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Complete List of Authors:	Huntington, Susie; Aquarius Population Health Limited Burns, Richéal; Aquarius Population Health Limited Harding- Esch, Emma; Public Health England, HIV & STI; St George's University of London, Applied Diagnostic Research and Evaluation Unit, Institute for Infection & Immunity Harvey , Michael; Aquarius Population Health Limited Hill-Tout, Rachel; St George's University Hospitals NHS Foundation Trust Fuller, Sebastian; St George's University of London, Applied Diagnostic Research and Evaluation Unit, Institute for Infection & Immunity Adams, Elisabeth; Aquarius Population Health Limited Sadiq, S. Tariq; Public Health England, HIV & STI; St George's University of London, Applied Diagnostic Research and Evaluation Unit, Institute for Infection & Immunity
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Evaluating the costs, benefits and cost-effectiveness of multi-pathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees

Susie E Huntington[1], Richéal M Burns[1], Emma Harding-Esch[2,3], Michael J Harvey[1], Rachel Hill-Tout[4], Sebastian S Fuller[3], *Elisabeth J Adams[1], *S Tariq Sadiq[2,3,4]

1. Aquarius Population Health, 58a Highgate High Street, London, N6 5HX, UK
2. HIV/STI Department, National Infection Service, Public Health England, 61 Colindale Avenue, London, NW9 5EQ, UK
3. Applied Diagnostic Research and Evaluation Unit, Institute for Infection and Immunity, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK
4. St George's University Hospitals NHS Foundation Trust, Blackshaw Road, Tooting, London, SW17 0QT.

*Joint senior authors.

Correspondence to: Dr Tariq Sadiq ssadiq@sgul.ac.uk. Tel: 020 8725 5740/3355 Institute for Infection and Immunity, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK

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Abstract

Objectives: To quantify the costs, benefits and cost-effectiveness of three multi-pathogen point-of-care (POC) testing strategies for detecting common sexually transmitted infections (STIs) compared with standard laboratory testing.

Design: Modelling study.

Setting: Genitourinary medicine (GUM) services in England.

Population: A hypothetical cohort of 965,988 people, representing the annual number attending GUM services symptomatic of lower genitourinary tract infection.

Interventions: The decision tree model considered costs and reimbursement to GUM services associated with diagnosing and managing STIs. Three strategies using hypothetical point-of-care tests (POCTs) were compared to standard care (SC) using laboratory-based testing. The strategies were: A) dual POC test (POCT) for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG); B) triplex POCT for CT-NG and *Mycoplasma genitalium* (MG); C) quadruplex POCT for CT-NG-MG and *Trichomonas vaginalis* (TV). Data came from published literature and unpublished estimates.

Primary and secondary outcome measures: Primary outcomes were total costs and benefits (quality-adjusted life years [QALYs]) for each strategy (2016 GB £) and associated incremental cost-effectiveness ratios (ICERs) between each of the POC strategies and SC. Secondary outcomes were inappropriate treatment of STIs, onward STI transmission, pelvic inflammatory disease in women, time to cure and total attendances.

Results: In the base-case analysis, POC strategy C, a quadruplex POCT, was the most cost-effective relative to the other strategies, with an ICER of £36,585 per QALY gained compared to SC when using micro-costing, and cost-savings of £26,451,382 when using tariff costing. POC strategy C also generated the most benefits, with 240,467 fewer clinic attendances, 808 fewer onward STI transmissions, and 235,135 averted inappropriate treatments compared to SC.

Conclusions: Many benefits can be achieved by using multi-pathogen POCTs to improve STI diagnosis and management. Further evidence is needed on the underlying prevalence of STIs and SC delivery in the UK to reduce uncertainty in economic analyses.

Strengths and limitations of this study

- The main strength of this study is that it presents the first estimates of the potential public health impact of multi-pathogen POCT strategies made possible by emerging diagnostic technologies.
- The model used inputs from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion and in incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.
- The main limitations were the paucity of published data on treatment pathways and gaps in treatment guidelines, which made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, or percentage returning to clinics after initial treatment.

Introduction

Continued high transmission rates of sexually transmitted infections (STIs) that cause treatable lower genital tract discharge syndromes (GDS) are a major public health concern. This causes significant reproductive-health long-term sequelae[1-4] and frequently necessitates empirical therapy to minimise treatment delay, which often results in misdirected treatment, poor antimicrobial stewardship and the spread of antimicrobial resistance.[5,6] Among the common causes of GDS, there were 107,252 and 39,696 diagnoses of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG), respectively, made in English genitourinary medicine (GUM) services in 2015 [7], with smaller numbers of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) diagnoses.

The decision to give empirical antimicrobial therapy in symptomatic patients is usually guided by results of immediate microscopy of genital discharge, but this has low sensitivity, missing up to half of NG/TV infections in women [8] and particularly poor specificity for predicting CT or MG. Accurate routine diagnosis, which requires laboratory-based nucleic acid amplification tests (NAATs), can take up to two weeks for results to be processed and most GUM services do not routinely conduct NAATs for MG or TV. Many patients are presumptively treated with either azithromycin or doxycycline, which are effective against CT but respectively cure only two-thirds and one-third of MG infections [9] and neither antimicrobial is effective against TV.[9]

Emerging technologies are being developed that allow rapid and accurate point-of-care tests (POCTs) for multiple sexually transmitted infections, solutions which could address these challenges and help improve patient and public health outcomes. However, health services are under increasing financial pressure, and implementing new technologies may be prohibitively costly for both providers and commissioners of healthcare. There is currently only one commercially available rapid NAAT for CT and NG, which has equivalent performance to laboratory NAATs (Cepheid GeneXpert).[10] Previous economic evaluations of NAAT POCTs for CT and NG indicate that they are likely to provide a cost-effective strategy for screening GUM attendees.[5,11] To inform decision making by groups developing multi-pathogen POCTs and clinics which would likely use such tests, we assessed costs, benefits and cost-effectiveness of three testing strategies using hypothetical NAAT POCTs for A) CT-NG, B) CT-NG-MG and C) CT-NG-MG-TV compared with laboratory-based CT-NG NAAT testing.

Methods

Creating a model structure

A decision tree model was constructed using Microsoft Excel (v.2016) to simulate a hypothetical cohort of people with symptoms of a lower genitourinary tract infection attending English GUM services. The base-case analysis, using assumptions provided in Supplementary Table 1, compared complete pathway costs of three point-of-care (POC) strategies to the current practice of using microscopy plus a laboratory CT-NG NAAT. The POC strategies used microscopy plus a hypothetical POCT that provides results in 30 minutes for A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Microscopy was used in all POC strategies as it can detect other conditions and infections not covered by the POCTs, as well as diagnosing NG and TV. The strategies were chosen in response to recent developments in STI POCT technology, reflecting pathogen configurations and performance characteristics.[12,13]

Outcomes

Primary outcomes were total costs and benefits measured by quality adjusted life years (QALYs) for each strategy and associated incremental cost-effectiveness ratios (ICERs, see equation) between each of the POC strategies and standard care (SC). The ICER provides information on the additional cost per unit of additional benefit between an option and the next less expensive alternative.

$$ICERx = \frac{Cost_{POCx} - Cost_{Current\ Practice}}{QALY_{POCx} - QALY_{Current\ Practice}}$$

Secondary outcomes assessed the wider health benefits and included inappropriate treatment of STIs (defined as unnecessary treatment of people with no STI plus incorrect treatment for people with an STI), onward transmission of the four STIs, pelvic inflammatory disease (PID), a serious complication of CT, NG and MG infections in women, time to cure and total GUM attendances.

Patient pathways

Three senior clinicians at St George's University Hospitals NHS Foundation Trust, London outlined current and hypothetical POC pathways for symptomatic patients (**Error! Reference source not found.**). We assumed that treatment pathways did not vary by subgroup but that MSM had diagnostic tests from three anatomical sites (genital, pharyngeal, and rectal) at initial visit and MSW and women only had genital swabs. The model accounted for single or dual infections with NG, CT, MG and/or TV.

The cost of treating PID, was included in the model but other long-term complications associated with STI infection (e.g. infertility) and adverse drug events associated with treatment were not considered. The proportion of patients lost-to-follow-up (LTFU) was estimated. It was assumed that anyone remaining in follow-up consented to diagnostic testing and, if diagnosed, accepted treatment. The decision framework assumed that individuals had a maximum of three follow-up visits and then exited the model. Drug resistance was not considered. The time horizon for the model was 56 days. It was assumed that treatment was started on the day of diagnosis.

Epidemiology and clinical parameters

A short online survey, distributed to members of the British Association for Sexual Health and HIV (BASHH), was used to collect data on the percentage of patients attending GUM services that are symptomatic, the percentage of patients returning after initial visits, as well as MG testing protocols, as limited data were available from published literature. The survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK (Supplementary Table 2).

The total annual number of people attending English GUM services for STI testing was obtained from national surveillance data (GUMCAD 2015 data).[7] This was combined with the clinician survey results on the proportion of symptomatic attendees, to estimate 965,988 total symptomatic attendees and by subgroup (590,787 women, 259,064 men-who-have-sex-with-women [MSW] and 116,137 men-who-have-sex-with-men [MSM]). We assumed that hypothetical POCTs had similar sensitivity and specificity to the best performing currently available CT-NG POCTs.[10] The prevalence of CT, NG, MG and TV in GUM attendees (Table 1, variables 12-21) was estimated using published studies and preliminary findings from the PRECISE Study [14], a study evaluating POCTs conducted by St George's, University of London and Public Health England.

Cost and utility parameters

All costs are given in 2015/16 prices (GB, £) and inflated to 2015/16 costs when based on previous estimates using the Hospital and Community Health Services (HCHS) Inflation Indices 2015.[15] The model considered two perspectives for costs: 1) costs to GUM services (micro-costing) associated with testing and management of NG/CT/MG/TV infections plus the cost of treating PID [16] and 2) NHS tariff reimbursements clinics would receive based on attendances (Table 2). Micro-costing was calculated by adapting an existing pathway model [17] which considers costs of staff time, diagnostic kit, drugs, and other consumables. The tariff, an estimated average first and follow-up attendance cost used for commissioning and cross-charging [18], was estimated using the draft 2015/16 NHS tariff for first and

follow-up GUM attendances. Fixed tariffs are not affected by how treatment is administered (oral/intramuscular) or the number of tests performed.

Costs of implementing a change in practice, including training costs, were not considered. Costs associated with testing and treating other causes of lower genitourinary tract symptoms were not considered.

Utilities, measures of health-related quality of life, were used in calculating QALYs for the health states (asymptomatic, symptomatic, or awaiting test results) incorporated in the decision analytic framework (**Error! Reference source not found.** 2).

Scenario and sensitivity analysis

As well as the base-case analysis, 32 scenarios were assessed deterministically, where one or more key parameters were varied (Supplementary Table 3). Scenarios included: higher STI prevalence; lower sensitivity and specificity of POCTs; differing microscopy use; cheaper POCTs; and different LTFU rates.

We performed a second order Monte Carlo probabilistic sensitivity analysis (PSA) to estimate ICERs. We converted model inputs from discrete values to distributions. For cost inputs, we used a normal distribution and varied each cost by 20% for the standard deviation. We correlated costs of POCTs against the least expensive option to ensure test costs would change equivalently to the same degree with each simulation. For clinical parameters, we used beta and normal distributions for probabilities and uniform distributions for test performance. For utilities, normal distributions were used. The PSA included 5000 simulations and was performed using recommended procedures [19]. Probabilities that strategies were cost-effective at a range of willingness-to-pay (WTP) thresholds per QALY gained were presented in cost-effectiveness acceptability curves (CEACs). CEACs were generated for each subgroup and the total population. Threshold costs for POCTs at which POC strategies would become cost-saving were calculated to the nearest £0.25.

Results

Using micro-costing, the estimated annual cost of testing and managing CT, NG, MG and TV infections in 965,988 symptomatic individuals attending GUM was £113,058,655 using SC. This was the cheapest strategy to clinical services, with POC strategies A, B and C being increasingly expensive at £118,704,963 (5% increase), £124,842,003 (10.4% increase), and £125,313,136 (10.8% increase), respectively (Table 3). The opposite was true when using tariff costs, with SC being the most expensive for commissioners of sexual health care at £172,364,138, and POC strategy C being the least expensive, at £145,912,757 (Table 3).

Most of the total care pathway cost was the initial attendance cost. In SC, total pathway costs for women were £65,122,097, of this 93% (£60,432,050) were initial attendance costs. For POC strategy C, total pathway costs for women were £69,285,504, of which 98% (£68,041,383) were initial attendance costs.

POC strategy C provided most benefits to the full cohort. POC strategies A, B, and C increased QALYs by 124, 94 and 335, respectively compared to SC (**Error! Reference source not found.** 3 and Table 4). Time to cure was shorter and the number of total clinic visits, onward STI transmissions and PID cases were fewer in POC strategies than in SC. Compared to SC, POC strategy C resulted in 240,467 fewer clinic visits, 808 fewer onward STI transmissions, 235,135 averted inappropriate treatments and 112 fewer cases of PID.

ICERs associated with the base-case model are presented in Table 4. POC C highlights cost-effectiveness relative to other strategies yielding an ICER of £36,585 per QALY gained compared to SC when using micro-costing and cost-savings of £26,451,382 when using tariff costing.

CEACs are presented in **Error! Reference source not found.**. Using micro-costing, for a WTP of £30,000/QALY, the upper threshold adopted by NICE [20], SC had a 50% probability of being cost-effective overall, a 17% probability for women, a 2% probability for MSW and a 99% probability for MSM, relative to the POC strategies. For a WTP of £25,000, POC C dominates, i.e. is cheaper and yields more benefits than the other POC strategies for the total cohort, women and MSW. For MSM, SC dominates all strategies across the thresholds examined. For MSW, POC A had 65% probability of being cost-effective at a WTP threshold of £10,000 per QALY gained.

Results of 32 scenario analyses are summarised in Supplementary Tables 4-7. The proportion of patients given presumptive treatment (scenarios 21-24) impacted costs hugely. When no presumptive treatment was given (scenario 21), the cost per QALY was £7,339 and £9,092 more than SC for POC

strategies B and C respectively, whilst POC strategy A was dominated by SC. When all patients without a diagnosis were presumptively treated for CT, MG or TV, according to which infections had been ruled out (scenario 24), POC strategies A and C were dominated by SC and POC strategy B cost £64,300/QALY more than SC.

When the utility score for being symptomatic was 10% less than base-case (scenario 25), cost per QALY was £15,627 more for POC strategy C than for SC. If microscopy was no longer used in POC strategies (scenario 13), cost per QALY was £16,204 and £29,594 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC.

If MG and TV prevalence were as high as the estimated prevalence in the US [21,22] (scenario 2), cost per QALY was £20,530 and £25,548 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC. When POCTs were priced the same as the SC test (scenario 31), POC strategies B and C were cost-saving (using micro-costing).

Holding all other parameters constant, POC strategies would be cost-saving compared to SC, if POCTs cost £19.25, £13.50 and £21.00, respectively for POCTs A, B and C.

DISCUSSION

Principle findings

This study compared costs, benefits and cost-effectiveness of a laboratory-based CT-NG NAAT, with three POC strategies for: A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Using our initial assumptions, for the total population using the micro-costing approach to assess direct costs to health-care services, each POC strategy cost more than SC but yielded additional benefits. The proportion of patients given presumptive treatment and the cost of the POCT kit both impacted the costs hugely. Results indicated that different strategies would be cost-effective for different patient sub-groups depending on the WTP threshold in place. POC strategy A was most cost-effective for MSW, POC strategy C for women, and SC for MSM. Whether using different testing strategies on different patient groups would be practical or acceptable was beyond the scope of this research and requires further investigation. Different results were obtained when tariff reimbursement costs were used, with POC strategy C costing the least and providing the most benefits.

Strengths and weaknesses

Our analysis has several strengths. This is the first study to compare the cost-effectiveness of the three different STI POC strategies with SC. Comparable and consistent methods were used to construct a model with input from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion. The model incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.

Potential limitations should be considered. While it is thought that most UK clinicians follow British Association for Sexual Health and HIV (BASHH) guidelines for STI testing and treatment [9,23], there is diversity in the testing and management strategies employed to meet specific patient needs, both within and between clinics. This diversity, the paucity of published data on treatment pathways and gaps in treatment guidelines, made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, or percentage returning to clinics after initial treatment. We tried to overcome this by collecting data using an online survey for GUM clinicians, albeit from a small sample size. There were few published data on utilities and sexual behaviour whilst symptomatic with an STI, whilst waiting for test results and whilst being on treatment for an STI. Both qualitative and quantitative research is needed in this area to inform future health economic analyses and to understand preferences for and impact on patients of introducing POC testing.

The costs associated with long-term complications of STIs were not considered [24]. This limitation means that the results are conservative, as the costs associated with SC are likely to be underestimated. However, the long-term benefits for a single round of testing were thought to be very low and to not have a major impact on the magnitude of results.

Comparing the results to other studies. POC pathways generated some cost savings, primarily because patients had fewer return visits. However, these did not outweigh the higher cost of the POCTs compared to laboratory-based NAATs when estimating total pathway costs. This means that if POC testing was used, there would be expected overall cost increases based on the analysis using the micro-costing approach. This differs from previous modelling, in which a CT-NG POCT was cost saving compared to laboratory testing [5]. In the Turner *et al.* model, the cost of a POC attendance was £6.95 cheaper than the cost of an SC attendance since the asymptomatic POC pathway was redesigned. In our model, the cost of attendance for a symptomatic patient was the same whether samples were sent to a laboratory or performed in clinic, since all symptomatic clinic attendees would require examination and microscopy.

Implications for public health, clinicians and people using GUM services

POC strategy C significantly decreased the numbers of inappropriate antibiotics given compared to SC, with over 235,000 fewer inappropriate treatments. Many of these treatments are likely to include azithromycin, which when inappropriately given can encourage spread of macrolide antibiotic resistance in MG infections [6]. POC strategy C also increased costs for health providers while decreasing tariff costs for commissioners, unless the "freed-up" capacity enabled by POC strategy C was used for STI screening appointments and initial assessments for symptomatic people. Although this would likely have a positive impact on public health, given GUM services in England face increasing pressure on their services with more than 2 million new attendances annually [7], while local authorities equally face fiscal pressures, this work demonstrates the potential tensions between different cost-consequences for procurers and providers and public health benefits when considering implementation of novel health technologies.

For people using GUM services, there are numerous benefits to POC testing compared to SC. People would need fewer clinic visits, saving them time and reducing LTFU and reducing their costs such as out-of-pocket expenses and productivity losses. Receiving a diagnosis at the initial attendance reduces anxiety compared to waiting for test results [25]. A negative result from a multi-pathogen POCT will support the development of clearer guidelines for clinicians, which could also reassure patients,

particularly those with vague genital tract symptoms. Receiving effective treatment at initial attendance is likely to reduce the duration of symptoms and reproductive health sequelae.[1,2]

POCTs can also generate public health benefits from swifter diagnosis and treatment, for example, POC strategy C led to an estimated 43% fewer onward transmissions of STIs compared to SC. The ability to diagnose or rule out specific infections at first attendance enables accurate treatment and reduces inappropriate antibiotic use, crucial for good antibiotic stewardship, the economic benefits of which are substantial.[26]

Unanswered questions and future research

Although a rapid test for CT and NG is used in some GUM services, multi-pathogen configurations of CT-NG-MG-TV POCTs are not currently available. As such, likely pathways for POC strategies had to be designed based on expert opinion. Published audits of GUM patient pathways would be a useful addition to the literature. To reduce uncertainty in economic analyses around STIs, further evidence is also needed on underlying STI prevalence and the risk of onward STI transmission.

Patient pathways and testing protocols vary between sites and different sites see different proportions of people from the three sub-groups. As such, the costs of changing to a POC strategy will vary between sites as will the benefits and costs not considered in the model. Validated and easy to use computational tools for clinics and commissioners, which assess the economic impact of implementing any one of the POC strategies, using local population data, would increase understanding across stakeholders.

Conclusion

In conclusion, the results suggest that although potentially more expensive, a quadruplex test for CT-NG-MG-TV is more cost-effective than SC and the other testing strategies, providing the most additional benefits to patients. Cost implications are driven by the cost of POCTs and would vary somewhat in different geographical areas due to differences in the subgroup mix and the prevalence of the four STIs.

Footnotes

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Contributors: All authors were involved in the conception and design of the research. STS, EHE, RHT and SF provided input into current clinical practice relating to patient pathways in GUM. SH estimated all parameter inputs and drafted the manuscript with support from EA and MH. RB developed the model with input from EA, SH and MH. All authors contributed to the interpretation of the model and approved the final version. STS acts as guarantor of the study.

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Ethical approval: Not required.

All authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency: The senior author (STS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: no additional data available.

