Screening and treatment for reducing the prevalence of *Chlamydia trachomatis*

Matrix Insight, in collaboration with Imperial College London, Kings College London and Bazian Ltd, were commissioned by Health England to undertake a research study to develop and apply a method for prioritising investments in preventative interventions for England. Seventeen preventative health interventions were included in the study. Each intervention was evaluated in terms of the following criteria: reach; inequality score; cost-effectiveness; and affordability. This report presents the results of the analysis for one of the interventions: screening and treatment for reducing the prevalence of *Chlamydia trachomatis*. The full report of the study is available from the ***H.E.L.P.*** website.

Summary

Description of the intervention
Opportunistic screening for *Chlamydia trachomatis* in women attending antenatal, abortion, colposcopy and family planning clinics. Women were asked either to provide a first-void urine sample or to allow an endocervical swab to be taken. Urine samples were obtained at booking antenatal visit or on admission for abortion. The endocervical swabs were taken at the time of colposcopy or at the abortion clinic. Samples were then analysed. Positive results were confirmed by repeat testing of the original sample. The presence of symptoms or signs of *C. trachomatis* infection was explored systematically and recorded.

Criteria	Measure	Value	Certainty
1. Reach			
Percentage of population affected by the condition and that could potentially benefit from the intervention.	Sexually active women aged 16-49 as a percentage of population aged 15 and above in England (ONS, 2005 and 2009).	11.33%	★★
2. Inequality score			
Ratio of the percentage of disadvantaged population to the percentage of the general population that could potentially benefit from the intervention.	Assumption	1	★
3. Cost-effectiveness			
Cost of the intervention per QALY gained (in £2007/08)	See cost-effectiveness	£892	★★
Net cost of the intervention per QALY gained (in £2007/08)	See cost-effectiveness	£370	★★
Timing of benefits	QALY gain and cost savings are estimated to occur in the short term (within 12 months of the intervention).		
4. Affordability			
Total cost of implementing the intervention at the national level	Multiple of eligible individuals and unit cost of the intervention	Less than £100 million	★★

Key to certainty grading scales

★ Low quality evidence

★★ Medium quality evidence

★★★ High quality evidence

Box 1. Cost per QALY gained

A quality adjusted life year (QALY) is a simple way of combining quality of life with length of life.
One QALY is equivalent to one year in full health. The cost per QALY gained is therefore the cost of achieving one extra year of full health. Its calculation is based on the following formula:

$$cost\ per\ QALY\ gained = \frac{incremental\ cost\ of\ intervention}{QALYs\ gained}$$

The net cost per QALY gained is the cost per QALY considering the incremental cost of the intervention as well as the cost saved through health treatment avoided. Its calculation is based on the following formula:

$$net\ cost\ per\ QALY\ gained = \frac{incremental\ cost\ of\ intervention - cost\ savings}{QALYs\ gained}$$

Cost effectiveness

Cost. Opportunistic screening for *Chlamydia trachomatis* in hospital-based antenatal and gynaecology clinics, and community-based family planning clinics cost £14 per person more than usual care (£2007/08).

Effect. Compared to usual care, opportunistic screening for *Chlamydia trachomatis* in hospital-based antenatal and gynaecology clinics, and community-based family planning clinics identifies cases of Chlamydia that would otherwise be untreated. The baseline probability of identifying someone with Chlamydia through opportunistic screening is 0%. The probability following the intervention is 100%. This effect is consistent with Norman et al (2004).

Benefits. The benefits of the intervention derive from identifying and treating cases of *C. trachomatis* that would be undetected otherwise. Two types of benefits are considered: QALYs and health care cost savings. Based on the QALYs gained and the health care cost savings of identifying cases of *C. trachomatis* in a population with a 12.7% prevalence of *C. trachomatis* is associated with the following benefits:

- An additional 0.016 QALYs per person
- Cost savings of £8.32 per person (£2007/08)

Please refer to decision model for details on how the QALY gain and cost savings were calculated.

