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## **Cost-effectiveness of abandoning microscopy of urethral smears for asymptomatic non-chlamydial non-gonococcal urethritis in men in the UK**

### **Appendix 1**

#### Model Assumptions

All assumptions were confirmed and agreed with clinical experts within the team before the analysis was carried out. The following assumptions were made:

- Symptomatic patients are index patients with symptoms due to their underlying infection
- An HIV and syphilis blood test is administered 5% of the time in a GP setting (expert opinion)
- All patients in all settings receive a NAAT test for Chlamydia and Gonorrhoea
- A GP consultation takes 11.7 minutes which is the average for a surgery consultation (1)
- All patients in a GUM setting are seen 50% by a doctor and 50% by a band 7 (clinical specialist) nurse (Expert opinion)
- Partner notification is conducted with all symptomatic patients in a GUM setting by a band 7 nurse and this takes 12 minutes (2)
- No formal partner notification is conducted in a GP setting, with just brief 'words of advice' to encourage sexual partners to attend for testing and treatment being given which was not considered in this economic analysis
- Taking case history takes 5 minutes for asymptomatic patients in a GUM setting (Expert opinion – study team)
- Taking case history takes 10 minutes for symptomatic patients in a GUM setting (Expert opinion – study team)
- Examination of a female patient in a GUM setting takes 10 minutes (Expert opinion – study team)
- Examination of a male patient in a GUM setting takes 5 minutes (Expert opinion – study team)
- A single dose (1g) of azithromycin is given as treatment for NGNCU
- For all microscopy tests implemented it takes 10 minutes for a lab technician to obtain and report the results of the microscopy test (Expert opinion – study team)

- The treatment for PID considered in this study is intramuscular ceftriaxone 500mg single dose followed by oral Doxycycline 100 mg twice daily plus metronidazole 400mg twice daily for 14 days (3)
- All notified partners are assessed and presumptively treated in a GUM location and are asymptomatic (Expert opinion – study team)
- The cost of PID does not include the cost of assisted reproduction

#### Resource Use and Costs

The ranges for the costs were taken by firstly describing the variation in the length of time of the procedures through the use of a gamma distribution with the mean = standard error and taking the values at the 5% and 95% points (with the minimum consultation time set to 2 minutes). And then secondly where more than one member of staff is assumed to contribute to an examination the cheapest and more expensive members of staff would be assumed to conduct the examination for the low and upper values of the range respectively. Some costs are unit costs and as such have a fixed cost that does not vary.

Resource	Unit Cost	Range	Source
NAAT nucleic acid amplification test - "NAAT"	£9.27		£7.35 for a swab 2005 prices = cost of hands-on time + equipment and consumables cost per test [7]
HIV test	£8.47		Rapid test kit £5-£11 (13) (mid-point 2014/15 prices)
Syphilis test	£2		EIA Assume £2
Microscopy test (including staff costs)	£7		NHS reference costs 2014-15 HRG DAPS07 Microscopy
Lab Technician (10 minutes of staff time) to obtain and report results of microscopy test	£3.33	£0.67-£10	Clinical support worker nursing (community) £20 /hr (12) <a href="#">(Range 2min-30min)</a>
Staff time to give results for Microscopy at Genitourinary Medicine (5 minutes of staff time)	£6.75	£2.70-£20.25	5 minutes with Nurse advanced (£81 / hour) (12) <a href="#">(Range 2min – 15min)</a>
Azithromycin – drug cost for treatment	£6.44		BNF accessed 21st June 2016 250mg tablets 4-tab pack £6.44
General Practice visit (excluding testing costs)	£44	£7.50-£131.25	GP includes direct care staff costs (with qualification costs, £225/hr) Assume 11.7 min surgery consultation (12) <a href="#">(Range 2min-35min)</a>
Cost of Partner Notification in GUM setting – administered to all symptomatic patients	£16.2	£2.70-£48.60	12 minutes with Nurse Advanced (£81 / hour) (12) <a href="#">(Range 2min-36min)</a>
Partner Notification leaflets + condoms given out during partner notification	£1.00		Assumed cost
Asymptomatic female at GUM clinic - Case history + Exam (13 minutes of staff time) 50% with Band 7 nurse and 50% with GP	£27.30	£2.70-£111.15	Nurse advanced cost per hour in surgery excluding qualification costs (£81 / hour) + GP excluding direct care staff costs (without qualification costs) (£171 / hr patient contact) (12) <a href="#">(Range 2min – 53min)</a>
Symptomatic female at GUM clinic - Case history + Exam (18 minutes of staff time) 50% with Band 7 nurse and 50% with GP	£37.80	£1.35-£153.90	"" <a href="#">Range (2min-73min)</a>
Asymptomatic male at GUM clinic – Case history + Exam (10 minutes of staff time) 50% with Band 7 nurse and 50% with GP	£21	£2.70-£85.50	"" <a href="#">Range (2min-41min)</a>
Symptomatic male at GUM – Case history + Exam (15 minutes of staff time) 50% with Band 7 nurse and 50% with GP	£31.50	£2.70-£128.25	"" <a href="#">Range (2min-62min)</a>
Cost of treating PID	£14.52		Ceftriaxone 500mg single dose, (1g vial) £9.58; Doxycycline 100mg twice daily for 14 days 100mg 8-cap pack £0.55 x 4; and Metronidazole 400mg twice daily for 14 days, 21-tab pack £1.37 x 2
Ectopic Pregnancy	£436.48		MA18C medical termination of pregnancy – less than 14 weeks gestation, elective inpatient NHS ref costs 14-15
Infertility	£587.02		£428 in 2003 (14) Using the hospital and community health services (HCHS) index to inflate to 2014 price 2002/03 index = 213.7 2014/15 index = 293.1. One cycle of treatment assumed per case