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Table 1. Epidemiological and clinical parameters

	Variable	Value			Distribution	Number			Comments, Reference
		Women	MSW	MSM		Women	MSW	MSM	
1	Initial clinic attendances	61%	27%	12%	Beta	590,787	259,064	116,137	Clinician survey results
2	CT infection	6.5%	23.3%	6.2%	Beta	38,401	60,362	7,200	W [14,27,28]; MSW [14,29]; MSM [14]
3	NG infection	0.7%	3.4%	38.1%	Beta	4,136	8,808	44,248	W [14,27,28]; MSW [14,29]; MSM [14]
4	MG infection	4.2%	12.3%	9.3%	Beta	24,813	31,865	10,801	W [14]; MSW [14,29]; MSW [14]
5	TV infection	4.4%	0.0%	0.0%	Beta	25,995	-	-	W [14,27,28,30]; MSW [14]; MSM estimate
6	CT NG co-infection	0.3%	2.2%	6.2%	Beta	1,772	5,699	7,200	W [14,27]; MSW, MSW [14]
7	CT MG co-infection	1.6%	2.8%	0.0%	Beta	9,453	7,254	-	W, MSW, MSW [14]
8	CT TV co-infection	0.2%	0.0%	0.0%	Beta	1,182	-	-	W [14,27,28]; MSW [14]; MSM estimate
9	NG MG co-infection	0.6%	0.6%	1.0%	Beta	3,545	1,554	1,161	W, MSW, MSM [14]
10	NG TV co-infection	0.4%	0.0%	0.0%	Beta	2,363	-	-	W [28]; MSW [14]; MSM estimate
11	MG TV co-infection	1.0%	0.0%	0.0%	Beta	5,908	-	-	W [14]; MSW, MSM estimate
12	Sensitivity of microscopy for detecting NG	40%	75%	75%	Uniform	Estimate based on published studies and clinical experience [8]			
13	Specificity of microscopy for detecting NG	100%	100%	100%	Uniform	Estimate based on published studies and clinical experience [8]			
14	Sensitivity of microscopy for detecting TV	50%	50%	50%	Uniform	Assumption based on clinical experience			
15	Specificity of microscopy for detecting TV	100%	100%	100%	Uniform	Assumption based on clinical experience			
16	Sensitivity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [23]			
17	Specificity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [23]			
18	Sensitivity of POCTs for CT/NG/MG/TV	95%	95%	95%	Uniform	Estimate based on tests currently available [10]			
19	Specificity of POCTs for CT/TV/MG	96%	96%	96%	Uniform	Estimate based on tests currently available [10]			
20	Specificity of POCTs for NG	98%	98%	98%	Uniform	Estimate based on tests currently available [10]			
21	CT infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [2]			
22	NG infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [31]			
23	MG infection - probability of PID	4%	-	-	Normal	Estimate based on published studies [1]			
24	TV infection - probability of PID	0%	-	-	Normal	Assumption			
25	Microscopy at first attendance	84%	84%	84%	Uniform	Assumption, clinician survey results			
26	Presumptive treatment for CT	50%	50%	50%	Normal	Estimate based on clinical practice			
27	Proportion of MG infections cured by CT	67%	67%	67%	Uniform	Estimate based on published studies [9]			

treatment

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with women*;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; NGU, non-gonococcal urethritis; PID, pelvic inflammatory disease; POCT, point-of-care test; TV, *Trichomonas vaginalis*.

Table 2. Model input parameters: costs and utilities

Utilities			
Asymptomatic health state	1.00	Assume an otherwise healthy population	
Symptomatic health state	0.93		Sri, 2016 [25]
Waiting for diagnosis (symptomatic) health state	0.93	Assume the same as symptomatic	Sri, 2016 [25]
Treatment complete i.e. returned to asymptomatic state	1.00	Assume they return to asymptomatic	
PID diagnosis health state	0.80		Smith, 2008 [32]
Costs			
Tariff cost of initial visit plus treatment management	£141.00	Draft National Tariff Payment System: 2015/16	[18]
Initial clinic visit of symptomatic patient (micro-costing)	£103.71	Patient pathway adapted from a previous model	Adams, 2014 [a 17]
Management of STI (oral medication) on same day as assessment[b,c]	£29.19	Excludes drug cost	Adams, 2014 [a 17]
Management of STI (oral medication) at return visit after results[b,c]	£31.32	Excludes drug cost	Adams, 2014 [a 17]
Management of STI (medication via injection) on same day as assessment[c]	£43.79	Excludes drug cost	Adams, 2014 [a 17]
Management of STI (medication via injection) on return visit after results[c]	£44.32	Excludes drug cost and GC culture/typing lab processing	Adams, 2014 [a 17]
Standard CT/NG NAAT laboratory diagnostic test[d]	£13.17		Adams, 2014 [a 17]
POCT CT-NG[d]	£24.00	Assumption based on cost of products currently available	
POCT CT-NG-MG[d]	£29.00	Assumption based on cost of products currently available	
POCT CT-NG-MG-TV[d]	£34.00	Assumption based on cost of products currently available	
Tariff cost of return visit	£110.00	Draft National Tariff Payment System: 2015/16	[18]
Return clinic visit of symptomatic patient (micro-costing)	£83.25	Patient pathway adapted from a previous model	Adams, 2014 [a 17]
NG test of cure using standard NAAT laboratory test	£41.73		Adams, 2014 [a 17]
NG test of cure using POC A	£55.93		Adams, 2014 [a 17]
Cost of drug treatment (1st line) for CT	£1.20	Where 95% of patients receive 1g Azithromycin and 5% receive Doxycycline 100mg twice daily for 7 days	BNF, 2016 [33]
Cost of drug treatment (1st line) for NG	£5.95	Single dose Ceftriaxone 500mg deep intramuscular injection	BNF, 2016 [33]

		with single dose 1g Azithromycin	
Cost of drug treatment (1st line) for MG	£1.87	Doxycycline 100mg twice daily for 7 days	BNF, 2016 [33]
Cost of drug treatment (1st line) for TV	£0.36	Metronidazole 2g orally in a single dose	BNF, 2016 [33]
Cost associated with treatment of short-term PID	£180.52		Aghaizu, 2011 [16]

BNF, British National Formulary; CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; PID, pelvic inflammatory disease; POC, point-of-care; TV, *Trichomonas vaginalis*.

[a]Costs were inflated to 2015/16 costs using the Hospital and Community Health Services (HCHS) Inflation Indices 2015 produced by the Personal Social Services Research Unit.[15] No data were available for inflation from 2014/15 to 2015/16 so it was assumed to the same as between 2013/2014 and 2014/15. The UK consumer price index for health services shows similar annual growth in this sector from 2014 which validates this assumption.

[b]The cost of management of MG/TV infection is assumed to be the same as the costs associated with management of CT infection.

[c]These costs vary due to the difference in administrative staff time for patient registration if the patient is treated on the same day or on a subsequent visit.

[d]MSM have samples from three sites (urethral, rectal, pharyngeal) tested at the initial visit, whereas women and MSW typically have one sample taken.

Table 3. The costs, QALYs, average time to cure, inappropriate treatment and follow-up visits in SC and three POC strategies for symptomatic people attending GUM services

Sub-group	Strategy	Model Outcomes: Total costs (micro-costing)	Total costs (tariff)	Total QALYs	Average time to cure (days)	Inappropriate treatments	Mean number of visits/person	Return clinic visits[1]	Infected partners	PID cases in women
All	SC	£113,058,655	£172,364,138	146,532	4.3	258,395	1.3	328,726	1,876	176
	POC A	£118,704,963	£151,956,910	146,656	2.3	109,135	1.1	143,205	1,414	119
	POC B	£124,842,003	£152,288,107	146,626	2.1	200,865	1.2	146,216	1,451	64
	POC C	£125,313,136	£145,912,757	146,867	1.1	23,260	1.1	88,259	1,068	64
Women	SC	£65,122,097	£99,714,696	89,533	4.4	176,604	1.3	149,216	764	176
	POC A	£66,938,018	£88,960,028	89,584	2.4	76,322	1.1	51,446	524	119
	POC B	£69,853,645	£89,101,615	89,554	2.2	128,806	1.1	52,733	535	64
	POC C	£69,285,504	£85,008,982	89,718	1.1	1,607	1.0	15,528	260	64
MSW	SC	£29,572,989	£46,813,874	39,342	4.3	54,860	1.4	93,507	459	-
	POC A	£29,995,704	£40,111,202	39,389	2.1	20,957	1.1	32,574	343	-
	POC B	£31,717,478	£40,614,444	39,380	2.0	54,863	1.1	37,149	360	-
	POC C	£31,373,674	£38,724,875	39,443	1.2	13,218	1.1	19,971	285	-
MSM	SC	£18,363,569	£25,835,568	17,658	4.1	26,931	1.7	86,002	653	-
	POC A	£21,771,241	£22,885,680	17,684	2.3	11,855	1.5	59,185	546	-
	POC B	£23,270,880	£22,572,047	17,692	1.5	17,196	1.5	56,334	556	-
	POC C	£24,653,958	£22,178,900	17,706	1.2	8,436	1.5	52,760	524	-

[1]Return clinic visit for results and treatment, a test of cure (routine for NG) or because they remain symptomatic.

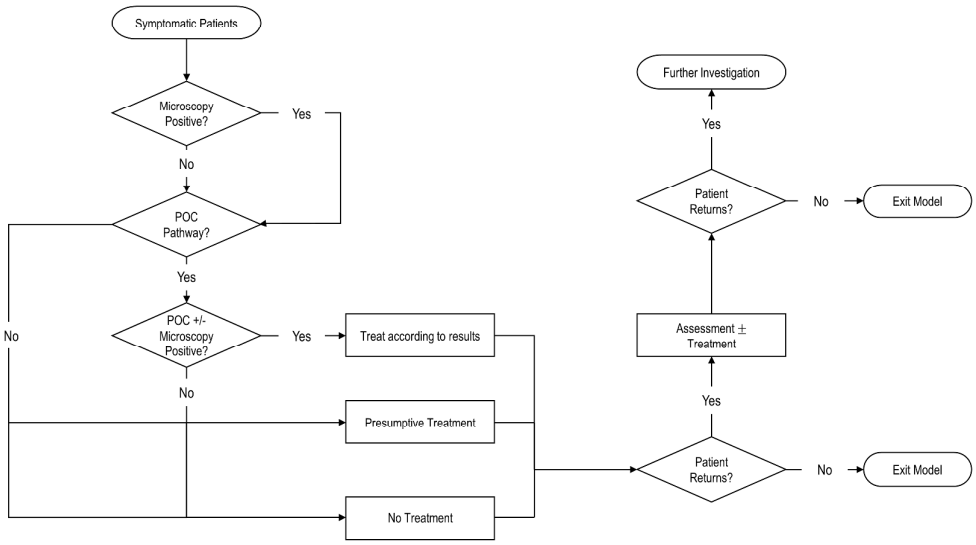
MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; PID, pelvic inflammatory disease; QALY, quality-adjusted life year.

Table 4. Cost differences for SC and POC strategies

Sub-group	Comparison	QALY difference	Micro-costing		Tariff costs	
			Cost difference	ICER (£/QALY gained)	Cost difference	ICER (£/QALY gained)
All	POC A vs SC	124	£5,646,309	£45,516	-£20,407,228	**Cost-Saving**
	POC B vs SC	94	£11,783,348	£125,197	-£20,076,031	**Cost-Saving**
	POC C vs SC	335	£12,254,482	£36,585	-£26,451,382	**Cost-Saving**
	POC B vs A	-30	£6,137,039	**Dominated**	£331,197	**Dominated**
	POC C vs B	241	£471,133	£1,956	-£6,375,350	**Cost-Saving**
Women	POC A vs SC	51	£1,815,921	£35,608	-£10,754,668	**Cost-Saving**
	POC B vs SC	21	£4,731,548	£222,568	-£10,613,081	**Cost-Saving**
	POC C vs SC	185	£4,163,407	£22,448	-£14,705,715	**Cost-Saving**
	POC B vs A	-30	£2,915,627	**Dominated**	£141,587	**Dominated**
	POC C vs B	164	-£568,141	**Cost-Saving**	-£4,092,634	**Cost-Saving**
MSW	POC A vs SC	47	£422,715	£9,005	-£6,702,672	**Cost-Saving**
	POC B vs SC	38	£2,144,488	£56,104	-£6,199,430	**Cost-Saving**
	POC C vs SC	102	£1,800,685	£17,724	-£8,088,999	**Cost-Saving**
	POC B vs A	-9	£1,721,773	**Dominated**	£503,242	**Dominated**
	POC C vs B	63	-£343,804	**Cost-Saving**	-£1,889,570	**Cost-Saving**
MSM	POC A vs SC	26	£3,407,672	£130,508	-£2,949,888	**Cost-Saving**
	POC B vs SC	35	£4,907,312	£141,683	-£3,263,521	**Cost-Saving**
	POC C vs SC	48	£6,290,390	£131,319	-£3,656,668	**Cost-Saving**
	POC B vs A	9	£1,499,639	£175,909	-£313,633	**Cost-Saving**
	POC C vs B	13	£1,383,078	£104,258	-£393,147	**Cost-Saving**

ICER, incremental cost-effectiveness ratios, MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; QALY, quality-adjusted life year.

Figure 1. Diagram showing simplified patient flow through the model



Standard care (SC): 50% of people not diagnosed with NG or TV by microscopy will be presumptively treated for CT. The treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs (i.e. not CT/NG/MG/TV). We assume this treatment is not effective against TV or NG. Incorrectly treated patients with NG infection will be diagnosed by NAAT, and return (minus those LTFU) to receive treatment. Other returning patients may receive presumptive treatment for MG and TV.

POC strategy A: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for MG and TV. We assume that this treatment is effective against CT, MG, TV, and against all other non-specific bacterial STIs. We assume that this treatment is not effective against NG. Patients not initially presumptively treated but who return to the clinic are then presumptively treated with MG and TV treatment.

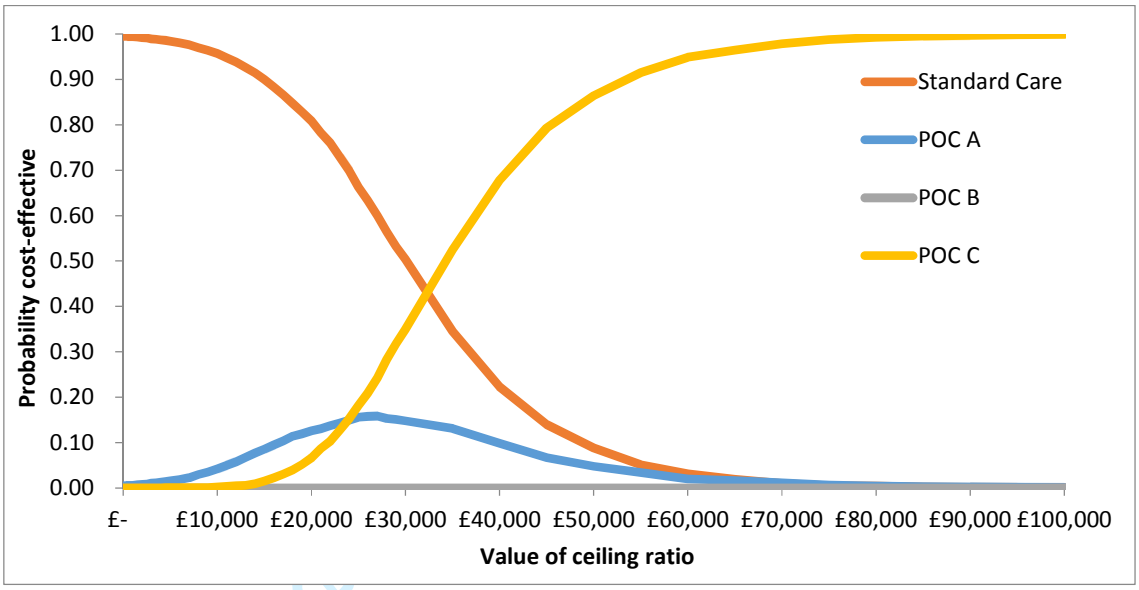
POC strategy B: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for TV. We assume this treatment is effective against TV, and against all other non-specific bacterial STIs. We assume this treatment is not effective against CT, MG, or NG.

POC strategy C: 100% of people who are not diagnosed by microscopy or POC would be presumptively treated using azithromycin. We assume this treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs. We assume this treatment is not effective against TV or NG. If any treated patients return they will be categorised as 'investigate further'. The

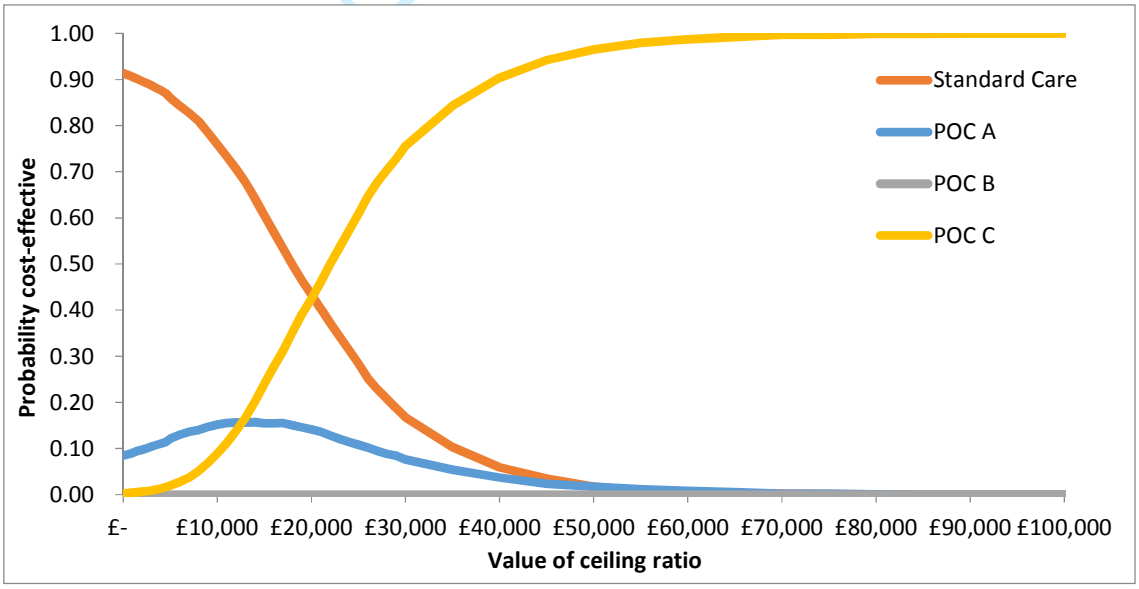
cost of the 'investigate further' is the cost of a standard return appointment which includes microscopy.

