

APPENDIX

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

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

Calculation of overtreatment

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

Table A2 Calculation of overtreatment

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

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

Table A3 Additional scenario analyses

Scenario		BASELINE	6 Higher prevalence	7 Lower proportion treated presumptively	8 Higher proportion treated presumptively	9 Long time to treat	10 Lower QALYs	11 Lower proportion symptomatic	12 Higher proportion symptomatic	13 Increase relative risk of symptomatics	14 No presumptive treatment	15 Increase relative risk of symptomatics presumptive treatment
		CT=3.6%, 7.4% NG=2.5%, 0.9% Sympt=5%, 8%	Double baseline prevalence		100% presumptive treatment	Rx time=21 days	25% lower symptoms/positive diagnosis/complications	15%, 20%				
Standard Care	Cost	£15,627,887	£20,833,130	£12,865,267	£15,651,162	£15,654,528	£15,627,887	£10,497,195	£27,415,395	£15,569,091	£11,396,310	£11,397,425
	QALY	84,012	83,966	84,027	84,012	84,011	83,885	84,038	83,971	84,013	84,056	84,056
	Transmissions	7,561	4,882	6,319	7,648	3,383	7,561	7,981	7,256	7,582	8,439	8,439
	PID	223	21	221	223	89	223	225	219	242	90	200
Overtreatment	95,382	5,605	71,524	95,382	95,382	95,382	95,382	40,073	183,161	93,628	81	71
Point of Care	Cost	£103,873,872	£108,716,604	£103,873,872	£103,873,872	£103,873,872	£103,873,872	£98,998,214	£110,679,468	£103,873,668	£103,874,165	£103,874,164
	QALY	84,059	84,008	84,059	84,059	84,059	83,986	84,059	84,059	84,059	84,059	84,059
	Transmissions	7,561	4,882	6,319	7,648	3,383	7,561	7,981	7,256	7,582	8,439	8,439
	PID	223	21	221	223	89	223	225	219	242	90	200
Overtreatment	95,382	5,605	71,524	95,382	95,382	95,382	95,382	40,073	183,161	93,628	81	71
Difference (POC-SC)	Cost	-£1,754,015	-£2,116,526	-£8,991,395	-£1,777,290	-£1,780,656	-£1,754,015	-£8,498,981	-£6,735,928	-£1,695,422	-£7,522,146	-£7,523,261
	QALY	46	41	32	47	47	102	21	88	46	2	2
	Transmissions	-17,561	-34,882	-16,319	-17,648	-33,383	-17,561	-17,981	-17,256	-17,582	-18,439	-18,439
	PID	-189	-353	-187	-189	-354	-189	-190	-186	-209	-154	-164
Overtreatment	-95,382	-85,605	-71,524	-95,382	-95,382	-95,382	-40,073	-183,161	-93,628	-81	-71	

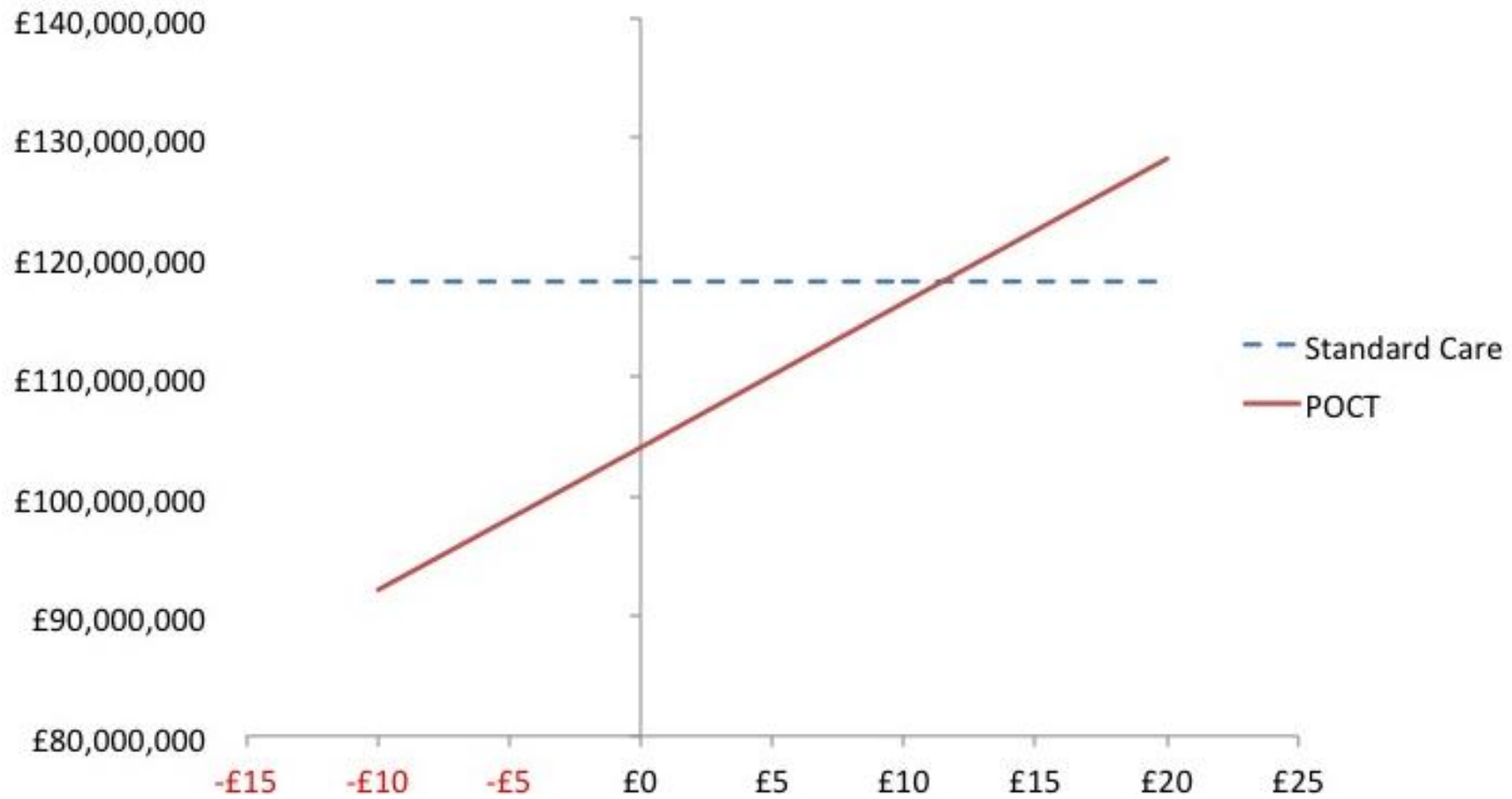
Table A4 Partner pathway results for those currently treated epidemiologically as contacts of infected individuals.

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

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

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

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



Further description and discussion of presumptive and epidemiological treatment

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

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

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

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

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

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

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

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

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

Ineffective or sub-optimal treatment

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

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

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