**Table 2:** Resource use and costs

## Sensitivity Analysis

Two scenarios were examined to assess the impact of increasing and decreasing the costs applied in the study as follows:

- Minimize costs - All costs are set to a minimum by taking the lowest realistic length of time for all consultations in all settings (minimum 2 minutes). Where two staff members undertake a consultation at baseline, in this scenario only the lowest paid is assumed to carry out the consultation.
- Maximize costs – All costs are set to a maximum by taking the highest realistic length of time for each consultation. Where two staff members undertake a consultation at baseline, the highest paid of the staff members is assumed to carry out the entire consultation.

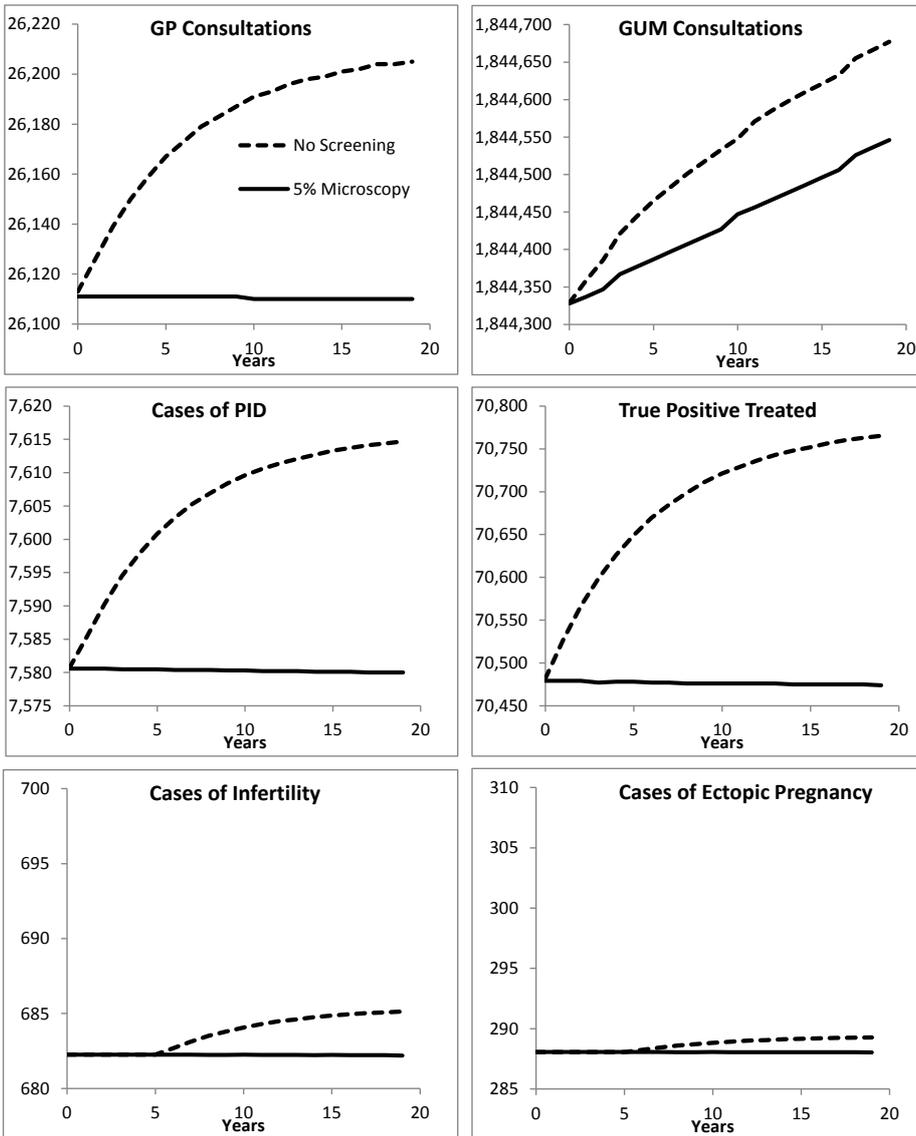
In addition, three further outputs from the transmission model were also analysed to assess their impact on the model results. These were median results (Median) from the 215 parameter sets of the transmission dynamic model, and the upper (Upper) and lower (Lower) results from the 95% range of values.