Figure 2. Cost-effectiveness acceptability curve: point-of-care (POC) strategies vs standard care

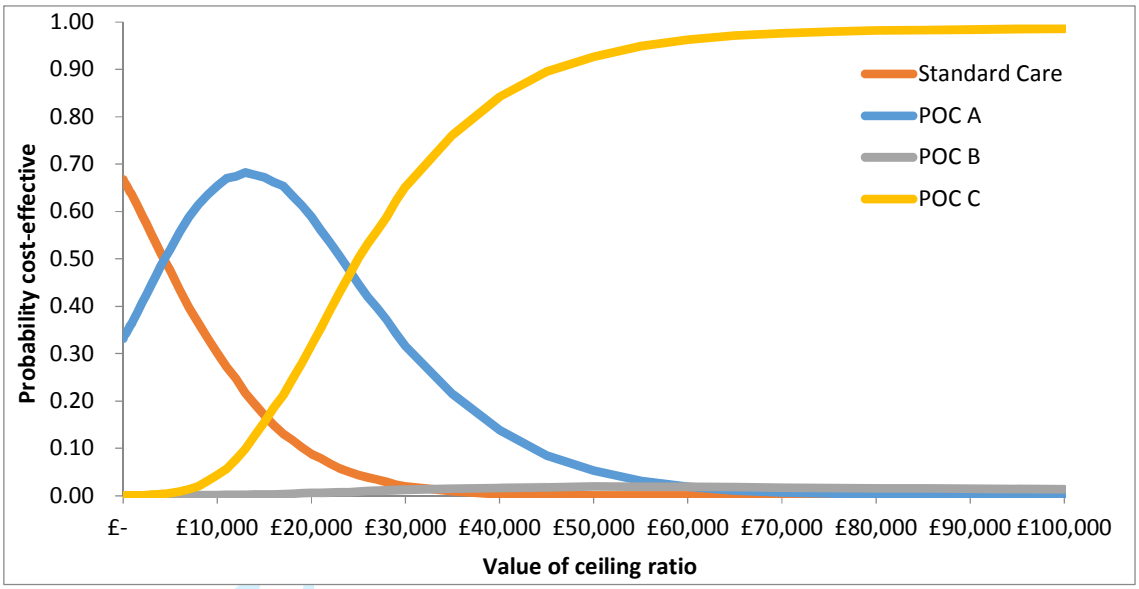
a. All



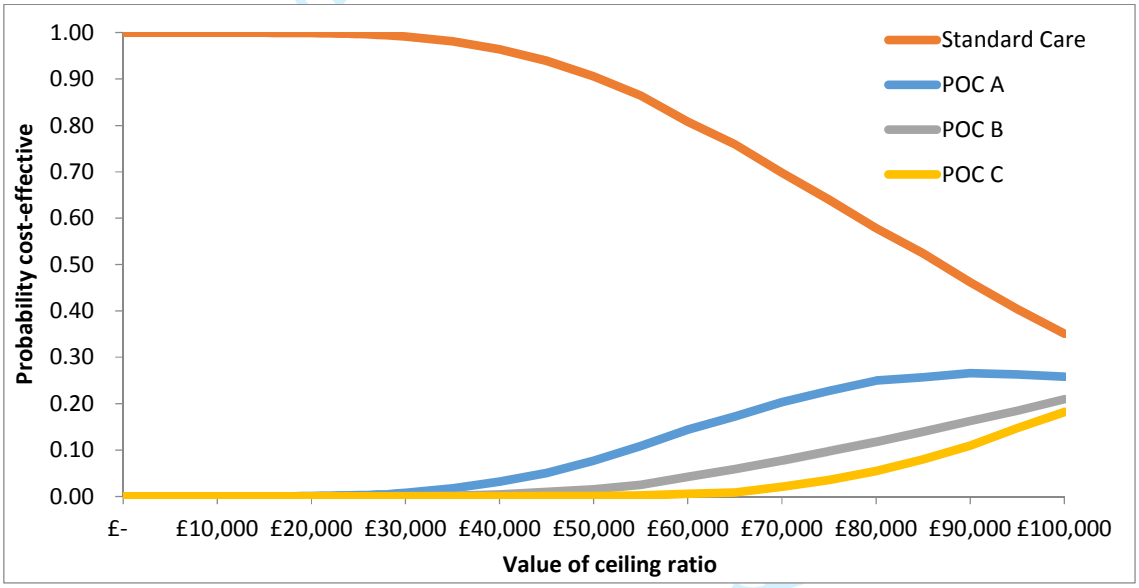
b. Women



c. Men-who-have-sex-with-women



d. Men-who-have-sex-with-men



POC, point-of-care strategy

Supplementary Table 1. Key model assumptions

1	The decision framework assumes that after a maximum of 3 courses of treatment the individual would be cured. In standard care, this could take up to 56 days in total; therefore, the cycle length is one day and time horizon is 56 days.
2	Screening options will confirm diagnosis between 1-21 days; treatment options will last for a maximum of 7 days and 2 weekly cycles are imposed between treatment regimens. In current practice, we assume that individuals return on day 8 for test results in the base-case.
3	The sensitivity (true positive) and specificity (true negative) of POCT for each infection does not vary across the different POC strategies nor does it vary between patient sub-groups.
4	The model accounts for the impact of single and dual infections (CT, NG, TV and MG).
5	The proportion lost-to-follow-up varies by STI and gender due to the nature of symptoms and severity of individual STIs.
6	STI symptoms remain at the same clinical level of severity across the time horizon.
7	The model incorporates an 'Other Infection' category which includes all other infections that cause similar lower genital symptoms diagnosed initially (day 0) that rule out an initial diagnosis of CT/NG/MG/TV. These may include candida and allergic reactions. The proportion of the cohort who we assume fall into the "Other infection" category is 1 in 2 for women, 1 in 3 for MSW and 1 in 4 for MSM. We vary this assumption in scenario analysis.
8	Once results from screening options are confirmed those with a confirmed STI are treated and partners are made aware of the infection to access treatment.
9	Each index infection is assumed to have 1 partner for women and MSW and 2 partners for MSM per 7-day period; this assumption, as well as the number of sexual acts per week, is varied in sensitivity analysis.
10	In the absence of any data on changes in sexual behaviour following diagnosis with an STI, it is assumed sexual behaviour is not changed due to a diagnosis. This assumption affords the identification of all potential transmissions; however, taken at face value would be an overestimation of transmissions.
11	The model assumes STI transmission rates are constant over the duration of exposure.
12	The model assumes different treatment regimens for the different infections as informed by clinical guidance.
13	The model assumes the correct treatment for true CT/NG/MG/TV infection is 100% efficacious and ignores antibiotic resistant strains in NG and MG, thereby underestimating the total costs associated with STI infection.
14	The model does not include re-infections.
15	The model does not consider adverse events associated with treatment options.
16	The model does not consider long-term complications associated with STI infection.
17	The model limits sub-group analysis to women, MSW and MSM; treatment pathways do not vary by sub-group.

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; POCT, point of care test; STI, sexually transmitted infection, TV, *Trichomonas vaginalis*.

Supplementary Table 2. Summary of GUM clinician survey (October 2016) relevant to patient pathways

Survey question	Median	Lowest	Highest
Roughly how many patients attend your service every month?	1,700	80	6,000
What proportion of your patients are MSM?	10%	5%	100%
What proportion of your patients are MSW?	30%	0%	85%
What proportion of your patients are women?	53%	0%	60%
What proportion of MSM attend with a symptomatic lower genital tract infection?	50%	5%	90%
What proportion of MSW attend with a symptomatic lower genital tract infection?	40%	0%	90%
What proportion of women attend with a symptomatic lower genital tract infection?	50%	0%	80%
What proportion of symptomatic men have a swab that is sent for microscopy?	80%	25%	100%
What proportion of symptomatic men have a swab that is sent for culture?	60%	5%	100%
What proportion of symptomatic women have a swab that is sent for microscopy?	88%	0%	100%
What proportion of symptomatic women have a swab that is sent for culture?	58%	0%	100%
What proportion of MSM are tested for MG?	0%	0%	10%
What proportion of MSW are tested for MG?	0%	0%	20%
What proportion of women are tested for MG?	0%	0%	15%
Men who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	50%	5%	100%
Of those who return, what proportion receive further tests?	25%	0%	80%
Of those who return, what proportion receive presumptive treatment for another infection?	18%	5%	90%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	23%	0%	65%
Women who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	30%	0%	75%
Of those who return, what proportion receive further tests?	50%	10%	100%
Of those who return, what proportion receive presumptive treatment for another infection?	28%	5%	100%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	20%	0%	85%

CT, *Chlamydia trachomatis;* GP, General Practice; GUM, genitourinary medicine; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; TV, *Trichomonas vaginalis*.

The online survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK.

Supplementary Table 3. Scenarios assessed

1	Higher prevalence of MG and TV (double the current estimated prevalence)
2	Higher prevalence of MG and TV based on estimated prevalence in symptomatic patients in the US (MG: women 21.1%; men 19.3% and TV: women 25.9%; men 6.3%)
3	Increase proportion with 'Other infection' as follows: women: 66.6%, MSW: 50%, MSM: 50%
4	Decrease proportion with 'Other infection' as follows: women: 33.3%, MSW: 25%, MSM: 20%
5	100% increase the rate of LTFU
6	50% decrease the rate of LTFU
7	Specificity/sensitivity of POCT is 75%
8	Specificity/sensitivity of POCT is 80%
9	Specificity/sensitivity of POCT is 85%
10	Specificity/sensitivity of POCT is 85% for NG (but unaltered for CT, MG and TV)
11	Specificity/sensitivity of POCT is 85% for CT (but unaltered for NG, MG and TV)
12	Specificity/sensitivity of POCT is 85% for MG (but unaltered for CT, NG and TV)
13	No microscopy used in any testing strategy
14	50% people get microscopy
15	75% people get microscopy
16	100% people get microscopy
17	84% use of microscopy in current pathway and no use of microscopy in the POC strategy C
18	No microscopy for men (only) in POC strategy C
19	No microscopy for women (only) in POC strategy C
20	Use of microscopy in POC strategy C only after a negative test result
21	No presumptive treatment for CT
22	25% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
23	75% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
24	100% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
25	Use 10% reduction in symptomatic utility scores
26	Excluding the cost of PID (as not all PID will be treated in the GUM service)
27	Inclusion of the drug costs for doxycycline as treatment for anyone NG/CT/MG/TV negative
28	POCT CT-NG costs the same as laboratory based NAAT
29	POCT CT-NG-MG cost the same as laboratory based NAAT
30	POCT CT-NG-MG-TV costs the same as laboratory based NAAT
31	All POCTs cost the same as laboratory based NAAT
32	All POCTs cost £2 less than in base-case

CT, *Chlamydia trachomatis;* GUM, genitourinary medicine; LTFU, lost-to-follow-up; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*; POC, point-of-care; POCT, point-of-care test; TV, *Trichomonas vaginalis;* US, United States (of America).

Supplementary Table 4. Cost-effectiveness comparison for scenario analyses using micro-costings - All

All	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£ 17,389	£ 41,381	£7,153	Dominated
2	Dominated	£ 20,530	£ 56,548	£8,228	Dominated
3	£ 224,378	£ 22,979	£ 69,517	£12,300	Dominated
4	Dominated	£ 15,818	£ 24,163	£7,107	£6,353
5	Dominated	£ 19,691	£ 35,749	£9,196	Dominated
6	Dominated	£ 19,363	£ 36,221	£9,196	Dominated
7	Dominated	£ 21,665	£ 82,996	£8,870	Dominated
8	Dominated	£ 21,220	£ 69,561	£8,865	Dominated
9	Dominated	£ 20,735	£ 57,596	£8,891	Dominated
10	Dominated	£ 19,726	£ 39,414	£8,986	Dominated
11	Dominated	£ 20,431	£ 43,314	£8,265	Dominated
12	Dominated	£ 19,647	£ 40,917	£10,034	Dominated
13	Dominated	£ 16,204	£ 29,594	£8,703	Dominated
14	Dominated	£ 18,061	£ 33,245	£8,989	Dominated
15	Dominated	£ 19,088	£ 35,286	£9,140	Dominated
16	Dominated	£ 20,191	£ 37,493	£9,297	Dominated
17	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
18	Dominated	£ 19,476	£ 28,889	£9,196	£7,998
19	Dominated	£ 19,476	£ 23,566	£9,196	£14,332
20	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
21	Dominated	£7,339	£9,092	£3,792	£2,859
22	Dominated	£ 12,055	£ 18,039	£5,910	£552
23	Dominated	£ 32,870	£ 91,155	£14,987	Dominated
24	Dominated	£ 64,300	Dominated	£27,913	Dominated
25	£ 46,988	£ 17,310	£ 15,627	£10,948	£4,554
26	Dominated	£ 19,510	£ 36,120	£9,211	Dominated
27	Dominated	£ 19,476	£ 37,040	£9,196	Dominated
28	£ 43,475	£ 19,476	£ 36,060	£21,718	Dominated
29	Dominated	Cost-saving	£ 36,060	Cost-saving	Dominated
30	Dominated	£ 19,476	Cost-saving	£9,196	£74,924
31	£ 43,475	Cost-saving	Cost-saving	£218	£20,817
32	Dominated	£ 16,667	£ 31,058	£9,196	Dominated

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 5. Cost-effectiveness comparison for scenario analyses using micro-costings - Women

Women	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£8,843	£ 25,961	£4,199	Dominated
2	Dominated	£8,932	£ 52,744	£3,587	Dominated
3	Dominated	£ 13,611	£ 46,391	£7,257	Dominated
4	Dominated	£6,915	£ 10,406	£3,249	£5,070
5	Dominated	£9,013	£ 21,182	£4,368	£1,662
6	Dominated	£8,827	£ 22,264	£4,368	£1,662
7	Dominated	£8,012	£ 48,866	£3,769	£180
8	Dominated	£8,124	£ 41,683	£3,848	£350
9	Dominated	£8,279	£ 34,918	£3,954	£588
10	Dominated	£8,732	£ 22,995	£4,249	£1,398
11	Dominated	£8,597	£ 25,567	£3,827	£1,542
12	Dominated	£8,630	£ 24,992	£4,563	£1,556
13	Dominated	£8,344	£ 19,947	£4,136	£2,008
14	Dominated	£8,661	£ 21,070	£4,271	£1,808
15	Dominated	£8,829	£ 21,658	£4,341	£1,702
16	Dominated	£9,004	£ 22,264	£4,415	£1,590
17	Dominated	£8,891	Cost-saving	£4,368	£14,160
18	Dominated	£8,891	£ 21,874	£4,368	£1,662
19	Dominated	£8,891	Cost-saving	£4,368	£14,160
20	Dominated	£8,891	Cost-saving	£4,368	£14,160
21	Dominated	£4,042	£1,678	£1,846	£6,724
22	Dominated	£6,046	£8,172	£2,856	£4,238
23	Dominated	£ 13,250	£ 69,756	£6,878	Dominated
24	Dominated	£ 20,769	Dominated	£11,866	Dominated
25	Dominated	£9,256	£9,545	£5,197	£7,575
26	Dominated	£8,930	£ 21,981	£4,383	£1,662
27	Dominated	£8,891	£ 23,150	£4,368	£951
28	Dominated	£8,891	£ 21,874	£6,916	£1,662
29	Dominated	£ 143	£ 21,874	Cost-saving	Dominated
30	Dominated	£8,891	Cost-saving	£4,368	£23,924
31	Dominated	£ 143	Cost-saving	Cost-saving	£10,304
32	Dominated	£6,671	£ 15,666	£4,368	£1,662

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 6. Cost-effectiveness comparison for scenario analyses using micro-costings - MSW

MSW	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£12,263	£22,566	£21,976	£39,978	£20,481
2	£6,136	£21,655	£20,324	£70,648	£17,318
3	£6,705	£20,051	£33,219	£53,907	£163,024
4	£10,163	£104,518	£12,897	Dominated	Cost-saving
5	£12,052	£61,168	£19,205	Dominated	Cost-saving
6	£7,525	£53,665	£16,992	Dominated	Cost-saving
7	£265,801	Dominated	£64,478	Dominated	Cost-saving
8	£100,276	Dominated	£50,420	Dominated	Cost-saving
9	£49,716	Dominated	£38,304	Dominated	Cost-saving
10	£10,139	£60,983	£19,061	Dominated	Cost-saving
11	£44,559	£243,310	£28,123	Dominated	Cost-saving
12	£9,005	£109,035	£22,985	Dominated	Cost-saving
13	£5,013	£44,501	£15,654	Dominated	Cost-saving
14	£7,253	£50,948	£16,857	Dominated	Cost-saving
15	£8,521	£54,669	£17,490	Dominated	Cost-saving
16	£9,906	£58,793	£18,147	Dominated	Cost-saving
17	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
18	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
19	£9,005	£56,104	£17,724	Dominated	Cost-saving
20	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
21	Cost-saving	Cost-saving	Cost-saving	£20,002	£929
22	Cost-saving	£9,663	£4,599	£121,977	Cost-saving
23	£80,063	Dominated	£62,970	Dominated	Cost-saving
24	Dominated	Dominated	Dominated	Dominated	Cost-saving
25	£3,870	£24,112	£7,614	Dominated	Cost-saving
26	£9,005	£56,104	£17,724	Dominated	Cost-saving
27	£9,005	£56,104	£18,456	Dominated	Cost-saving
28	Cost-saving	£56,104	£17,724	Dominated	Cost-saving
29	£9,005	£2,696	£17,724	£36,667	£26,789
30	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
31	Cost-saving	£2,696	Cost-saving	Dominated	Cost-saving
32	Cost-saving	£42,549	£12,624	Dominated	Cost-saving

MSW, Men-who-have-sex-with-women; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 7. Cost-effectiveness comparisons for scenario analyses using micro-costings - MSM

MSM	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£137,378	£95,423	£139,260	£49,813	Dominated
2	£119,952	£83,250	£145,988	£42,999	Dominated
3	£91,163	£83,961	£332,964	£71,307	Dominated
4	£140,882	£160,599	£115,724	£235,703	£52,018
5	£135,796	£145,798	£134,186	£175,909	£104,258
6	£127,894	£139,636	£1,044	£175,909	£1,317
7	£833,775	£2,053,305	£350,136	Dominated	£78,956
8	£425,499	£591,462	£268,835	£4,264,237	£84,090
9	£271,627	£324,923	£211,896	£579,296	£89,914
10	£191,294	£191,613	£173,306	£192,369	£130,727
11	£168,341	£173,675	£143,342	£187,785	£85,861
12	£130,508	£167,524	£141,202	£406,528	£88,559
13	£47,590	£64,826	£74,079	£189,798	£126,208
14	£80,744	£98,423	£101,384	£181,298	£112,461
15	£113,144	£127,453	£122,040	£177,307	£106,349
16	£175,783	£175,089	£151,216	£173,474	£100,673
17	£130,508	£141,683	£131,189	£175,909	£83,111
18	£130,508	£141,683	£131,189	£175,909	£83,111
19	£130,508	£141,683	£131,319	£175,909	£104,258
20	£130,508	£141,683	£131,189	£175,909	£83,111
21	£60,065	£77,460	£84,981	£164,890	£116,909
22	£85,266	£101,948	£103,897	£170,152	£110,577
23	£235,470	£217,337	£174,644	£182,233	£97,951
24	£747,941	£417,789	£253,365	£189,212	£91,656
25	£56,093	£60,884	£56,420	£75,544	£44,773
26	£130,508	£141,683	£131,319	£175,909	£104,258
27	£130,508	£141,683	£131,648	£175,909	£105,447
28	Cost-saving	£141,683	£131,319	£869,045	£104,258
29	£130,508	Cost-saving	£131,319	Cost-saving	£681,008
30	£130,508	£141,683	Cost-saving	£175,909	Cost-saving
31	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving
32	£130,508	£141,683	£131,319	£175,909	£104,258

MSM, Men-who-have-sex-with-men; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P1, L1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	P2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	P4, L20-30
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	P5, L3-7
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	P5, L6-7
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	P6, L13-21
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	P5, L11-14
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	P5, L26
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	P25
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	P6, 24-26 P24, Table
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A

			N/A
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	P5-6
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	P24, Table 4 P6, L13-26
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	P24, Table 4
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	P33, Figure 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	P20, Table 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	P7, 14-24
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	P21, Table 3 P24, Table 4
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	P28, Table 7 P27, Table 6
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	N/A

		of methodological assumptions (such as discount rate, study perspective).	N/A
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	P30-33
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	P35 Figure 2 P30-33
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	P10-12
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	P13, L18-21
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	P13, L9-17

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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A modelling-based evaluation of the costs, benefits and cost-effectiveness of multi-pathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees

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A modelling-based evaluation of the costs, benefits and cost-effectiveness of multi-pathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees

Susie E Huntington[1], Richéal M Burns[1], Emma Harding-Esch[3,4], Michael J Harvey[1], Rachel Hill-Tout[5], Sebastian S Fuller[4], *Elisabeth J Adams[1], *S Tariq Sadiq[3,4,5]

1. Aquarius Population Health, 58a Highgate High Street, London, N6 5HX, UK
2. Health Economics and Policy Analysis Centre (HEPAC), NUI Galway, Ireland.
3. HIV/STI Department, National Infection Service, Public Health England, 61 Colindale Avenue, London, NW9 5EQ, UK
4. St George's Institute for Infection and Immunity, Applied Diagnostic Research and Evaluation Unit, University of London, Cranmer Terrace, London, SW17 0RE, UK
5. St George's University Hospitals NHS Foundation Trust, Blackshaw Road, Tooting, London, SW17 0QT.

*Joint senior authors.

Correspondence to: Dr Tariq Sadiq ssadiq@sgul.ac.uk. Tel: 020 8725 5740/3355 Institute for Infection and Immunity, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK

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Abstract

Objectives: To quantify the costs, benefits and cost-effectiveness of three multi-pathogen point-of-care (POC) testing strategies for detecting common sexually transmitted infections (STIs) compared with standard laboratory testing.

Design: Modelling study.

Setting: Genitourinary medicine (GUM) services in England.

Population: A hypothetical cohort of 965,988 people, representing the annual number attending GUM services symptomatic of lower genitourinary tract infection.

Interventions: The decision tree model considered costs and reimbursement to GUM services associated with diagnosing and managing STIs. Three strategies using hypothetical point-of-care tests (POCTs) were compared to standard care (SC) using laboratory-based testing. The strategies were: A) dual POC test (POCT) for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG); B) triplex POCT for CT-NG and *Mycoplasma genitalium* (MG); C) quadruplex POCT for CT-NG-MG and *Trichomonas vaginalis* (TV). Data came from published literature and unpublished estimates.

Primary and secondary outcome measures: Primary outcomes were total costs and benefits (quality-adjusted life years [QALYs]) for each strategy (2016 GB £) and associated incremental cost-effectiveness ratios (ICERs) between each of the POC strategies and SC. Secondary outcomes were inappropriate treatment of STIs, onward STI transmission, pelvic inflammatory disease in women, time to cure and total attendances.

Results: In the base-case analysis, POC strategy C, a quadruplex POCT, was the most cost-effective relative to the other strategies, with an ICER of £36,585 per QALY gained compared to SC when using micro-costing, and cost-savings of £26,451,382 when using tariff costing. POC strategy C also generated the most benefits, with 240,467 fewer clinic attendances, 808 fewer onward STI transmissions, and 235,135 averted inappropriate treatments compared to SC.

Conclusions: Many benefits can be achieved by using multi-pathogen POCTs to improve STI diagnosis and management. Further evidence is needed on the underlying prevalence of STIs and SC delivery in the UK to reduce uncertainty in economic analyses.

Strengths and limitations of this study

- The main strength of this study is that it presents the first estimates of the potential public health impact of multi-pathogen POCT strategies made possible by emerging diagnostic technologies.
- The model used inputs from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion and in incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.
- The main limitations were the paucity of published data on treatment pathways including efficacy of treatment and gaps in treatment guidelines, which made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, or percentage returning to clinics after initial treatment.

Introduction

Continued high transmission rates of sexually transmitted infections (STIs) that cause treatable lower genital tract discharge syndromes (GDS) are a major public health concern. This causes significant reproductive-health long-term sequelae[1-4] and frequently necessitates empirical therapy to minimise treatment delay, which often results in misdirected treatment, poor antimicrobial stewardship and the spread of antimicrobial resistance.[5,6] Among the common causes of GDS, there were 107,252 and 39,696 diagnoses of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG), respectively, made in English genitourinary medicine (GUM) services in 2015 [7], with smaller numbers of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) diagnoses.

The decision to give empirical antimicrobial therapy in symptomatic patients is usually guided by results of immediate microscopy of genital discharge, but this has low sensitivity, missing up to half of NG/TV infections in women [8] and particularly poor specificity for predicting CT or MG. Accurate routine diagnosis, which requires laboratory-based nucleic acid amplification tests (NAATs), can take up to two weeks for results to be processed and most GUM services do not routinely conduct NAATs for MG or TV. Many patients are presumptively treated with either azithromycin or doxycycline, which are effective against CT but respectively cure only two-thirds and one-third of MG infections [9] and neither antimicrobial is effective against TV.[9]

Emerging technologies are being developed that allow rapid and accurate point-of-care tests (POCTs) for multiple sexually transmitted infections, solutions which could address these challenges and help improve patient and public health outcomes. However, health services are under increasing financial pressure, and implementing new technologies may be prohibitively costly for both providers and commissioners of healthcare. There is currently only one commercially available rapid NAAT for CT and NG, which has equivalent performance to laboratory NAATs (Cepheid GeneXpert).[10] Previous economic evaluations of NAAT POCTs for CT and NG indicate that they are likely to provide a cost-effective strategy for screening GUM attendees.[5,11] To inform decision making by groups developing multi-pathogen POCTs and clinics which would likely use such tests, we assessed costs, benefits and cost-effectiveness of three testing strategies using hypothetical NAAT POCTs for A) CT-NG, B) CT-NG-MG and C) CT-NG-MG-TV compared with laboratory-based CT-NG NAAT testing.

Methods

Creating a model structure

A decision tree model was constructed using Microsoft Excel (v.2016) to simulate a hypothetical cohort of people with symptoms of a lower genitourinary tract infection attending English GUM services. The base-case or primary analysis, using assumptions provided in Supplementary Table 1, compared complete pathway costs of three point-of-care (POC) strategies to the current practice of using microscopy plus a laboratory CT-NG NAAT. The POC strategies used microscopy plus a hypothetical POCT that provides results in 30 minutes for A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Microscopy was used in all POC strategies as it can detect other conditions and infections not covered by the POCTs, as well as diagnosing NG and TV. The strategies were chosen in response to recent developments in STI POCT technology, reflecting pathogen configurations and performance characteristics.[12,13]

Outcomes

Primary outcomes were total costs and benefits, measured by quality adjusted life years (QALYs) for each strategy and associated incremental cost-effectiveness ratios (ICERs, see equation) between each of the POC strategies and standard care (SC). The ICER provides information on the additional cost per unit of additional benefit between an option and the next less expensive alternative.

$$ICERx = \frac{Cost_{POCx} - Cost_{Current\ Practice}}{QALY_{POCx} - QALY_{Current\ Practice}}$$

Secondary outcomes assessed the wider health benefits and included inappropriate treatment of STIs (defined as unnecessary treatment of people with no STI plus incorrect treatment for people with an STI), onward transmission of the four STIs, pelvic inflammatory disease (PID), a serious complication of CT, NG and MG infections in women, time to cure and total GUM attendances.

Patient pathways

Three senior clinicians at St George's University Hospitals NHS Foundation Trust, London outlined current and hypothetical POC pathways for symptomatic patients (Figure 1). We assumed that treatment pathways did not vary by subgroup but that MSM had diagnostic tests from three anatomical sites (genital, pharyngeal, and rectal) at initial visit and MSW and women only had genital swabs. The model accounted for single or dual infections with NG, CT, MG and/or TV.

The cost of treating PID, was included in the model but other long-term complications associated with STI infection (e.g. infertility) and adverse drug events associated with treatment were not considered. The proportion of patients lost-to-follow-up (LTFU) was estimated. It was assumed that anyone remaining in follow-up consented to diagnostic testing and, if diagnosed, accepted treatment. The decision framework assumed that individuals had a maximum of three follow-up visits and then exited the model. Drug resistance was not considered. The time horizon for the model was 56 days. It was assumed that treatment was started on the day of diagnosis.

Epidemiology and clinical parameters

A short online survey, distributed to members of the British Association for Sexual Health and HIV (BASHH), was used to collect data on the percentage of patients attending GUM services that are symptomatic, the percentage of patients returning after initial visits, as well as MG testing protocols, as limited data were available from published literature. The survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK (Supplementary Table 2).

The total annual number of people attending English GUM services for STI testing was obtained from national surveillance data (GUMCAD 2015 data).[7] This was combined with the clinician survey results on the proportion of symptomatic attendees, to estimate 965,988 total symptomatic attendees and by subgroup (590,787 women, 259,064 men-who-have-sex-with-women [MSW] and 116,137 men-who-have-sex-with-men [MSM]). We assumed that hypothetical POCTs had similar sensitivity and specificity to the best performing currently available CT-NG POCTs.[10] The prevalence of CT, NG, MG and TV in GUM attendees (Table 1, variables 12-21) was estimated using published studies and preliminary findings from the PRECISE Study [14], a study evaluating POCTs conducted by St George's, University of London and Public Health England.

Table 1. Epidemiological and clinical parameters

	Variable	Value			Distribution	Number			Comments, Reference
		Women	MSW	MSM		Women	MSW	MSM	
1	Initial clinic attendances	61%	27%	12%	Beta	590,787	259,064	116,137	Clinician survey results
2	CT infection	6.5%	23.3%	6.2%	Beta	38,401	60,362	7,200	W [14,15,16]; MSW [14,17]; MSM [14]
3	NG infection	0.7%	3.4%	38.1%	Beta	4,136	8,808	44,248	W [14,15,16]; MSW [14,17]; MSM [14]
4	MG infection	4.2%	12.3%	9.3%	Beta	24,813	31,865	10,801	W [14]; MSW [14,17]; MSW [14]
5	TV infection	4.4%	0.0%	0.0%	Beta	25,995	-	-	W [14,15,16,18]; MSW [14]; MSM estimate
6	CT NG co-infection	0.3%	2.2%	6.2%	Beta	1,772	5,699	7,200	W [14,15]; MSW, MSW [14]
7	CT MG co-infection	1.6%	2.8%	0.0%	Beta	9,453	7,254	-	W, MSW, MSW [14]
8	CT TV co-infection	0.2%	0.0%	0.0%	Beta	1,182	-	-	W [14,15,16]; MSW [14]; MSM estimate
9	NG MG co-infection	0.6%	0.6%	1.0%	Beta	3,545	1,554	1,161	W, MSW, MSM [14]
10	NG TV co-infection	0.4%	0.0%	0.0%	Beta	2,363	-	-	W [16]; MSW [14]; MSM estimate
11	MG TV co-infection	1.0%	0.0%	0.0%	Beta	5,908	-	-	W [14]; MSW, MSM estimate
12	Sensitivity of microscopy for detecting NG	40%	75%	75%	Uniform	Estimate based on published studies and clinical experience [8]			
13	Specificity of microscopy for detecting NG	100%	100%	100%	Uniform	Estimate based on published studies and clinical experience [8]			
14	Sensitivity of microscopy for detecting TV	50%	50%	50%	Uniform	Assumption based on clinical experience			
15	Specificity of microscopy for detecting TV	100%	100%	100%	Uniform	Assumption based on clinical experience			
16	Sensitivity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [19]			
17	Specificity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [19]			
18	Sensitivity of POCTs for CT/NG/MG/TV	95%	95%	95%	Uniform	Estimate based on tests currently available [10]			
19	Specificity of POCTs for CT/TV/MG	96%	96%	96%	Uniform	Estimate based on tests currently available [10]			
20	Specificity of POCTs for NG	98%	98%	98%	Uniform	Estimate based on tests currently available [10]			
21	CT infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [2]			
22	NG infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [20]			
23	MG infection - probability of PID	4%	-	-	Normal	Estimate based on published studies [1]			
24	TV infection - probability of PID	0%	-	-	Normal	Assumption			
25	Microscopy at first attendance	84%	84%	84%	Uniform	Assumption, clinician survey results			
26	Presumptive treatment for CT	50%	50%	50%	Normal	Estimate based on clinical practice			
27	Proportion of MG infections cured by CT treatment	67%	67%	67%	Uniform	Estimate based on published studies [9]			

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with women*;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; NGU, non-gonococcal urethritis; PID, pelvic inflammatory disease; POCT, point-of-care test; TV, *Trichomonas vaginalis*.

Cost and utility parameters

All costs are given in 2015/16 prices (GB, £) and inflated to 2015/16 costs when based on previous estimates using the Hospital and Community Health Services (HCHS) Inflation Indices 2015.[21] The model considered two perspectives for costs: 1) costs to GUM services (micro-costing) associated with testing and management of NG/CT/MG/TV infections plus the cost of treating PID [22] and 2) NHS tariff reimbursements clinics would receive based on attendances (Table 2). Micro-costing was calculated by adapting an existing pathway model [23] which considers costs of staff time, diagnostic kit, drugs, and other consumables. The tariff, an estimated average first and follow-up attendance cost used for commissioning and cross-charging [24], was estimated using the draft 2015/16 NHS tariff for first and follow-up GUM attendances. Fixed tariffs are not affected by how treatment is administered (oral/intramuscular) or the number of tests performed.

Table 2. Model input parameters: costs and utilities

Utilities			
Asymptomatic health state	1.00	Assume an otherwise healthy population	
Symptomatic health state	0.93		Sri, 2016 [25]
Waiting for diagnosis (symptomatic) health state	0.93	Assume the same as symptomatic	Sri, 2016 [25]
Treatment complete i.e. returned to asymptomatic state	1.00	Assume they return to asymptomatic	
PID diagnosis health state	0.80		Smith, 2008 [26]
Costs			
Tariff cost of initial visit plus treatment management	£141.00	Draft National Tariff Payment System: 2015/16	[24]
Initial clinic visit of symptomatic patient (micro-costing)	£103.71	Patient pathway adapted from a previous model	Adams, 2014 [a 23]
Management of STI (oral medication) on same day as assessment[b,c]	£29.19	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (oral medication) at return visit after results[b,c]	£31.32	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (medication via injection) on same day as assessment[c]	£43.79	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (medication via injection) on return visit after results[c]	£44.32	Excludes drug cost and GC culture/typing lab processing	Adams, 2014 [a 23]
Standard CT/NG NAAT laboratory diagnostic test[d]	£13.17		Adams, 2014 [a 23]
POCT CT-NG[d]	£24.00	Assumption based on cost of products currently available	
POCT CT-NG-MG[d]	£29.00	Assumption based on cost of products currently available	
POCT CT-NG-MG-TV[d]	£34.00	Assumption based on cost of products currently available	
Tariff cost of return visit	£110.00	Draft National Tariff Payment System: 2015/16	[24]
Return clinic visit of symptomatic patient (micro-costing)	£83.25	Patient pathway adapted from a previous model	Adams, 2014 [a 23]
NG test of cure using standard NAAT laboratory test	£41.73		Adams, 2014 [a 23]
NG test of cure using POC A	£55.93		Adams, 2014 [a 23]
Cost of drug treatment (1st line) for CT	£1.20	Where 95% of patients receive 1g Azithromycin and 5% receive Doxycycline 100mg twice daily for 7 days	BNF, 2016 [27]
Cost of drug treatment (1st line) for NG	£5.95	Single dose Ceftriaxone 500mg deep intramuscular injection	BNF, 2016 [27]

		with single dose 1g Azithromycin	
Cost of drug treatment (1st line) for MG	£1.87	Doxycycline 100mg twice daily for 7 days	BNF, 2016 [27]
Cost of drug treatment (1st line) for TV	£0.36	Metronidazole 2g orally in a single dose	BNF, 2016 [27]
Cost associated with treatment of short-term PID	£180.52		Aghaizu, 2011 [22]

BNF, British National Formulary; CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; PID, pelvic inflammatory disease; POC, point-of-care; TV, *Trichomonas vaginalis*.

[a]Costs were inflated to 2015/16 costs using the Hospital and Community Health Services (HCHS) Inflation Indices 2015 produced by the Personal Social Services Research Unit.[21] No data were available for inflation from 2014/15 to 2015/16 so it was assumed to the same as between 2013/2014 and 2014/15. The UK consumer price index for health services shows similar annual growth in this sector from 2014 which validates this assumption.

[b]The cost of management of MG/TV infection is assumed to be the same as the costs associated with management of CT infection.

[c]These costs vary due to the difference in administrative staff time for patient registration if the patient is treated on the same day or on a subsequent visit.

[d]MSM have samples from three sites (urethral, rectal, pharyngeal) tested at the initial visit, whereas women and MSW typically have one sample taken.

Costs of implementing a change in practice, including training costs, were not considered. Costs associated with testing and treating other causes of lower genitourinary tract symptoms were not considered.

Utilities, measures of health-related quality of life, were used in calculating QALYs for the health states (asymptomatic, symptomatic, or awaiting test results) incorporated in the decision analytic framework (Table 2).

Scenario and sensitivity analysis

As well as the base-case analysis, 32 further scenarios were assessed deterministically i.e. where one or more key parameters were varied based on changing the assumption of that parameter(s) while holding all others at the base-case level (Supplementary Table 3). Scenarios included: higher STI prevalence; lower sensitivity and specificity of POCTs; differing microscopy use; cheaper POCTs; and different LTFU rates.

We performed a second order Monte Carlo probabilistic sensitivity analysis (PSA), consistent with best practice, to estimate base-case ICERs. We converted model inputs from discrete values to distributions. For cost inputs, we used a normal distribution and varied each cost by 20% for the standard deviation. We correlated costs of POCTs against the least expensive option to ensure test costs would change equivalently to the same degree with each simulation. For clinical parameters, we used beta and normal distributions for probabilities and uniform distributions for test performance. For utilities, normal distributions were used. The PSA included 5000 simulations and was performed using recommended procedures [28]. Probabilities that strategies were cost-effective at a range of willingness-to-pay (WTP) thresholds per QALY gained were presented in cost-effectiveness acceptability curves (CEACs). CEACs were generated for each subgroup and the total population. Threshold costs for POCTs at which POC strategies would become cost-saving were calculated to the nearest £0.25.

Results

Using micro-costing, the estimated annual cost of testing and managing CT, NG, MG and TV infections in 965,988 symptomatic individuals attending GUM was £113,058,655 using SC. This was the cheapest strategy to clinical services, with POC strategies A, B and C being increasingly expensive at £118,704,963 (5% increase), £124,842,003 (10.4% increase), and £125,313,136 (10.8% increase), respectively (Table 3). The opposite was true when using tariff costs, with SC being the most expensive for commissioners of sexual health care at £172,364,138, and POC strategy C being the least expensive, at £145,912,757 (Table 3).

Table 3. The costs, QALYs, average time to cure, inappropriate treatment and follow-up visits in SC and three POC strategies for symptomatic people attending GUM services

Sub-group	Strategy	Model Outcomes: Total costs (micro-costing)	Total costs (tariff)	Total QALYs	Average time to cure (days)	Inappropriate treatments	Mean number of visits/person	Return clinic visits[1]	Infected partners	PID cases in women
All	SC	£113,058,655	£172,364,138	146,532	4.3	258,395	1.3	328,726	1,876	176
	POC A	£118,704,963	£151,956,910	146,656	2.3	109,135	1.1	143,205	1,414	119
	POC B	£124,842,003	£152,288,107	146,626	2.1	200,865	1.2	146,216	1,451	64
	POC C	£125,313,136	£145,912,757	146,867	1.1	23,260	1.1	88,259	1,068	64
Women	SC	£65,122,097	£99,714,696	89,533	4.4	176,604	1.3	149,216	764	176
	POC A	£66,938,018	£88,960,028	89,584	2.4	76,322	1.1	51,446	524	119
	POC B	£69,853,645	£89,101,615	89,554	2.2	128,806	1.1	52,733	535	64
	POC C	£69,285,504	£85,008,982	89,718	1.1	1,607	1.0	15,528	260	64
MSW	SC	£29,572,989	£46,813,874	39,342	4.3	54,860	1.4	93,507	459	-
	POC A	£29,995,704	£40,111,202	39,389	2.1	20,957	1.1	32,574	343	-
	POC B	£31,717,478	£40,614,444	39,380	2.0	54,863	1.1	37,149	360	-
	POC C	£31,373,674	£38,724,875	39,443	1.2	13,218	1.1	19,971	285	-
MSM	SC	£18,363,569	£25,835,568	17,658	4.1	26,931	1.7	86,002	653	-
	POC A	£21,771,241	£22,885,680	17,684	2.3	11,855	1.5	59,185	546	-
	POC B	£23,270,880	£22,572,047	17,692	1.5	17,196	1.5	56,334	556	-
	POC C	£24,653,958	£22,178,900	17,706	1.2	8,436	1.5	52,760	524	-

[1]Return clinic visit for results and treatment, a test of cure (routine for NG) or because they remain symptomatic.

MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; PID, pelvic inflammatory disease; QALY, quality-adjusted life year.

Most of the total care pathway cost was the initial attendance cost. In SC, total pathway costs for women were £65,122,097, of this 93% (£60,432,050) were initial attendance costs. For POC strategy C, total pathway costs for women were £69,285,504, of which 98% (£68,041,383) were initial attendance costs.

POC strategy C provided most benefits to the full cohort. POC strategies A, B, and C increased QALYs by 124, 94 and 335, respectively compared to SC (Table 3 and Table 4). Time to cure was shorter and the number of total clinic visits, onward STI transmissions and PID cases were fewer in POC strategies than in SC. Compared to SC, POC strategy C resulted in 240,467 fewer clinic visits, 808 fewer onward STI transmissions, 235,135 averted inappropriate treatments and 112 fewer cases of PID.

Table 4. Cost differences for SC and POC strategies

Sub-group	Comparison	QALY difference	Micro-costing		Tariff costs	
			Cost difference	ICER (£/QALY gained)	Cost difference	ICER (£/QALY gained)
All	POC A vs SC	124	£5,646,309	£45,516	-£20,407,228	**Cost-Saving**
	POC B vs SC	94	£11,783,348	£125,197	-£20,076,031	**Cost-Saving**
	POC C vs SC	335	£12,254,482	£36,585	-£26,451,382	**Cost-Saving**
	POC B vs A	-30	£6,137,039	**Dominated**	£331,197	**Dominated**
	POC C vs B	241	£471,133	£1,956	-£6,375,350	**Cost-Saving**
Women	POC A vs SC	51	£1,815,921	£35,608	-£10,754,668	**Cost-Saving**
	POC B vs SC	21	£4,731,548	£222,568	-£10,613,081	**Cost-Saving**
	POC C vs SC	185	£4,163,407	£22,448	-£14,705,715	**Cost-Saving**
	POC B vs A	-30	£2,915,627	**Dominated**	£141,587	**Dominated**
	POC C vs B	164	-£568,141	**Cost-Saving**	-£4,092,634	**Cost-Saving**
MSW	POC A vs SC	47	£422,715	£9,005	-£6,702,672	**Cost-Saving**
	POC B vs SC	38	£2,144,488	£56,104	-£6,199,430	**Cost-Saving**
	POC C vs SC	102	£1,800,685	£17,724	-£8,088,999	**Cost-Saving**
	POC B vs A	-9	£1,721,773	**Dominated**	£503,242	**Dominated**
	POC C vs B	63	-£343,804	**Cost-Saving**	-£1,889,570	**Cost-Saving**
MSM	POC A vs SC	26	£3,407,672	£130,508	-£2,949,888	**Cost-Saving**
	POC B vs SC	35	£4,907,312	£141,683	-£3,263,521	**Cost-Saving**
	POC C vs SC	48	£6,290,390	£131,319	-£3,656,668	**Cost-Saving**
	POC B vs A	9	£1,499,639	£175,909	-£313,633	**Cost-Saving**
	POC C vs B	13	£1,383,078	£104,258	-£393,147	**Cost-Saving**

ICER, incremental cost-effectiveness ratios, MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; QALY, quality-adjusted life year.