Further one-way sensitivity analysis of key parameters was also investigated, with particular attention paid to parameters that were estimated through expert opinion. In addition the time horizon was also varied to show its impact on conclusions drawn from the model.

## Appendix II

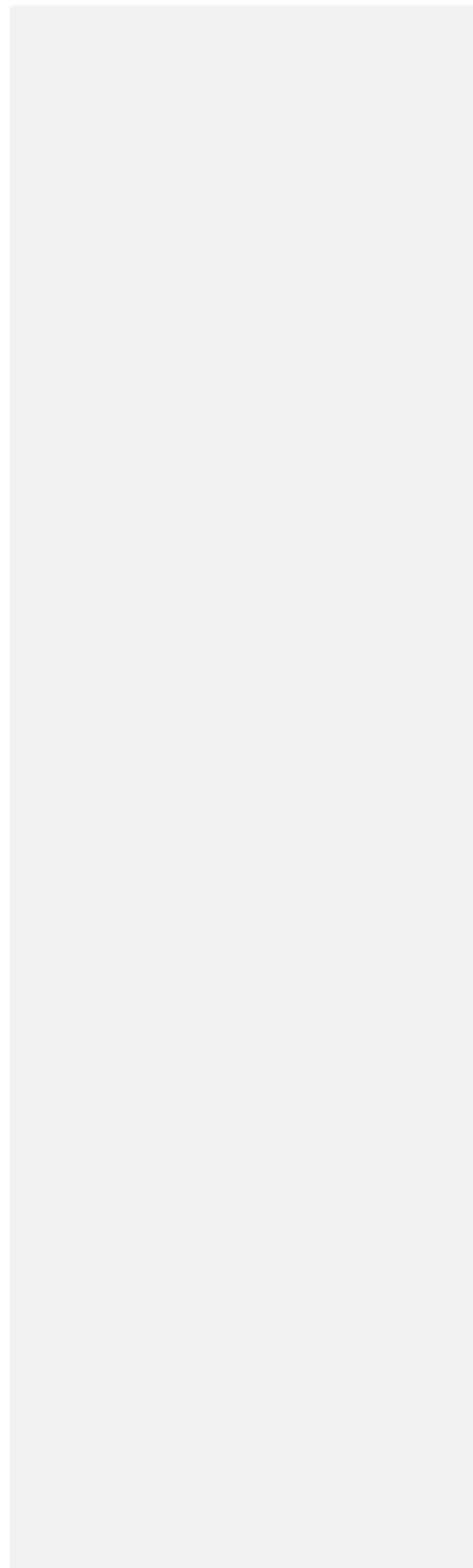
### Mean Output from the Transmission Model

The following graphs provide a summary of the mean output from the transmission model which was utilized in this economic analysis at baseline for each of the two scenarios considered in this study.



**Figure A1:** Output from the transmission model used in the baseline economic analysis with variation in the testing strategy

It can be seen from Figure A1 that increasing the coverage of microscopy leads to an increase in the annual number of consultations in both GP and GUM locations. Moreover this increasing coverage also has a positive impact on reducing the number of cases of PID averted, the number of cases of infertility, and the number of cases of ectopic pregnancy. It also lowers the number of true positive patients with NGNCU being treated, due to its impact on onward transmission.



### Appendix III

#### Sensitivity Analysis -Results

The two scenarios examined in this study consider the impact of reducing and increasing multiple cost parameters to see their cumulative impact on the results obtained from the model.