ICERs associated with the base-case model are presented in Table 4. POC C highlights cost-effectiveness relative to other strategies yielding an ICER of £36,585 per QALY gained compared to SC when using micro-costing estimates. When incorporating NHS tariff costing, this represents a potential cost-savings of £26,451,382 relative to current practice.

CEACs are presented in Figures 2-5. Using micro-costing, for a WTP of £30,000/QALY, the upper threshold adopted by NICE [29], SC had a 50% probability of being cost-effective overall, a 17% probability for women, a 2% probability for MSW and a 99% probability for MSM, relative to the POC strategies. For a WTP of £25,000, POC C dominates, i.e. is cheaper and yields more benefits than the other POC strategies for the total cohort, women and MSW. For MSM, SC dominates all strategies across the thresholds examined. For MSW, POC A had 65% probability of being cost-effective at a WTP threshold of £10,000 per QALY gained.

Results of 32 scenario analyses are summarised in Supplementary Tables 4-7. The proportion of patients given presumptive treatment (scenarios 21-24) impacted costs hugely. When no presumptive treatment was given (scenario 21), the cost per QALY was £7,339 and £9,092 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC. When all patients without a diagnosis were presumptively treated for CT, MG or TV, according to which infections had been ruled out (scenario 24), POC strategies A and C were dominated by SC and POC strategy B cost £64,300/QALY more than SC.

When the utility score for being symptomatic was 10% less than base-case (scenario 25), cost per QALY was £15,627 more for POC strategy C than for SC. If microscopy was no longer used in POC strategies (scenario 13), cost per QALY was £16,204 and £29,594 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC.

If MG and TV prevalence were as high as the estimated prevalence in the US [30,31] (scenario 2), cost per QALY was £20,530 and £25,548 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC. When POCTs were priced the same as the SC test (scenario 31), POC strategies B and C were cost-saving (using micro-costing).

Holding all other parameters constant using base-case assumptions, POC strategies would be cost-saving compared to SC, if POCTs cost £19.25, £13.50 and £21.00, respectively for POCTs A, B and C.

DISCUSSION

Principle findings

This study compared costs, benefits and cost-effectiveness of a laboratory-based CT-NG NAAT, with three POC strategies for: A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Using our initial assumptions for the total population using the micro-costing approach to assess direct costs to health-care services, each POC strategy cost more than SC, but yielded additional benefits. The proportion of patients given presumptive treatment and the cost of the POCT kit both impacted the costs hugely. Results indicated that different strategies would be cost-effective for different patient sub-groups depending on the WTP threshold in place. POC strategy A was most cost-effective for MSW, POC strategy C for women, and SC for MSM. Whether using different testing strategies on different patient groups would be practical or acceptable was beyond the scope of this research and requires further investigation. Different results were obtained when tariff reimbursement costs were used, with POC strategy C costing the least and providing the most benefits.

Strengths and weaknesses

Our analysis has several strengths. This is the first study to compare the cost-effectiveness of the three different STI POC strategies with SC. Comparable and consistent methods were used to construct a model with inputs from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion. The model incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.

Potential limitations should be considered. While it is thought that most UK clinicians follow British Association for Sexual Health and HIV (BASHH) guidelines for STI testing and treatment [9,19], there is diversity in the testing and management strategies employed to meet specific patient needs, both within and between clinics. This diversity, the paucity of published data on treatment pathways and gaps in treatment guidelines, made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, the percentage returning to clinics after initial treatment and the percentage of patients attending with symptoms – all parameters which are likely to vary somewhat between clinics. We tried to overcome this using different scenario analysis and by collecting data using an online survey for GUM clinicians, albeit from a small sample size. Data from the survey showed high variation between clinics for some parameters. For example, the percentage of patients attending with symptoms ranged from 0% to 90%. There were few published data on

utilities and sexual behaviour whilst symptomatic with an STI, whilst waiting for test results and whilst being on treatment for an STI. Both qualitative and quantitative research is needed in this area to inform future health economic analyses and to understand preferences for and impact on patients of introducing POC testing.

The staffing and consumable cost data used in the model were average costs. In reality, different sites use staff of different grades and salaries to perform similar tasks and negotiate different costs for consumables, implying an inevitable variation in how cost effective the different strategies would be for different sites.

The costs associated with long-term complications of STIs were not considered [32]. This limitation means that the results are conservative, as the costs associated with SC are likely to be underestimated. However, the long-term benefits for a single round of testing were thought to be very low and to not have a major impact on the magnitude of results.

Comparing the results to other studies. POC pathways generated some cost savings, primarily because patients had fewer return visits. However, these did not outweigh the higher cost of the POCTs compared to laboratory-based NAATs when estimating total pathway costs. This means that if POC testing was used, there would be expected overall cost increases based on the analysis using the micro-costing approach. This differs from previous modelling, in which a CT-NG POCT was cost saving compared to laboratory testing [5]. In the Turner *et al.* model, the cost of a POC attendance was £6.95 cheaper than the cost of an SC attendance since the asymptomatic POC pathway was redesigned. In our model, the cost of attendance for a symptomatic patient was the same whether samples were sent to a laboratory or performed in clinic, since all symptomatic clinic attendees would require examination and microscopy.

Implications for public health, clinicians and people using GUM services

POC strategy C significantly decreased the numbers of inappropriate antibiotics given compared to SC, with over 235,000 fewer inappropriate treatments. Many of these treatments are likely to include azithromycin, which when inappropriately given can encourage spread of macrolide antibiotic resistance in MG infections [6]. POC strategy C also increased costs for health providers while decreasing tariff costs for commissioners, unless the “freed-up” capacity enabled by POC strategy C was used for STI screening appointments and initial assessments for symptomatic people. Although this would likely have a positive impact on public health, given GUM services in England face increasing pressure on

their services with more than 2 million new attendances annually [7], while local authorities equally face fiscal pressures, this work demonstrates the potential tensions between different cost-consequences for procurers and providers and public health benefits when considering implementation of novel health technologies.

For people using GUM services, there are numerous benefits to POC testing compared to SC. People would need fewer clinic visits, saving them time and reducing LTFU and reducing their costs such as out-of-pocket expenses and productivity losses. Receiving a diagnosis at the initial attendance reduces anxiety compared to waiting for test results [25]. A negative result from a multi-pathogen POCT will support the development of clearer guidelines for clinicians, which could also reassure patients, particularly those with vague genital tract symptoms. Receiving effective treatment at initial attendance is likely to reduce the duration of symptoms and reproductive health sequelae.[1,2]

POCTs can also generate public health benefits from swifter diagnosis and treatment, for example, POC strategy C led to an estimated 43% fewer onward transmissions of STIs compared to SC. The ability to diagnose or rule out specific infections at first attendance enables accurate treatment and reduces inappropriate antibiotic use, crucial for good antibiotic stewardship, the economic benefits of which are substantial and well documented.[33]

Unanswered questions and future research

Although a rapid test for CT and NG is used in some GUM services, multi-pathogen configurations of CT-NG-MG-TV POCTs are not currently available. As such, likely pathways for POC strategies had to be designed based on expert opinion. Published audits of GUM patient pathways would be a useful addition to the literature. To reduce uncertainty in economic analyses around STIs, further evidence is also needed on underlying STI prevalence and the risk of onward STI transmission.

Patient pathways and testing protocols vary between sites and different sites see different proportions of people from the three sub-groups. As such, the costs of changing to a POC strategy will vary between sites as will the benefits and costs not considered in the model. Validated and easy to use computational tools for clinics and commissioners, which assess the economic impact of implementing any one of the POC strategies, using local population data, would increase understanding across stakeholders.

Conclusion

In conclusion, the results suggest that although potentially more expensive, a quadruplex test for CT-NG-MG-TV is more cost-effective than SC and the other testing strategies assessed, providing the most additional benefits to patients. Cost implications are driven by the cost of POCTs and would vary somewhat in different geographical areas due to differences in the subgroup mix and the prevalence of the four STIs.

Footnotes

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All authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency: The senior author (STS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: no additional data available.

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Figure 1. Diagram showing simplified patient flow through the model

Standard care (SC): 50% of people not diagnosed with NG or TV by microscopy will be presumptively treated for CT. The treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs (i.e. not CT/NG/MG/TV). We assume this treatment is not effective against TV or NG. Incorrectly treated patients with NG infection will be diagnosed by NAAT, and return (minus those LTFU) to receive treatment. Other returning patients may receive presumptive treatment for MG and TV.

POC strategy A: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for MG and TV. We assume that this treatment is effective against CT, MG, TV, and against all other non-specific bacterial STIs. We assume that this treatment is not effective against NG. Patients not initially presumptively treated but who return to the clinic are then presumptively treated with MG and TV treatment.

POC strategy B: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for TV. We assume this treatment is effective against TV, and against all other non-specific bacterial STIs. We assume this treatment is not effective against CT, MG, or NG.

POC strategy C: 100% of people who are not diagnosed by microscopy or POC would be presumptively treated using azithromycin. We assume this treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs. We assume this treatment is not effective against TV or NG. If any treated patients return they will be categorised as 'investigate further'. The cost of the 'investigate further' is the cost of a standard return appointment which includes microscopy.

Figure 2. Cost-effectiveness acceptability curves (CEACs): point-of-care test (POCT) strategies vs standard care

Footnote: MSM, men who have sex with men; MSW men who have sex with women; W, women.

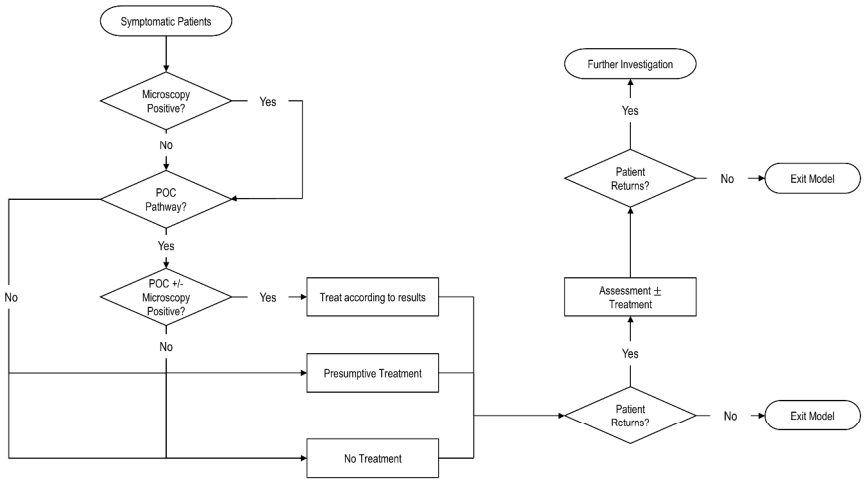

Figure 1.

338x190mm (300 x 300 DPI)

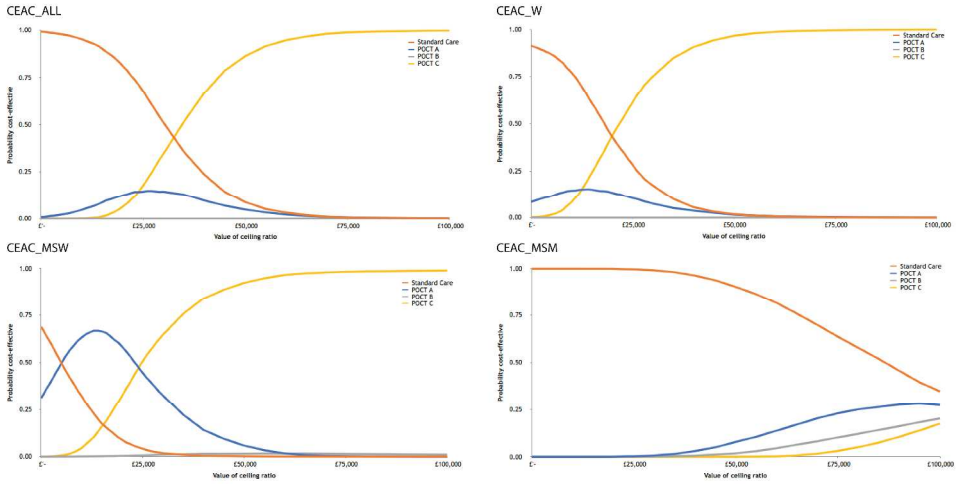

Figure 2 Cost-effectiveness acceptability curves (CEACs): point-of-care test (POCT) strategies vs standard care

596x309mm (300 x 300 DPI)

Supplementary Table 1. Key model assumptions

1	The decision framework assumes that after a maximum of 3 courses of treatment the individual would be cured. In standard care, this could take up to 56 days in total; therefore, the cycle length is one day and time horizon is 56 days.
2	Screening options will confirm diagnosis between 1-21 days; treatment options will last for a maximum of 7 days and 2 weekly cycles are imposed between treatment regimens. In current practice, we assume that individuals return on day 8 for test results in the base-case.
3	The sensitivity (true positive) and specificity (true negative) of POCT for each infection does not vary across the different POC strategies nor does it vary between patient sub-groups.
4	The model accounts for the impact of single and dual infections (CT, NG, TV and MG).
5	The proportion lost-to-follow-up varies by STI and gender due to the nature of symptoms and severity of individual STIs.
6	STI symptoms remain at the same clinical level of severity across the time horizon.
7	The model incorporates an 'Other Infection' category which includes all other infections that cause similar lower genital symptoms diagnosed initially (day 0) that rule out an initial diagnosis of CT/NG/MG/TV. These may include candida and allergic reactions. The proportion of the cohort who we assume fall into the "Other infection" category is 1 in 2 for women, 1 in 3 for MSW and 1 in 4 for MSM. We vary this assumption in scenario analysis.
8	Once results from screening options are confirmed those with a confirmed STI are treated and partners are made aware of the infection to access treatment.
9	Each index infection is assumed to have 1 partner for women and MSW and 2 partners for MSM per 7-day period; this assumption, as well as the number of sexual acts per week, is varied in sensitivity analysis.
10	In the absence of any data on changes in sexual behaviour following diagnosis with an STI, it is assumed sexual behaviour is not changed due to a diagnosis. This assumption affords the identification of all potential transmissions; however, taken at face value would be an overestimation of transmissions.
11	The model assumes STI transmission rates are constant over the duration of exposure.
12	The model assumes different treatment regimens for the different infections as informed by clinical guidance.
13	The model assumes the correct treatment for true CT/NG/MG/TV infection is 100% efficacious and ignores antibiotic resistant strains in NG and MG, thereby underestimating the total costs associated with STI infection.
14	The model does not include re-infections.
15	The model does not consider adverse events associated with treatment options.
16	The model does not consider long-term complications associated with STI infection.
17	The model limits sub-group analysis to women, MSW and MSM; treatment pathways do not vary by sub-group.

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; POCT, point of care test; STI, sexually transmitted infection, TV, *Trichomonas vaginalis*.

Supplementary Table 2. Summary of GUM clinician survey (October 2016) relevant to patient pathways

Survey question	Median	Lowest	Highest
Roughly how many patients attend your service every month?	1,700	80	6,000
What proportion of your patients are MSM?	10%	5%	100%
What proportion of your patients are MSW?	30%	0%	85%
What proportion of your patients are women?	53%	0%	60%
What proportion of MSM attend with a symptomatic lower genital tract infection?	50%	5%	90%
What proportion of MSW attend with a symptomatic lower genital tract infection?	40%	0%	90%
What proportion of women attend with a symptomatic lower genital tract infection?	50%	0%	80%
What proportion of symptomatic men have a swab that is sent for microscopy?	80%	25%	100%
What proportion of symptomatic men have a swab that is sent for culture?	60%	5%	100%
What proportion of symptomatic women have a swab that is sent for microscopy?	88%	0%	100%
What proportion of symptomatic women have a swab that is sent for culture?	58%	0%	100%
What proportion of MSM are tested for MG?	0%	0%	10%
What proportion of MSW are tested for MG?	0%	0%	20%
What proportion of women are tested for MG?	0%	0%	15%
Men who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	50%	5%	100%
Of those who return, what proportion receive further tests?	25%	0%	80%
Of those who return, what proportion receive presumptive treatment for another infection?	18%	5%	90%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	23%	0%	65%
Women who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	30%	0%	75%
Of those who return, what proportion receive further tests?	50%	10%	100%
Of those who return, what proportion receive presumptive treatment for another infection?	28%	5%	100%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	20%	0%	85%

CT, *Chlamydia trachomatis;* GP, General Practice; GUM, genitourinary medicine; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; TV, *Trichomonas vaginalis*.

The online survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK.

Supplementary Table 3. Scenarios assessed

1	Higher prevalence of MG and TV (double the current estimated prevalence)
2	Higher prevalence of MG and TV based on estimated prevalence in symptomatic patients in the US (MG: women 21.1%; men 19.3% and TV: women 25.9%; men 6.3%)
3	Increase proportion with 'Other infection' as follows: women: 66.6%, MSW: 50%, MSM: 50%
4	Decrease proportion with 'Other infection' as follows: women: 33.3%, MSW: 25%, MSM: 20%
5	100% increase the rate of LTFU
6	50% decrease the rate of LTFU
7	Specificity/sensitivity of POCT is 75%
8	Specificity/sensitivity of POCT is 80%
9	Specificity/sensitivity of POCT is 85%
10	Specificity/sensitivity of POCT is 85% for NG (but unaltered for CT, MG and TV)
11	Specificity/sensitivity of POCT is 85% for CT (but unaltered for NG, MG and TV)
12	Specificity/sensitivity of POCT is 85% for MG (but unaltered for CT, NG and TV)
13	No microscopy used in any testing strategy
14	50% people get microscopy
15	75% people get microscopy
16	100% people get microscopy
17	84% use of microscopy in current pathway and no use of microscopy in the POC strategy C
18	No microscopy for men (only) in POC strategy C
19	No microscopy for women (only) in POC strategy C
20	Use of microscopy in POC strategy C only after a negative test result
21	No presumptive treatment for CT
22	25% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
23	75% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
24	100% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
25	Use 10% reduction in symptomatic utility scores
26	Excluding the cost of PID (as not all PID will be treated in the GUM service)
27	Inclusion of the drug costs for doxycycline as treatment for anyone NG/CT/MG/TV negative
28	POCT CT-NG costs the same as laboratory based NAAT
29	POCT CT-NG-MG cost the same as laboratory based NAAT
30	POCT CT-NG-MG-TV costs the same as laboratory based NAAT
31	All POCTs cost the same as laboratory based NAAT
32	All POCTs cost £2 less than in base-case

CT, *Chlamydia trachomatis;* GUM, genitourinary medicine; LTFU, lost-to-follow-up; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*; POC, point-of-care; POCT, point-of-care test; TV, *Trichomonas vaginalis;* US, United States (of America).

Supplementary Table 4. Cost-effectiveness comparison for scenario analyses using micro-costings - All

All	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£ 17,389	£ 41,381	£7,153	Dominated
2	Dominated	£ 20,530	£ 56,548	£8,228	Dominated
3	£ 224,378	£ 22,979	£ 69,517	£12,300	Dominated
4	Dominated	£ 15,818	£ 24,163	£7,107	£6,353
5	Dominated	£ 19,691	£ 35,749	£9,196	Dominated
6	Dominated	£ 19,363	£ 36,221	£9,196	Dominated
7	Dominated	£ 21,665	£ 82,996	£8,870	Dominated
8	Dominated	£ 21,220	£ 69,561	£8,865	Dominated
9	Dominated	£ 20,735	£ 57,596	£8,891	Dominated
10	Dominated	£ 19,726	£ 39,414	£8,986	Dominated
11	Dominated	£ 20,431	£ 43,314	£8,265	Dominated
12	Dominated	£ 19,647	£ 40,917	£10,034	Dominated
13	Dominated	£ 16,204	£ 29,594	£8,703	Dominated
14	Dominated	£ 18,061	£ 33,245	£8,989	Dominated
15	Dominated	£ 19,088	£ 35,286	£9,140	Dominated
16	Dominated	£ 20,191	£ 37,493	£9,297	Dominated
17	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
18	Dominated	£ 19,476	£ 28,889	£9,196	£7,998
19	Dominated	£ 19,476	£ 23,566	£9,196	£14,332
20	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
21	Dominated	£7,339	£9,092	£3,792	£2,859
22	Dominated	£ 12,055	£ 18,039	£5,910	£552
23	Dominated	£ 32,870	£ 91,155	£14,987	Dominated
24	Dominated	£ 64,300	Dominated	£27,913	Dominated
25	£ 46,988	£ 17,310	£ 15,627	£10,948	£4,554
26	Dominated	£ 19,510	£ 36,120	£9,211	Dominated
27	Dominated	£ 19,476	£ 37,040	£9,196	Dominated
28	£ 43,475	£ 19,476	£ 36,060	£21,718	Dominated
29	Dominated	Cost-saving	£ 36,060	Cost-saving	Dominated
30	Dominated	£ 19,476	Cost-saving	£9,196	£74,924
31	£ 43,475	Cost-saving	Cost-saving	£218	£20,817
32	Dominated	£ 16,667	£ 31,058	£9,196	Dominated

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 5. Cost-effectiveness comparison for scenario analyses using micro-costings - Women

Women	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£8,843	£ 25,961	£4,199	Dominated
2	Dominated	£8,932	£ 52,744	£3,587	Dominated
3	Dominated	£ 13,611	£ 46,391	£7,257	Dominated
4	Dominated	£6,915	£ 10,406	£3,249	£5,070
5	Dominated	£9,013	£ 21,182	£4,368	£1,662
6	Dominated	£8,827	£ 22,264	£4,368	£1,662
7	Dominated	£8,012	£ 48,866	£3,769	£180
8	Dominated	£8,124	£ 41,683	£3,848	£350
9	Dominated	£8,279	£ 34,918	£3,954	£588
10	Dominated	£8,732	£ 22,995	£4,249	£1,398
11	Dominated	£8,597	£ 25,567	£3,827	£1,542
12	Dominated	£8,630	£ 24,992	£4,563	£1,556
13	Dominated	£8,344	£ 19,947	£4,136	£2,008
14	Dominated	£8,661	£ 21,070	£4,271	£1,808
15	Dominated	£8,829	£ 21,658	£4,341	£1,702
16	Dominated	£9,004	£ 22,264	£4,415	£1,590
17	Dominated	£8,891	Cost-saving	£4,368	£14,160
18	Dominated	£8,891	£ 21,874	£4,368	£1,662
19	Dominated	£8,891	Cost-saving	£4,368	£14,160
20	Dominated	£8,891	Cost-saving	£4,368	£14,160
21	Dominated	£4,042	£1,678	£1,846	£6,724
22	Dominated	£6,046	£8,172	£2,856	£4,238
23	Dominated	£ 13,250	£ 69,756	£6,878	Dominated
24	Dominated	£ 20,769	Dominated	£11,866	Dominated
25	Dominated	£9,256	£9,545	£5,197	£7,575
26	Dominated	£8,930	£ 21,981	£4,383	£1,662
27	Dominated	£8,891	£ 23,150	£4,368	£951
28	Dominated	£8,891	£ 21,874	£6,916	£1,662
29	Dominated	£ 143	£ 21,874	Cost-saving	Dominated
30	Dominated	£8,891	Cost-saving	£4,368	£23,924
31	Dominated	£ 143	Cost-saving	Cost-saving	£10,304
32	Dominated	£6,671	£ 15,666	£4,368	£1,662

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 6. Cost-effectiveness comparison for scenario analyses using micro-costings - MSW

MSW	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£12,263	£22,566	£21,976	£39,978	£20,481
2	£6,136	£21,655	£20,324	£70,648	£17,318
3	£6,705	£20,051	£33,219	£53,907	£163,024
4	£10,163	£104,518	£12,897	Dominated	Cost-saving
5	£12,052	£61,168	£19,205	Dominated	Cost-saving
6	£7,525	£53,665	£16,992	Dominated	Cost-saving
7	£265,801	Dominated	£64,478	Dominated	Cost-saving
8	£100,276	Dominated	£50,420	Dominated	Cost-saving
9	£49,716	Dominated	£38,304	Dominated	Cost-saving
10	£10,139	£60,983	£19,061	Dominated	Cost-saving
11	£44,559	£243,310	£28,123	Dominated	Cost-saving
12	£9,005	£109,035	£22,985	Dominated	Cost-saving
13	£5,013	£44,501	£15,654	Dominated	Cost-saving
14	£7,253	£50,948	£16,857	Dominated	Cost-saving
15	£8,521	£54,669	£17,490	Dominated	Cost-saving
16	£9,906	£58,793	£18,147	Dominated	Cost-saving
17	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
18	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
19	£9,005	£56,104	£17,724	Dominated	Cost-saving
20	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
21	Cost-saving	Cost-saving	Cost-saving	£20,002	£929
22	Cost-saving	£9,663	£4,599	£121,977	Cost-saving
23	£80,063	Dominated	£62,970	Dominated	Cost-saving
24	Dominated	Dominated	Dominated	Dominated	Cost-saving
25	£3,870	£24,112	£7,614	Dominated	Cost-saving
26	£9,005	£56,104	£17,724	Dominated	Cost-saving
27	£9,005	£56,104	£18,456	Dominated	Cost-saving
28	Cost-saving	£56,104	£17,724	Dominated	Cost-saving
29	£9,005	£2,696	£17,724	£36,667	£26,789
30	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
31	Cost-saving	£2,696	Cost-saving	Dominated	Cost-saving
32	Cost-saving	£42,549	£12,624	Dominated	Cost-saving

MSW, Men-who-have-sex-with-women; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 7. Cost-effectiveness comparisons for scenario analyses using micro-costings - MSM

MSM	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£137,378	£95,423	£139,260	£49,813	Dominated
2	£119,952	£83,250	£145,988	£42,999	Dominated
3	£91,163	£83,961	£332,964	£71,307	Dominated
4	£140,882	£160,599	£115,724	£235,703	£52,018
5	£135,796	£145,798	£134,186	£175,909	£104,258
6	£127,894	£139,636	£1,044	£175,909	£1,317
7	£833,775	£2,053,305	£350,136	Dominated	£78,956
8	£425,499	£591,462	£268,835	£4,264,237	£84,090
9	£271,627	£324,923	£211,896	£579,296	£89,914
10	£191,294	£191,613	£173,306	£192,369	£130,727
11	£168,341	£173,675	£143,342	£187,785	£85,861
12	£130,508	£167,524	£141,202	£406,528	£88,559
13	£47,590	£64,826	£74,079	£189,798	£126,208
14	£80,744	£98,423	£101,384	£181,298	£112,461
15	£113,144	£127,453	£122,040	£177,307	£106,349
16	£175,783	£175,089	£151,216	£173,474	£100,673
17	£130,508	£141,683	£131,189	£175,909	£83,111
18	£130,508	£141,683	£131,189	£175,909	£83,111
19	£130,508	£141,683	£131,319	£175,909	£104,258
20	£130,508	£141,683	£131,189	£175,909	£83,111
21	£60,065	£77,460	£84,981	£164,890	£116,909
22	£85,266	£101,948	£103,897	£170,152	£110,577
23	£235,470	£217,337	£174,644	£182,233	£97,951
24	£747,941	£417,789	£253,365	£189,212	£91,656
25	£56,093	£60,884	£56,420	£75,544	£44,773
26	£130,508	£141,683	£131,319	£175,909	£104,258
27	£130,508	£141,683	£131,648	£175,909	£105,447
28	Cost-saving	£141,683	£131,319	£869,045	£104,258
29	£130,508	Cost-saving	£131,319	Cost-saving	£681,008
30	£130,508	£141,683	Cost-saving	£175,909	Cost-saving
31	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving
32	£130,508	£141,683	£131,319	£175,909	£104,258

MSM, Men-who-have-sex-with-men; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P1, L1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	P2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	P4, L20-30
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	P5
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	P5
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	P9, L3
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	P5
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	P2, P9
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	P9
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	P5
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A

			N/A
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	P5-6
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	P9,10,11
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	P9,10,11
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Figure 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	SuppTable 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	P12
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Table 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Table 3 & 4
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	N/A

		of methodological assumptions (such as discount rate, study perspective).	N/A
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	P18, 19
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	P18
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	P19
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	P20
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	P20

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

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A modelling-based evaluation of the costs, benefits and cost-effectiveness of multi-pathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees

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A modelling-based evaluation of the costs, benefits and cost-effectiveness of multi-pathogen point-of-care tests for sexually transmitted infections in symptomatic genitourinary medicine clinic attendees

Susie E Huntington[1], Richéal M Burns[1], Emma Harding-Esch[3,4], Michael J Harvey[1], Rachel Hill-Tout[5], Sebastian S Fuller[4], *Elisabeth J Adams[1], *S Tariq Sadiq[3,4,5]

1. Aquarius Population Health, 58a Highgate High Street, London, N6 5HX, UK
2. Health Economics and Policy Analysis Centre (HEPAC), NUI Galway, Ireland.
3. HIV/STI Department, National Infection Service, Public Health England, 61 Colindale Avenue, London, NW9 5EQ, UK
4. St George's Institute for Infection and Immunity, Applied Diagnostic Research and Evaluation Unit, University of London, Cranmer Terrace, London, SW17 0RE, UK
5. St George's University Hospitals NHS Foundation Trust, Blackshaw Road, Tooting, London, SW17 0QT.

*Joint senior authors.

Correspondence to: Dr Tariq Sadiq ssadiq@sgul.ac.uk. Tel: 020 8725 5740/3355 Institute for Infection and Immunity, St George's, University of London, Cranmer Terrace, London, SW17 0RE, UK

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Abstract

Objectives: To quantify the costs, benefits and cost-effectiveness of three multi-pathogen point-of-care (POC) testing strategies for detecting common sexually transmitted infections (STIs) compared with standard laboratory testing.

Design: Modelling study.

Setting: Genitourinary medicine (GUM) services in England.

Population: A hypothetical cohort of 965,988 people, representing the annual number attending GUM services symptomatic of lower genitourinary tract infection.

Interventions: The decision tree model considered costs and reimbursement to GUM services associated with diagnosing and managing STIs. Three strategies using hypothetical point-of-care tests (POCTs) were compared to standard care (SC) using laboratory-based testing. The strategies were: A) dual POC test (POCT) for *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG); B) triplex POCT for CT-NG and *Mycoplasma genitalium* (MG); C) quadruplex POCT for CT-NG-MG and *Trichomonas vaginalis* (TV). Data came from published literature and unpublished estimates.

Primary and secondary outcome measures: Primary outcomes were total costs and benefits (quality-adjusted life years [QALYs]) for each strategy (2016 GB £) and associated incremental cost-effectiveness ratios (ICERs) between each of the POC strategies and SC. Secondary outcomes were inappropriate treatment of STIs, onward STI transmission, pelvic inflammatory disease in women, time to cure and total attendances.

Results: In the base-case analysis, POC strategy C, a quadruplex POCT, was the most cost-effective relative to the other strategies, with an ICER of £36,585 per QALY gained compared to SC when using micro-costing, and cost-savings of £26,451,382 when using tariff costing. POC strategy C also generated the most benefits, with 240,467 fewer clinic attendances, 808 fewer onward STI transmissions, and 235,135 averted inappropriate treatments compared to SC.

Conclusions: Many benefits can be achieved by using multi-pathogen POCTs to improve STI diagnosis and management. Further evidence is needed on the underlying prevalence of STIs and SC delivery in the UK to reduce uncertainty in economic analyses.

Strengths and limitations of this study

- The main strength of this study is that it presents the first estimates of the potential public health impact of multi-pathogen POCT strategies made possible by emerging diagnostic technologies.
- The model used inputs from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion and in incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.
- The main limitations were the paucity of published data on treatment pathways including efficacy of treatment and gaps in treatment guidelines, which made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, or percentage returning to clinics after initial treatment.

Introduction

Continued high transmission rates of sexually transmitted infections (STIs) that cause treatable lower genital tract discharge syndromes (GDS) are a major public health concern. This causes significant reproductive-health long-term sequelae[1-4] and frequently necessitates empirical therapy to minimise treatment delay, which often results in misdirected treatment, poor antimicrobial stewardship and the spread of antimicrobial resistance.[5,6] Among the common causes of GDS, there were 107,252 and 39,696 diagnoses of *Chlamydia trachomatis* (CT) and *Neisseria gonorrhoeae* (NG), respectively, made in English genitourinary medicine (GUM) services in 2015 [7], with smaller numbers of *Trichomonas vaginalis* (TV) and *Mycoplasma genitalium* (MG) diagnoses.

The decision to give empirical antimicrobial therapy in symptomatic patients is usually guided by results of immediate microscopy of genital discharge, but this has low sensitivity, missing up to half of NG/TV infections in women [8] and particularly poor specificity for predicting CT or MG. Accurate routine diagnosis, which requires laboratory-based nucleic acid amplification tests (NAATs), can take up to two weeks for results to be processed and most GUM services do not routinely conduct NAATs for MG or TV. Many patients are presumptively treated with either azithromycin or doxycycline, which are effective against CT but respectively cure only two-thirds and one-third of MG infections [9] and neither antimicrobial is effective against TV.[9]

Emerging technologies are being developed that allow rapid and accurate point-of-care tests (POCTs) for multiple sexually transmitted infections, solutions which could address these challenges and help improve patient and public health outcomes. However, health services are under increasing financial pressure, and implementing new technologies may be prohibitively costly for both providers and commissioners of healthcare. There is currently only one commercially available rapid NAAT for CT and NG, which has equivalent performance to laboratory NAATs (Cepheid GeneXpert).[10] Previous economic evaluations of NAAT POCTs for CT and NG indicate that they are likely to provide a cost-effective strategy for screening GUM attendees.[5,11] To inform decision making by groups developing multi-pathogen POCTs and clinics which would likely use such tests, we assessed costs, benefits and cost-effectiveness of three testing strategies using hypothetical NAAT POCTs for A) CT-NG, B) CT-NG-MG and C) CT-NG-MG-TV compared with laboratory-based CT-NG NAAT testing.

Methods

Creating a model structure

A decision tree model was constructed using Microsoft Excel (v.2016) to simulate a hypothetical cohort of people with symptoms of a lower genitourinary tract infection attending English GUM services. The base-case or primary analysis, using assumptions provided in Supplementary Table 1, compared complete pathway costs of three point-of-care (POC) strategies to the current practice of using microscopy plus a laboratory CT-NG NAAT. The POC strategies used microscopy plus a hypothetical POCT that provides results in 30 minutes for A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Microscopy was used in all POC strategies as it can detect other conditions and infections not covered by the POCTs, as well as diagnosing NG and TV. The strategies were chosen in response to recent developments in STI POCT technology, reflecting pathogen configurations and performance characteristics.[12,13]

Outcomes

Primary outcomes were total costs and benefits, measured by quality adjusted life years (QALYs) for each strategy and associated incremental cost-effectiveness ratios (ICERs, see equation) between each of the POC strategies and standard care (SC). The ICER provides information on the additional cost per unit of additional benefit between an option and the next less expensive alternative.

$$ICERx = \frac{Cost_{POCx} - Cost_{Current\ Practice}}{QALY_{POCx} - QALY_{Current\ Practice}}$$

Secondary outcomes assessed the wider health benefits and included inappropriate treatment of STIs (defined as unnecessary treatment of people with no STI plus incorrect treatment for people with an STI), onward transmission of the four STIs, pelvic inflammatory disease (PID), a serious complication of CT, NG and MG infections in women, time to cure and total GUM attendances.

Patient pathways

Three senior clinicians at St George's University Hospitals NHS Foundation Trust, London outlined current and hypothetical POC pathways for symptomatic patients (Figure 1). We assumed that treatment pathways did not vary by subgroup but that MSM had diagnostic tests from three anatomical sites (genital, pharyngeal, and rectal) at initial visit and MSW and women only had genital swabs. The model accounted for single or dual infections with NG, CT, MG and/or TV.

The cost of treating PID, was included in the model but other long-term complications associated with STI infection (e.g. infertility) and adverse drug events associated with treatment were not considered. The proportion of patients lost-to-follow-up (LTFU) was estimated. It was assumed that anyone remaining in follow-up consented to diagnostic testing and, if diagnosed, accepted treatment. The decision framework assumed that individuals had a maximum of three follow-up visits and then exited the model. Drug resistance was not considered. The time horizon for the model was 56 days. It was assumed that treatment was started on the day of diagnosis.

Epidemiology and clinical parameters

A short online survey, distributed to members of the British Association for Sexual Health and HIV (BASHH), was used to collect data on the percentage of patients attending GUM services that are symptomatic, the percentage of patients returning after initial visits, as well as MG testing protocols, as limited data were available from published literature. The survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK (Supplementary Table 2).

The total annual number of people attending English GUM services for STI testing was obtained from national surveillance data (GUMCAD 2015 data).[7] The number of GUM attendees who were symptomatic was then calculated using the median percentages reported in the clinician survey (50% of 1,181,574 for women; 40% of 647,661 for men-who-have-sex-with-women [MSW]; and 50% of 232,274 for men-who-have-sex-with-men [MSM]). The model simulated a total of 965,988 symptomatic attendees and by subgroup, 590,787 women, 259,064 MSW and 116,137 MSM. We assumed that hypothetical POCTs had similar sensitivity and specificity to the best performing currently available CT-NG POCTs.[10] The prevalence of CT, NG, MG and TV in GUM attendees (Table 1) was estimated using published studies and preliminary findings from the PRECISE Study [14], a study evaluating POCTs conducted by St George's, University of London and Public Health England.

Patient and public involvement

There was no involvement from patients or the public in the design of the evaluation.

Table 1. Epidemiological and clinical parameters

	Variable	Value			Distribution	Number			Comments, Reference
		Women	MSW	MSM		Women	MSW	MSM	
1	Initial clinic attendances	61%	27%	12%	Beta	590,787	259,064	116,137	Clinician survey results
2	CT infection	6.5%	23.3%	6.2%	Beta	38,401	60,362	7,200	W [14,15,16]; MSW [14,17]; MSM [14]
3	NG infection	0.7%	3.4%	38.1%	Beta	4,136	8,808	44,248	W [14,15,16]; MSW [14,17]; MSM [14]
4	MG infection	4.2%	12.3%	9.3%	Beta	24,813	31,865	10,801	W [14]; MSW [14,17]; MSW [14]
5	TV infection	4.4%	0.0%	0.0%	Beta	25,995	-	-	W [14,15,16,18]; MSW [14]; MSM estimate
6	CT NG co-infection	0.3%	2.2%	6.2%	Beta	1,772	5,699	7,200	W [14,15]; MSW, MSW [14]
7	CT MG co-infection	1.6%	2.8%	0.0%	Beta	9,453	7,254	-	W, MSW, MSW [14]
8	CT TV co-infection	0.2%	0.0%	0.0%	Beta	1,182	-	-	W [14,15,16]; MSW [14]; MSM estimate
9	NG MG co-infection	0.6%	0.6%	1.0%	Beta	3,545	1,554	1,161	W, MSW, MSM [14]
10	NG TV co-infection	0.4%	0.0%	0.0%	Beta	2,363	-	-	W [16]; MSW [14]; MSM estimate
11	MG TV co-infection	1.0%	0.0%	0.0%	Beta	5,908	-	-	W [14]; MSW, MSM estimate
12	Sensitivity of microscopy for detecting NG	40%	75%	75%	Uniform	Estimate based on published studies and clinical experience [8]			
13	Specificity of microscopy for detecting NG	100%	100%	100%	Uniform	Estimate based on published studies and clinical experience [8]			
14	Sensitivity of microscopy for detecting TV	50%	50%	50%	Uniform	Assumption based on clinical experience			
15	Specificity of microscopy for detecting TV	100%	100%	100%	Uniform	Assumption based on clinical experience			
16	Sensitivity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [19]			
17	Specificity of current NAAT test for CT-NG	97%	97%	97%	Uniform	Typical of best-performing tests currently used [19]			
18	Sensitivity of POCTs for CT/NG/MG/TV	95%	95%	95%	Uniform	Estimate based on tests currently available [10]			
19	Specificity of POCTs for CT/TV/MG	96%	96%	96%	Uniform	Estimate based on tests currently available [10]			
20	Specificity of POCTs for NG	98%	98%	98%	Uniform	Estimate based on tests currently available [10]			
21	CT infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [2]			
22	NG infection - probability of PID	16%	-	-	Normal	Estimate based on published studies [20]			
23	MG infection - probability of PID	4%	-	-	Normal	Estimate based on published studies [1]			
24	TV infection - probability of PID	0%	-	-	Normal	Assumption			
25	Microscopy at first attendance	84%	84%	84%	Uniform	Assumption, clinician survey results			
26	Presumptive treatment for CT	50%	50%	50%	Normal	Estimate based on clinical practice			
27	Proportion of MG infections cured by CT treatment	67%	67%	67%	Uniform	Estimate based on published studies [9]			

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with women*;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; NGU, non-gonococcal urethritis; PID, pelvic inflammatory disease; POCT, point-of-care test; TV, *Trichomonas vaginalis*.

Cost and utility parameters

All costs are given in 2015/16 prices (GB, £) and inflated to 2015/16 costs when based on previous estimates using the Hospital and Community Health Services (HCHS) Inflation Indices 2015.[21] The model considered two perspectives for costs: 1) costs to GUM services (micro-costing) associated with testing and management of NG/CT/MG/TV infections plus the cost of treating PID[22] and 2) NHS tariff reimbursements clinics would receive based on attendances (Table 2). Micro-costing was calculated by adapting an existing pathway model [23] and includes the cost of staff time, diagnostic kit, drugs, and other consumables. The tariff, an estimated average first and follow-up attendance cost used for commissioning and cross-charging[24], was estimated using the draft 2015/16 NHS tariff for first and follow-up GUM attendances. Fixed tariffs are not affected by how treatment is administered (oral/intramuscular) or the number of tests performed.