<b>Parameter</b>	<b>ICER</b>	<b>ICER</b>
	<b>/PID averted</b>	<b>/MOA</b>
Maximize Costs	£34,000	£108,500
Minimize Costs	£9,600	£30,500

**Table A1:** Sensitivity analysis results for the alternative cost scenarios for No Microscopy vs. 5% Microscopy

As shown in Table A1, by varying the costs applied in the model it can be seen that for No Microscopy vs. 5% Microscopy the ICER for PID averted ranges from £9,600-£30,500 while the ICER for MOA ranges from £34,000-£108,500.

#### Variations in Transmission Model Output

The sensitivity analysis above has only considered uncertainty in the parameters used in the economic evaluation and has until now only adopted mean values from the infectious disease model. In order to examine how uncertainty in the output from the infectious disease model affects the conclusions drawn from the economic model, a further series of outputs from the infectious disease model were also considered, these being the median results obtained from the 215 parameter sets along with upper and lower limits informed by the 95% ranges.

<b>Dynamic transmission model</b>	<b>ICER</b>
<b>output scenario</b>	<b>No Microscopy vs. 5% Microscopy</b>
	<b>Cost / Case of PID averted; Cost/ MOA</b>
Mean	£15,700; £49,900
Median	£39,100; £124,400
Upper	£30,400; £95,400
Lower	£10,800; £34,600

**Table A2:** ICER values for the outcomes of case of PID averted and major adverse event averted with variation in the infectious disease model output

By examining that impact of various plausible outputs from the TDM (Table A2), it can be seen that the range of ICER values for No Microscopy vs. 5% Microscopy for the outcome measure of case of PID averted treated range from £10,800-£39,100 and for major outcome averted range from £34,600-£124,400.

#### Time Horizon

In order to investigate the impact of the time horizon on the model results, the results from a range of alternatives are considered here. Table A3 shows the impact of varying the time horizon on the cost, the number of PID cases averted, and MOA. It can be seen that in the short term limited microscopy is least cost effective, but the intervention becomes more cost-effective the further the time horizon is extended into the future.

Time Horizon	Scenario	Cost	Cases of PID	ICER (PID case averted)	Major Outcomes	ICER (/MOA)
5 years	No Microscopy	£395,381,000	35,500		11,900	
	5% Microscopy	£397,087,000	35,400	£41,000	11,900	£146,600
10 years	No Microscopy	£728,324,000	65,400		22,000	
	5% Microscopy	£731,433,000	65,300	£22,600	22,000	£76,800
15 years	No Microscopy	£1,008,676,000	90,600		30,500	
	5% Microscopy	£1,012,950,000	90,400	£17,800	30,400	£57,900
20 years	No Microscopy	£1,244,736,000	111,800		37,600	
	5% Microscopy	£1,249,986,000	111,500	£15,700	37,500	£49,900

**Table A3:** Deterministic results for each of the outcomes considered in this study with variation in the time horizon

#### One-way sensitivity Analysis

The parameters, proportion of PID cases that are symptomatic and the delay from PID to infertility / ectopic pregnancy manifest were informed by expert opinion in this study, and as such it is necessary to examine their impact on the results from the model. Neither of these parameters had an impact on the ICER values for the main outcome measure used in this study, namely, cases of PID averted, but can impact on MOA. This is shown in the table A4.

<b>Parameter</b>	<b>ICER /PID averted</b>	<b>ICER /MOA</b>
Delay from PID to Infertility / ectopic pregnancy		
1 years	£15,600	£47,200
2	£15,700	£47,900
3	£15,700	£48,600
5 (Baseline)	£15,700	£49,900
10	£15,700	£52,900
15	£15,700	£55,300
Proportion of PID cases that are symptomatic		
20%	£15,700	£96,900
40	£15,700	£63,600
56 (Baseline)	£15,700	£49,900
60	£15,700	£47,400
80	£15,700	£37,700
100	£15,700	£31,300

**Table A4:** Results from one-way sensitivity analysis for No Microscopy vs. 5% Microscopy

It can be seen that varying these parameters has very little impact on the ICER values for the primary outcome measure of cost / case of PID averted. In the case of MOA, for the parameter estimated time to infertility / ectopic pregnancy manifest, as this is increased, 5% Microscopy becomes increasingly less cost-effective. For the proportion of PID cases that are symptomatic, increasing this value leads to the ICER values for MOA to decrease, thus making 5% Microscopy more cost-effective.

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