Table 2. Model input parameters: costs and utilities

Utilities			
Asymptomatic health state	1.00	Assume an otherwise healthy population	
Symptomatic health state	0.93		Sri, 2016 [25]
Waiting for diagnosis (symptomatic) health state	0.93	Assume the same as symptomatic	Sri, 2016 [25]
Treatment complete i.e. returned to asymptomatic state	1.00	Assume they return to asymptomatic	
PID diagnosis health state	0.80		Smith, 2008 [26]
Costs			
Tariff cost of initial visit plus treatment management	£141.00	Draft National Tariff Payment System: 2015/16	[24]
Initial clinic visit of symptomatic patient (micro-costing)	£103.71	Patient pathway adapted from a previous model	Adams, 2014 [a 23]
Management of STI (oral medication) on same day as assessment[b,c]	£29.19	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (oral medication) at return visit after results[b,c]	£31.32	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (medication via injection) on same day as assessment[c]	£43.79	Excludes drug cost	Adams, 2014 [a 23]
Management of STI (medication via injection) on return visit after results[c]	£44.32	Excludes drug cost and GC culture/typing lab processing	Adams, 2014 [a 23]
Standard CT/NG NAAT laboratory diagnostic test[d]	£13.17		Adams, 2014 [a 23]
POCT CT-NG[d]	£24.00	Assumption based on cost of products currently available	
POCT CT-NG-MG[d]	£29.00	Assumption based on cost of products currently available	
POCT CT-NG-MG-TV[d]	£34.00	Assumption based on cost of products currently available	
Tariff cost of return visit	£110.00	Draft National Tariff Payment System: 2015/16	[24]
Return clinic visit of symptomatic patient (micro-costing)	£83.25	Patient pathway adapted from a previous model	Adams, 2014 [a 23]
NG test of cure using standard NAAT laboratory test	£41.73		Adams, 2014 [a 23]
NG test of cure using POC A	£55.93		Adams, 2014 [a 23]
Cost of drug treatment (1st line) for CT	£1.20	Where 95% of patients receive 1g Azithromycin and 5% receive Doxycycline 100mg twice daily for 7 days	BNF, 2016 [27]
Cost of drug treatment (1st line) for NG	£5.95	Single dose Ceftriaxone 500mg deep intramuscular injection	BNF, 2016 [27]

		with single dose 1g Azithromycin	
Cost of drug treatment (1st line) for MG	£1.87	Doxycycline 100mg twice daily for 7 days	BNF, 2016 [27]
Cost of drug treatment (1st line) for TV	£0.36	Metronidazole 2g orally in a single dose	BNF, 2016 [27]
Cost associated with treatment of short-term PID	£180.52		Aghaizu, 2011 [22]

BNF, British National Formulary; CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* NAAT, nucleic acid amplification test*;* NG, *Neisseria gonorrhoea*; PID, pelvic inflammatory disease; POC, point-of-care; TV, *Trichomonas vaginalis*.

[a]Costs were inflated to 2015/16 costs using the Hospital and Community Health Services (HCHS) Inflation Indices 2015 produced by the Personal Social Services Research Unit.[21] No data were available for inflation from 2014/15 to 2015/16 so it was assumed to the same as between 2013/2014 and 2014/15. The UK consumer price index for health services shows similar annual growth in this sector from 2014 which validates this assumption.

[b]The cost of management of MG/TV infection is assumed to be the same as the costs associated with management of CT infection.

[c]These costs vary due to the difference in administrative staff time for patient registration if the patient is treated on the same day or on a subsequent visit.

[d]MSM have samples from three sites (urethral, rectal, pharyngeal) tested at the initial visit, whereas women and MSW typically have one sample taken.

Costs of implementing a change in practice, including training costs, were not considered. However, the unit costs used for staff time, which were considered, do incorporate the cost of training courses[21]. Costs associated with testing and treating other causes of lower genitourinary tract symptoms were not considered.

Utilities, measures of health-related quality of life, were used in calculating QALYs for the health states (asymptomatic, symptomatic, or awaiting test results) incorporated in the decision analytic framework (Table 2).

Scenario and sensitivity analysis

As well as the base-case analysis, 32 further scenarios were assessed deterministically i.e. where one or more key parameters were varied based on changing the assumption of that parameter(s) while holding all others at the base-case level (Supplementary Table 3). Scenarios included: higher STI prevalence; lower sensitivity and specificity of POCTs; differing microscopy use; cheaper POCTs; and different LTFU rates.

We performed a second order Monte Carlo probabilistic sensitivity analysis (PSA), consistent with best practice, to estimate base-case ICERs. We converted model inputs from discrete values to distributions. For cost inputs, we used a normal distribution and varied each cost by 20% for the standard deviation. We correlated costs of POCTs against the least expensive option to ensure test costs would change equivalently to the same degree with each simulation. For clinical parameters, we used beta and normal distributions for probabilities and uniform distributions for test performance. For utilities, normal distributions were used. The PSA included 5000 simulations and was performed using recommended procedures [28]. Probabilities that strategies were cost-effective at a range of willingness-to-pay (WTP) thresholds per QALY gained were presented in cost-effectiveness acceptability curves (CEACs). CEACs were generated for each subgroup and the total population. Threshold costs for POCTs at which POC strategies would become cost-saving were calculated to the nearest £0.25.

Results

Using micro-costing, the estimated annual cost of testing and managing CT, NG, MG and TV infections in 965,988 symptomatic individuals attending GUM was £113,058,655 using SC. This was the cheapest strategy to clinical services, with POC strategies A, B and C being increasingly expensive at £118,704,963 (5% increase), £124,842,003 (10.4% increase), and £125,313,136 (10.8% increase), respectively (Table 3). The opposite was true when using tariff costs, with SC being the most expensive for commissioners of sexual health care at £172,364,138, and POC strategy C being the least expensive, at £145,912,757 (Table 3).

Table 3. The costs, QALYs, average time to cure, inappropriate treatment and follow-up visits in SC and three POC strategies for symptomatic people attending GUM services

Sub-group	Strategy	Model Outcomes: Total costs (micro-costing)	Total costs (tariff)	Total QALYs	Average time to cure (days)	Inappropriate treatments	Mean number of visits/person	Return clinic visits[1]	Infected partners	PID cases in women
All	SC	£113,058,655	£172,364,138	146,532	4.3	258,395	1.3	328,726	1,876	176
	POC A	£118,704,963	£151,956,910	146,656	2.3	109,135	1.1	143,205	1,414	119
	POC B	£124,842,003	£152,288,107	146,626	2.1	200,865	1.2	146,216	1,451	64
	POC C	£125,313,136	£145,912,757	146,867	1.1	23,260	1.1	88,259	1,068	64
Women	SC	£65,122,097	£99,714,696	89,533	4.4	176,604	1.3	149,216	764	176
	POC A	£66,938,018	£88,960,028	89,584	2.4	76,322	1.1	51,446	524	119
	POC B	£69,853,645	£89,101,615	89,554	2.2	128,806	1.1	52,733	535	64
	POC C	£69,285,504	£85,008,982	89,718	1.1	1,607	1.0	15,528	260	64
MSW	SC	£29,572,989	£46,813,874	39,342	4.3	54,860	1.4	93,507	459	-
	POC A	£29,995,704	£40,111,202	39,389	2.1	20,957	1.1	32,574	343	-
	POC B	£31,717,478	£40,614,444	39,380	2.0	54,863	1.1	37,149	360	-
	POC C	£31,373,674	£38,724,875	39,443	1.2	13,218	1.1	19,971	285	-
MSM	SC	£18,363,569	£25,835,568	17,658	4.1	26,931	1.7	86,002	653	-
	POC A	£21,771,241	£22,885,680	17,684	2.3	11,855	1.5	59,185	546	-
	POC B	£23,270,880	£22,572,047	17,692	1.5	17,196	1.5	56,334	556	-
	POC C	£24,653,958	£22,178,900	17,706	1.2	8,436	1.5	52,760	524	-

[1]Return clinic visit for results and treatment, a test of cure (routine for NG) or because they remain symptomatic.

MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; PID, pelvic inflammatory disease; QALY, quality-adjusted life year.

Most of the total care pathway cost was the initial attendance cost. In SC, total pathway costs for women were £65,122,097, of this 93% (£60,432,050) were initial attendance costs. For POC strategy C, total pathway costs for women were £69,285,504, of which 98% (£68,041,383) were initial attendance costs.

POC strategy C provided most benefits to the full cohort. POC strategies A, B, and C increased QALYs by 124, 94 and 335, respectively compared to SC (Table 3 and Table 4). Time to cure was shorter and the number of total clinic visits, onward STI transmissions and PID cases were fewer in POC strategies than in SC. Compared to SC, POC strategy C resulted in 240,467 fewer clinic visits, 808 fewer onward STI transmissions, 235,135 averted inappropriate treatments and 112 fewer cases of PID.

Table 4. Cost differences for SC and POC strategies

Sub-group	Comparison	QALY difference	Micro-costing		Tariff costs	
			Cost difference	ICER (£/QALY gained)	Cost difference	ICER (£/QALY gained)
All	POC A vs SC	124	£5,646,309	£45,516	-£20,407,228	**Cost-Saving**
	POC B vs SC	94	£11,783,348	£125,197	-£20,076,031	**Cost-Saving**
	POC C vs SC	335	£12,254,482	£36,585	-£26,451,382	**Cost-Saving**
	POC B vs A	-30	£6,137,039	**Dominated**	£331,197	**Dominated**
	POC C vs B	241	£471,133	£1,956	-£6,375,350	**Cost-Saving**
Women	POC A vs SC	51	£1,815,921	£35,608	-£10,754,668	**Cost-Saving**
	POC B vs SC	21	£4,731,548	£222,568	-£10,613,081	**Cost-Saving**
	POC C vs SC	185	£4,163,407	£22,448	-£14,705,715	**Cost-Saving**
	POC B vs A	-30	£2,915,627	**Dominated**	£141,587	**Dominated**
	POC C vs B	164	-£568,141	**Cost-Saving**	-£4,092,634	**Cost-Saving**
MSW	POC A vs SC	47	£422,715	£9,005	-£6,702,672	**Cost-Saving**
	POC B vs SC	38	£2,144,488	£56,104	-£6,199,430	**Cost-Saving**
	POC C vs SC	102	£1,800,685	£17,724	-£8,088,999	**Cost-Saving**
	POC B vs A	-9	£1,721,773	**Dominated**	£503,242	**Dominated**
	POC C vs B	63	-£343,804	**Cost-Saving**	-£1,889,570	**Cost-Saving**
MSM	POC A vs SC	26	£3,407,672	£130,508	-£2,949,888	**Cost-Saving**
	POC B vs SC	35	£4,907,312	£141,683	-£3,263,521	**Cost-Saving**
	POC C vs SC	48	£6,290,390	£131,319	-£3,656,668	**Cost-Saving**
	POC B vs A	9	£1,499,639	£175,909	-£313,633	**Cost-Saving**
	POC C vs B	13	£1,383,078	£104,258	-£393,147	**Cost-Saving**

ICER, incremental cost-effectiveness ratios, MSW, men-who-have-sex-with-women; MSM, men-who-have-sex-with-men; POC, point-of-care; QALY, quality-adjusted life year.

ICERs associated with the base-case model are presented in Table 4. POC C highlights cost-effectiveness relative to other strategies yielding an ICER of £36,585 per QALY gained compared to SC when using micro-costing estimates. When incorporating NHS tariff costing, this represents a potential cost-savings of £26,451,382 relative to current practice.

CEACs are presented in Figure 2. Using micro-costing, for a WTP of £30,000/QALY, the upper threshold adopted by NICE [29], SC had a 50% probability of being cost-effective overall, a 17% probability for women, a 2% probability for MSW and a 99% probability for MSM, relative to the POC strategies. For a WTP of £25,000, POC C dominates, i.e. is cheaper and yields more benefits than the other POC strategies for the total cohort, women and MSW. For MSM, SC dominates all strategies across the thresholds examined. For MSW, POC A had 65% probability of being cost-effective at a WTP threshold of £10,000 per QALY gained.

Results of 32 scenario analyses are summarised in Supplementary Tables 4-7. The proportion of patients given presumptive treatment (scenarios 21-24) impacted costs hugely. When no presumptive treatment was given (scenario 21), the cost per QALY was £7,339 and £9,092 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC. When all patients without a diagnosis were presumptively treated for CT, MG or TV, according to which infections had been ruled out (scenario 24), POC strategies A and C were dominated by SC and POC strategy B cost £64,300/QALY more than SC.

When the utility score for being symptomatic was 10% less than base-case (scenario 25), cost per QALY was £15,627 more for POC strategy C than for SC. If microscopy was no longer used in POC strategies (scenario 13), cost per QALY was £16,204 and £29,594 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC.

If MG and TV prevalence were as high as the estimated prevalence in the US [30,31] (scenario 2), cost per QALY was £20,530 and £25,548 more than SC for POC strategies B and C respectively, whilst POC strategy A was dominated by SC. When POCTs were priced the same as the SC test (scenario 31), POC strategies B and C were cost-saving (using micro-costing).

Holding all other parameters constant using base-case assumptions, POC strategies would be cost-saving compared to SC, if POCTs cost £19.25, £13.50 and £21.00, respectively for POCTs A, B and C.

DISCUSSION

Principle findings

This study compared costs, benefits and cost-effectiveness of a laboratory-based CT-NG NAAT, with three POC strategies for: A) CT-NG; B) CT-NG-MG; C) CT-NG-MG-TV. Using our initial assumptions for the total population using the micro-costing approach to assess direct costs to health-care services, each POC strategy cost more than SC, but yielded additional benefits. The proportion of patients given presumptive treatment and the cost of the POCT kit both impacted the costs hugely. Results indicated that different strategies would be cost-effective for different patient sub-groups depending on the WTP threshold in place. POC strategy A was most cost-effective for MSW, POC strategy C for women, and SC for MSM. Whether using different testing strategies on different patient groups would be practical or acceptable was beyond the scope of this research and requires further investigation. Different results were obtained when tariff reimbursement costs were used, with POC strategy C costing the least and providing the most benefits.

Strengths and weaknesses

Our analysis has several strengths. This is the first study to compare the cost-effectiveness of the three different STI POC strategies with SC. Comparable and consistent methods were used to construct a model with inputs from multiple sources including published studies, published data (for costs), national surveillance data plus expert opinion. The model incorporated uncertainty in multiple input parameters by using a second order Monte Carlo PSA and numerous scenarios were assessed in sensitivity analysis.

Potential limitations should be considered. While it is thought that most UK clinicians follow British Association for Sexual Health and HIV (BASHH) guidelines for STI testing and treatment [9,19], there is diversity in the testing and management strategies employed to meet specific patient needs, both within and between clinics. This diversity, the paucity of published data on treatment pathways and gaps in treatment guidelines, made building a representative SC pathway problematic. There were few published data for some input parameters, for example, the percentage of patients who are presumptively treated without a microbiological result, the percentage returning to clinics after initial treatment and the percentage of patients attending with symptoms – all parameters which are likely to vary somewhat between clinics. We tried to overcome this using different scenario analysis and by collecting data using an online survey for GUM clinicians, albeit from a small sample size. Data from the survey showed high variation between clinics for some parameters. For example, the percentage of patients attending with symptoms ranged from 0% to 90%. There were few published data on

utilities and sexual behaviour whilst symptomatic with an STI, whilst waiting for test results and whilst being on treatment for an STI. Both qualitative and quantitative research is needed in this area to inform future health economic analyses and to understand preferences for and impact on patients of introducing POC testing.

The staffing and consumable cost data used in the model were average costs. In reality, different sites use staff of different grades and salaries to perform similar tasks and negotiate different costs for consumables, implying an inevitable variation in how cost effective the different strategies would be for different sites.

The costs associated with long-term complications of STIs were not considered [32]. This limitation means that the results are conservative, as the costs associated with SC are likely to be underestimated. However, the long-term benefits for a single round of testing were thought to be very low and to not have a major impact on the magnitude of results.

Comparing the results to other studies. POC pathways generated some cost savings, primarily because patients had fewer return visits. However, these did not outweigh the higher cost of the POCTs compared to laboratory-based NAATs when estimating total pathway costs. This means that if POC testing was used, there would be expected overall cost increases based on the analysis using the micro-costing approach. This differs from previous modelling, in which a CT-NG POCT was cost saving compared to laboratory testing [5]. In the Turner *et al.* model, the cost of a POC attendance was £6.95 cheaper than the cost of an SC attendance since the asymptomatic POC pathway was redesigned. In our model, the cost of attendance for a symptomatic patient was the same whether samples were sent to a laboratory or performed in clinic, since all symptomatic clinic attendees would require examination and microscopy.

Implications for public health, clinicians and people using GUM services

POC strategy C significantly decreased the numbers of inappropriate antibiotics given compared to SC, with over 235,000 fewer inappropriate treatments. Many of these treatments are likely to include azithromycin, which when inappropriately given can encourage spread of macrolide antibiotic resistance in MG infections [6]. POC strategy C also increased costs for health providers while decreasing tariff costs for commissioners, unless the “freed-up” capacity enabled by POC strategy C was used for STI screening appointments and initial assessments for symptomatic people. Although this would likely have a positive impact on public health, given GUM services in England face increasing pressure on their services with more than 2 million new attendances annually [7], while local authorities equally face fiscal pressures, this work demonstrates the potential tensions between different cost-consequences

for procurers and providers and public health benefits when considering implementation of novel health technologies. Whilst there are no triplex or quadruplex POC STI tests currently on the market, there is a least one multiplex STI POC assay in development.[33]

For people using GUM services, there are numerous benefits to POC testing compared to SC. People would need fewer clinic visits, saving them time and reducing LTFU and reducing their costs such as out-of-pocket expenses and productivity losses. Receiving a diagnosis at the initial attendance reduces anxiety compared to waiting for test results[25]. A negative result from a multi-pathogen POCT will support the development of clearer guidelines for clinicians, which could also reassure patients, particularly those with vague genital tract symptoms. Receiving effective treatment at initial attendance is likely to reduce the duration of symptoms and reproductive health sequelae.[1,2]

POCTs can also generate public health benefits from swifter diagnosis and treatment, for example, POC strategy C led to an estimated 43% fewer onward transmissions of STIs compared to SC. The ability to diagnose or rule out specific infections at first attendance enables accurate treatment and reduces inappropriate antibiotic use, crucial for good antibiotic stewardship, the economic benefits of which are substantial and well documented.[34]

Unanswered questions and future research

Although a rapid test for CT and NG is used in some GUM services, multi-pathogen configurations of CT-NG-MG-TV POCTs are not currently available. As such, likely pathways for POC strategies had to be designed based on expert opinion. Published audits of GUM patient pathways would be a useful addition to the literature. To reduce uncertainty in economic analyses around STIs, further evidence is also needed on underlying STI prevalence and the risk of onward STI transmission.

Patient pathways and testing protocols vary between sites and different sites see different proportions of people from the three sub-groups. As such, the costs of changing to a POC strategy will vary between sites as will the benefits and costs not considered in the model. Validated and easy to use computational tools for clinics and commissioners, which assess the economic impact of implementing any one of the POC strategies, using local population data, would increase understanding across stakeholders.

Conclusion

In conclusion, the results suggest that although potentially more expensive, a quadruplex test for CT-NG-MG-TV is more cost-effective than SC and the other testing strategies assessed, providing the most

additional benefits to patients. Cost implications are driven by the cost of POCTs and would vary somewhat in different geographical areas due to differences in the subgroup mix and the prevalence of the four STIs.

Footnotes

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Ethical approval: Not required.

All authors had full access to the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency: The senior author (STS) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported, that no important aspects of the study have been omitted, and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: no additional data available.

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Figure 1. Diagram showing simplified patient flow through the model

Standard care (SC): 50% of people not diagnosed with NG or TV by microscopy will be presumptively treated for CT. The treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs (i.e. not CT/NG/MG/TV). We assume this treatment is not effective against TV or NG. Incorrectly treated patients with NG infection will be diagnosed by NAAT, and return (minus those LTFU) to receive treatment. Other returning patients may receive presumptive treatment for MG and TV.

POC strategy A: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for MG and TV. We assume that this treatment is effective against CT, MG, TV, and against all other non-specific bacterial STIs. We assume that this treatment is not effective against NG. Patients not initially presumptively treated but who return to the clinic are then presumptively treated with MG and TV treatment.

POC strategy B: 50% of people not diagnosed by microscopy or POCT would be presumptively treated for TV. We assume this treatment is effective against TV, and against all other non-specific bacterial STIs. We assume this treatment is not effective against CT, MG, or NG.

POC strategy C: 100% of people who are not diagnosed by microscopy or POC would be presumptively treated using azithromycin. We assume this treatment is effective against CT, 67% of MG[9], and against all other non-specific bacterial STIs. We assume this treatment is not effective against TV or NG. If any treated patients return they will be categorised as 'investigate further'. The cost of the 'investigate further' is the cost of a standard return appointment which includes microscopy.

Figure 2. Cost-effectiveness acceptability curves (CEACs): point-of-care test (POCT) strategies vs standard care

Footnote: MSM, men who have sex with men; MSW men who have sex with women; W, women.

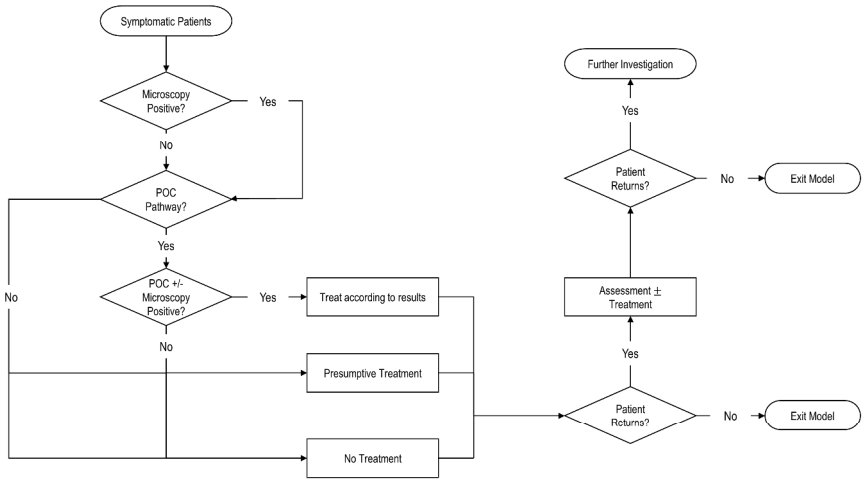

Figure 1.

338x190mm (300 x 300 DPI)

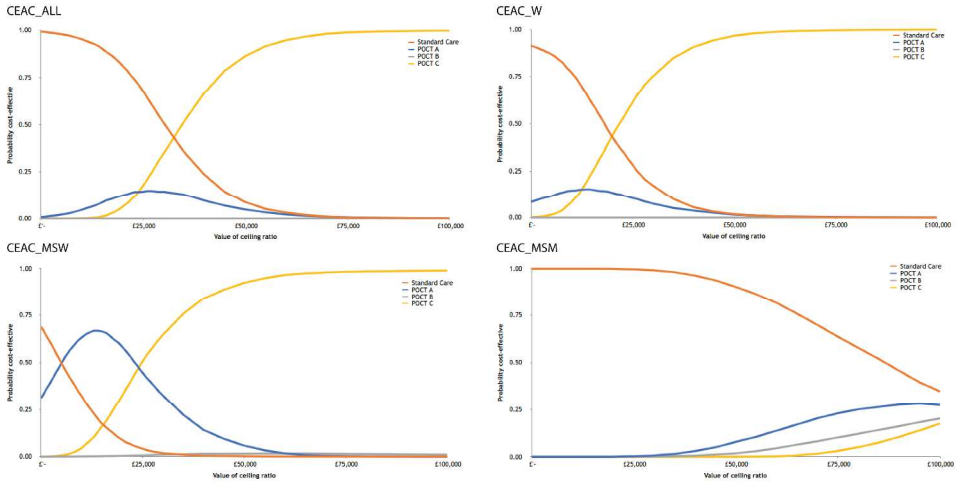

Figure 2 Cost-effectiveness acceptability curves (CEACs): point-of-care test (POCT) strategies vs standard care

596x309mm (300 x 300 DPI)

Supplementary Table 1. Key model assumptions

1	The decision framework assumes that after a maximum of 3 courses of treatment the individual would be cured. In standard care, this could take up to 56 days in total; therefore, the cycle length is one day and time horizon is 56 days.
2	Screening options will confirm diagnosis between 1-21 days; treatment options will last for a maximum of 7 days and 2 weekly cycles are imposed between treatment regimens. In current practice, we assume that individuals return on day 8 for test results in the base-case.
3	The sensitivity (true positive) and specificity (true negative) of POCT for each infection does not vary across the different POC strategies nor does it vary between patient sub-groups.
4	The model accounts for the impact of single and dual infections (CT, NG, TV and MG).
5	The proportion lost-to-follow-up varies by STI and gender due to the nature of symptoms and severity of individual STIs.
6	STI symptoms remain at the same clinical level of severity across the time horizon.
7	The model incorporates an 'Other Infection' category which includes all other infections that cause similar lower genital symptoms diagnosed initially (day 0) that rule out an initial diagnosis of CT/NG/MG/TV. These may include candida and allergic reactions. The proportion of the cohort who we assume fall into the "Other infection" category is 1 in 2 for women, 1 in 3 for MSW and 1 in 4 for MSM. We vary this assumption in scenario analysis.
8	Once results from screening options are confirmed those with a confirmed STI are treated and partners are made aware of the infection to access treatment.
9	Each index infection is assumed to have 1 partner for women and MSW and 2 partners for MSM per 7-day period; this assumption, as well as the number of sexual acts per week, is varied in sensitivity analysis.
10	In the absence of any data on changes in sexual behaviour following diagnosis with an STI, it is assumed sexual behaviour is not changed due to a diagnosis. This assumption affords the identification of all potential transmissions; however, taken at face value would be an overestimation of transmissions.
11	The model assumes STI transmission rates are constant over the duration of exposure.
12	The model assumes different treatment regimens for the different infections as informed by clinical guidance.
13	The model assumes the correct treatment for true CT/NG/MG/TV infection is 100% efficacious and ignores antibiotic resistant strains in NG and MG, thereby underestimating the total costs associated with STI infection.
14	The model does not include re-infections.
15	The model does not consider adverse events associated with treatment options.
16	The model does not consider long-term complications associated with STI infection.
17	The model limits sub-group analysis to women, MSW and MSM; treatment pathways do not vary by sub-group.

CT, *Chlamydia trachomatis;* MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; POCT, point of care test; STI, sexually transmitted infection, TV, *Trichomonas vaginalis*.

Supplementary Table 2. Summary of GUM clinician survey (October 2016) relevant to patient pathways

Survey question	Median	Lowest	Highest
Roughly how many patients attend your service every month?	1,700	80	6,000
What proportion of your patients are MSM?	10%	5%	100%
What proportion of your patients are MSW?	30%	0%	85%
What proportion of your patients are women?	53%	0%	60%
What proportion of MSM attend with a symptomatic lower genital tract infection?	50%	5%	90%
What proportion of MSW attend with a symptomatic lower genital tract infection?	40%	0%	90%
What proportion of women attend with a symptomatic lower genital tract infection?	50%	0%	80%
What proportion of symptomatic men have a swab that is sent for microscopy?	80%	25%	100%
What proportion of symptomatic men have a swab that is sent for culture?	60%	5%	100%
What proportion of symptomatic women have a swab that is sent for microscopy?	88%	0%	100%
What proportion of symptomatic women have a swab that is sent for culture?	58%	0%	100%
What proportion of MSM are tested for MG?	0%	0%	10%
What proportion of MSW are tested for MG?	0%	0%	20%
What proportion of women are tested for MG?	0%	0%	15%
Men who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	50%	5%	100%
Of those who return, what proportion receive further tests?	25%	0%	80%
Of those who return, what proportion receive presumptive treatment for another infection?	18%	5%	90%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	23%	0%	65%
Women who test negative for CT/NG			
What proportion return to your service for a follow-up appointment?	30%	0%	75%
Of those who return, what proportion receive further tests?	50%	10%	100%
Of those who return, what proportion receive presumptive treatment for another infection?	28%	5%	100%
What proportion are referred to / decide to attend another healthcare setting (e.g. GP)?	20%	0%	85%

CT, *Chlamydia trachomatis;* GP, General Practice; GUM, genitourinary medicine; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NG, *Neisseria gonorrhoea*; TV, *Trichomonas vaginalis*.

The online survey was completed by 23 GUM clinicians, 10 from London and 13 from elsewhere in the UK.

Supplementary Table 3. Scenarios assessed

1	Higher prevalence of MG and TV (double the current estimated prevalence)
2	Higher prevalence of MG and TV based on estimated prevalence in symptomatic patients in the US (MG: women 21.1%; men 19.3% and TV: women 25.9%; men 6.3%)
3	Increase proportion with 'Other infection' as follows: women: 66.6%, MSW: 50%, MSM: 50%
4	Decrease proportion with 'Other infection' as follows: women: 33.3%, MSW: 25%, MSM: 20%
5	100% increase the rate of LTFU
6	50% decrease the rate of LTFU
7	Specificity/sensitivity of POCT is 75%
8	Specificity/sensitivity of POCT is 80%
9	Specificity/sensitivity of POCT is 85%
10	Specificity/sensitivity of POCT is 85% for NG (but unaltered for CT, MG and TV)
11	Specificity/sensitivity of POCT is 85% for CT (but unaltered for NG, MG and TV)
12	Specificity/sensitivity of POCT is 85% for MG (but unaltered for CT, NG and TV)
13	No microscopy used in any testing strategy
14	50% people get microscopy
15	75% people get microscopy
16	100% people get microscopy
17	84% use of microscopy in current pathway and no use of microscopy in the POC strategy C
18	No microscopy for men (only) in POC strategy C
19	No microscopy for women (only) in POC strategy C
20	Use of microscopy in POC strategy C only after a negative test result
21	No presumptive treatment for CT
22	25% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
23	75% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
24	100% presumptive treatment for CT (of those not diagnosed with NG/TV in microscopy)
25	Use 10% reduction in symptomatic utility scores
26	Excluding the cost of PID (as not all PID will be treated in the GUM service)
27	Inclusion of the drug costs for doxycycline as treatment for anyone NG/CT/MG/TV negative
28	POCT CT-NG costs the same as laboratory based NAAT
29	POCT CT-NG-MG cost the same as laboratory based NAAT
30	POCT CT-NG-MG-TV costs the same as laboratory based NAAT
31	All POCTs cost the same as laboratory based NAAT
32	All POCTs cost £2 less than in base-case

CT, *Chlamydia trachomatis;* GUM, genitourinary medicine; LTFU, lost-to-follow-up; MG, *Mycoplasma genitalium;* MSM, men-who-have-sex-with-men; MSW, men-who-have-sex-with-women; NAAT, nucleic acid amplification test; NG, *Neisseria gonorrhoea*; POC, point-of-care; POCT, point-of-care test; TV, *Trichomonas vaginalis;* US, United States (of America).

Supplementary Table 4. Cost-effectiveness comparison for scenario analyses using micro-costings - All

All	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£ 17,389	£ 41,381	£7,153	Dominated
2	Dominated	£ 20,530	£ 56,548	£8,228	Dominated
3	£ 224,378	£ 22,979	£ 69,517	£12,300	Dominated
4	Dominated	£ 15,818	£ 24,163	£7,107	£6,353
5	Dominated	£ 19,691	£ 35,749	£9,196	Dominated
6	Dominated	£ 19,363	£ 36,221	£9,196	Dominated
7	Dominated	£ 21,665	£ 82,996	£8,870	Dominated
8	Dominated	£ 21,220	£ 69,561	£8,865	Dominated
9	Dominated	£ 20,735	£ 57,596	£8,891	Dominated
10	Dominated	£ 19,726	£ 39,414	£8,986	Dominated
11	Dominated	£ 20,431	£ 43,314	£8,265	Dominated
12	Dominated	£ 19,647	£ 40,917	£10,034	Dominated
13	Dominated	£ 16,204	£ 29,594	£8,703	Dominated
14	Dominated	£ 18,061	£ 33,245	£8,989	Dominated
15	Dominated	£ 19,088	£ 35,286	£9,140	Dominated
16	Dominated	£ 20,191	£ 37,493	£9,297	Dominated
17	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
18	Dominated	£ 19,476	£ 28,889	£9,196	£7,998
19	Dominated	£ 19,476	£ 23,566	£9,196	£14,332
20	Dominated	£ 19,476	£ 16,053	£9,196	£23,574
21	Dominated	£7,339	£9,092	£3,792	£2,859
22	Dominated	£ 12,055	£ 18,039	£5,910	£552
23	Dominated	£ 32,870	£ 91,155	£14,987	Dominated
24	Dominated	£ 64,300	Dominated	£27,913	Dominated
25	£ 46,988	£ 17,310	£ 15,627	£10,948	£4,554
26	Dominated	£ 19,510	£ 36,120	£9,211	Dominated
27	Dominated	£ 19,476	£ 37,040	£9,196	Dominated
28	£ 43,475	£ 19,476	£ 36,060	£21,718	Dominated
29	Dominated	Cost-saving	£ 36,060	Cost-saving	Dominated
30	Dominated	£ 19,476	Cost-saving	£9,196	£74,924
31	£ 43,475	Cost-saving	Cost-saving	£218	£20,817
32	Dominated	£ 16,667	£ 31,058	£9,196	Dominated

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 5. Cost-effectiveness comparison for scenario analyses using micro-costings - Women

Women	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	Dominated	£8,843	£ 25,961	£4,199	Dominated
2	Dominated	£8,932	£ 52,744	£3,587	Dominated
3	Dominated	£ 13,611	£ 46,391	£7,257	Dominated
4	Dominated	£6,915	£ 10,406	£3,249	£5,070
5	Dominated	£9,013	£ 21,182	£4,368	£1,662
6	Dominated	£8,827	£ 22,264	£4,368	£1,662
7	Dominated	£8,012	£ 48,866	£3,769	£180
8	Dominated	£8,124	£ 41,683	£3,848	£350
9	Dominated	£8,279	£ 34,918	£3,954	£588
10	Dominated	£8,732	£ 22,995	£4,249	£1,398
11	Dominated	£8,597	£ 25,567	£3,827	£1,542
12	Dominated	£8,630	£ 24,992	£4,563	£1,556
13	Dominated	£8,344	£ 19,947	£4,136	£2,008
14	Dominated	£8,661	£ 21,070	£4,271	£1,808
15	Dominated	£8,829	£ 21,658	£4,341	£1,702
16	Dominated	£9,004	£ 22,264	£4,415	£1,590
17	Dominated	£8,891	Cost-saving	£4,368	£14,160
18	Dominated	£8,891	£ 21,874	£4,368	£1,662
19	Dominated	£8,891	Cost-saving	£4,368	£14,160
20	Dominated	£8,891	Cost-saving	£4,368	£14,160
21	Dominated	£4,042	£1,678	£1,846	£6,724
22	Dominated	£6,046	£8,172	£2,856	£4,238
23	Dominated	£ 13,250	£ 69,756	£6,878	Dominated
24	Dominated	£ 20,769	Dominated	£11,866	Dominated
25	Dominated	£9,256	£9,545	£5,197	£7,575
26	Dominated	£8,930	£ 21,981	£4,383	£1,662
27	Dominated	£8,891	£ 23,150	£4,368	£951
28	Dominated	£8,891	£ 21,874	£6,916	£1,662
29	Dominated	£ 143	£ 21,874	Cost-saving	Dominated
30	Dominated	£8,891	Cost-saving	£4,368	£23,924
31	Dominated	£ 143	Cost-saving	Cost-saving	£10,304
32	Dominated	£6,671	£ 15,666	£4,368	£1,662

POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 6. Cost-effectiveness comparison for scenario analyses using micro-costings - MSW

MSW	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£12,263	£22,566	£21,976	£39,978	£20,481
2	£6,136	£21,655	£20,324	£70,648	£17,318
3	£6,705	£20,051	£33,219	£53,907	£163,024
4	£10,163	£104,518	£12,897	Dominated	Cost-saving
5	£12,052	£61,168	£19,205	Dominated	Cost-saving
6	£7,525	£53,665	£16,992	Dominated	Cost-saving
7	£265,801	Dominated	£64,478	Dominated	Cost-saving
8	£100,276	Dominated	£50,420	Dominated	Cost-saving
9	£49,716	Dominated	£38,304	Dominated	Cost-saving
10	£10,139	£60,983	£19,061	Dominated	Cost-saving
11	£44,559	£243,310	£28,123	Dominated	Cost-saving
12	£9,005	£109,035	£22,985	Dominated	Cost-saving
13	£5,013	£44,501	£15,654	Dominated	Cost-saving
14	£7,253	£50,948	£16,857	Dominated	Cost-saving
15	£8,521	£54,669	£17,490	Dominated	Cost-saving
16	£9,906	£58,793	£18,147	Dominated	Cost-saving
17	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
18	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
19	£9,005	£56,104	£17,724	Dominated	Cost-saving
20	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
21	Cost-saving	Cost-saving	Cost-saving	£20,002	£929
22	Cost-saving	£9,663	£4,599	£121,977	Cost-saving
23	£80,063	Dominated	£62,970	Dominated	Cost-saving
24	Dominated	Dominated	Dominated	Dominated	Cost-saving
25	£3,870	£24,112	£7,614	Dominated	Cost-saving
26	£9,005	£56,104	£17,724	Dominated	Cost-saving
27	£9,005	£56,104	£18,456	Dominated	Cost-saving
28	Cost-saving	£56,104	£17,724	Dominated	Cost-saving
29	£9,005	£2,696	£17,724	£36,667	£26,789
30	£9,005	£56,104	Cost-saving	Dominated	Cost-saving
31	Cost-saving	£2,696	Cost-saving	Dominated	Cost-saving
32	Cost-saving	£42,549	£12,624	Dominated	Cost-saving

MSW, Men-who-have-sex-with-women; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

Supplementary Table 7. Cost-effectiveness comparisons for scenario analyses using micro-costings - MSM

MSM	Cost-effectiveness comparison (£/QALY gained)				
Scenario	POC A vs SC	POC B vs SC	POC C vs SC	POC B vs POC A	POC C vs POC B
1	£137,378	£95,423	£139,260	£49,813	Dominated
2	£119,952	£83,250	£145,988	£42,999	Dominated
3	£91,163	£83,961	£332,964	£71,307	Dominated
4	£140,882	£160,599	£115,724	£235,703	£52,018
5	£135,796	£145,798	£134,186	£175,909	£104,258
6	£127,894	£139,636	£1,044	£175,909	£1,317
7	£833,775	£2,053,305	£350,136	Dominated	£78,956
8	£425,499	£591,462	£268,835	£4,264,237	£84,090
9	£271,627	£324,923	£211,896	£579,296	£89,914
10	£191,294	£191,613	£173,306	£192,369	£130,727
11	£168,341	£173,675	£143,342	£187,785	£85,861
12	£130,508	£167,524	£141,202	£406,528	£88,559
13	£47,590	£64,826	£74,079	£189,798	£126,208
14	£80,744	£98,423	£101,384	£181,298	£112,461
15	£113,144	£127,453	£122,040	£177,307	£106,349
16	£175,783	£175,089	£151,216	£173,474	£100,673
17	£130,508	£141,683	£131,189	£175,909	£83,111
18	£130,508	£141,683	£131,189	£175,909	£83,111
19	£130,508	£141,683	£131,319	£175,909	£104,258
20	£130,508	£141,683	£131,189	£175,909	£83,111
21	£60,065	£77,460	£84,981	£164,890	£116,909
22	£85,266	£101,948	£103,897	£170,152	£110,577
23	£235,470	£217,337	£174,644	£182,233	£97,951
24	£747,941	£417,789	£253,365	£189,212	£91,656
25	£56,093	£60,884	£56,420	£75,544	£44,773
26	£130,508	£141,683	£131,319	£175,909	£104,258
27	£130,508	£141,683	£131,648	£175,909	£105,447
28	Cost-saving	£141,683	£131,319	£869,045	£104,258
29	£130,508	Cost-saving	£131,319	Cost-saving	£681,008
30	£130,508	£141,683	Cost-saving	£175,909	Cost-saving
31	Cost-saving	Cost-saving	Cost-saving	Cost-saving	Cost-saving
32	£130,508	£141,683	£131,319	£175,909	£104,258

MSM, Men-who-have-sex-with-men; POCT, point-of-care test strategy; QALY, quality-adjusted life year.

CHEERS Checklist
Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards (CHEERS)—Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force,* provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	P1, L1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	P2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.	P4, L20-30
Methods			
Target population and subgroups	4	Describe characteristics of the base case population and subgroups analysed, including why they were chosen.	P5
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	P5
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	P9, L3
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	P5
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	P2, P9
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	P9
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.	P5
Measurement of effectiveness	11a	*Single study-based estimates:* Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	N/A

			N/A
	11b	*Synthesis-based estimates:* Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.	P5-6
Measurement and valuation of preference based outcomes	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	N/A
Estimating resources and costs	13a	*Single study-based economic evaluation:* Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	N/A
	13b	*Model-based economic evaluation:* Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.	P9,10,11
Currency, price date, and conversion	14	Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.	P9,10,11
Choice of model	15	Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.	Figure 1
Assumptions	16	Describe all structural or other assumptions underpinning the decision-analytical model.	SuppTable 1
Analytical methods	17	Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.	P12
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.	Table 1
Incremental costs and outcomes	19	For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.	Table 3 & 4
Characterising uncertainty	20a	*Single study-based economic evaluation:* Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	N/A

		of methodological assumptions (such as discount rate, study perspective).	N/A
	20b	*Model-based economic evaluation:* Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	P18, 19
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.	P18
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	P19
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	P20
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	P20

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp

The citation for the CHEERS Task Force Report is:
Husereau D, Drummond M, Petrou S, et al. Consolidated health economic evaluation reporting standards (CHEERS)—Explanation and elaboration: A report of the ISPOR health economic evaluations publication guidelines good reporting practices task force. Value Health 2013;16:231-50.