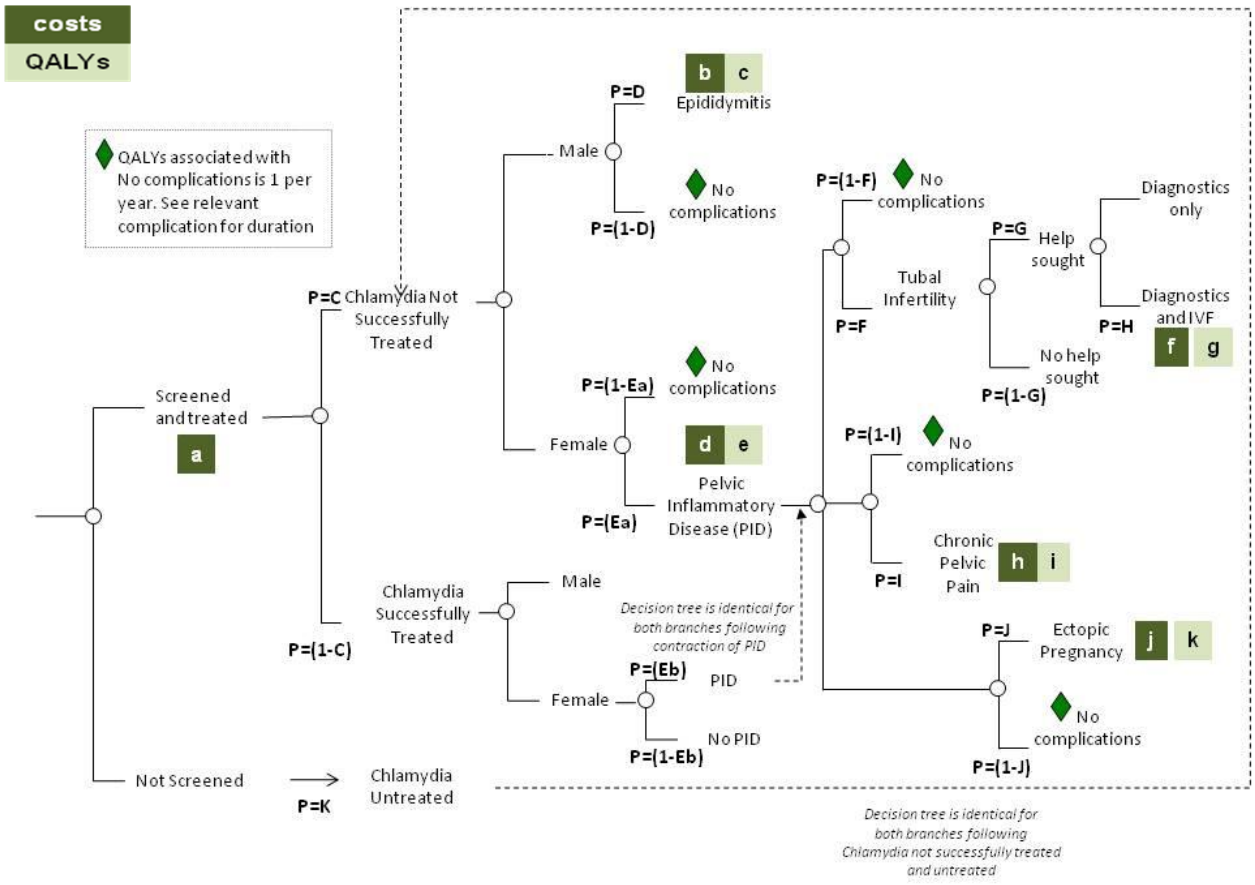
Decision model

A decision model was built to estimate the cost-effectiveness of the intervention. The model estimates the QALY gain and cost savings associated with the intervention.

Unless stated otherwise, the analysis was undertaken in accordance with H.M. Treasury's Green Book (HM Treasury, 2003). Specifically:

- Any costs and effects incurred more than one year after the intervention were discounted at 3.5%.
- Where necessary monetary values were converted in 2007/8 prices using Gross Domestic Product (GDP) deflators (HM Treasury, 2008).
- Where necessary monetary values were converted into pounds sterling using http://www.x-rates.com.

Figure 1. *Chlamydia trachomatis* screening model



The model draws the following estimates from the literature:

- The unit cost of the intervention (Table 1).
- The effect of the intervention on identifying and treating *Chlamydia trachomatis* (Table 1).
- The probabilities that untreated Chlamydia leads to health complications (Table 2).
- The impact of experiencing complications has on health care treatment costs (Table 3).
- The impact of experiencing complications on quality of life, measured in QALYs (Table 3).

Table 1. Intervention costs and effects

Description	Value	Assumptions and sources
Costs associated with identifying someone with Chlamydia using opportunistic screening	£14.21	Cost of opportunistic screening, which includes collecting, analysing and confirming positive results (Norman et al, 2004). It is assumed that everyone entering the model has Chlamydia. Assume that 100% people identified as having Chlamydia are treated.
Probability that Chlamydia is identified if present following the intervention	100%	Norman et al, 2004.
Probability that Chlamydia is identified if present without the intervention	0%	Norman et al, 2004.

Table 2. Transition probabilities associated with Chlamydia

Diagram reference	Description	Value	Assumptions and sources
C	Chlamydia not successfully treated	0.05	Cure rate from Norman et al (2004). Assuming 100% compliance with treatment.
D	Primary complications following Chlamydia infection in men.	0.03	Rates from Chesson et al (2008). Assumes that the only complication a male with Chlamydia can develop is Epididymitis and that following treatment of Chlamydia the probability of this complication attributable to Chlamydia is 0 (Chesson et al, 2008).
Ea	Primary complications following Chlamydia infection in women.	0.2	Rates from Chesson et al (2008). Assumes that the only primary complication a female with Chlamydia can develop is pelvic inflammatory disease (PID).
Eb	Probability of contracting PID if Chlamydia treatment successful	0.04	Chesson et al, (2008).
F	Development of tubal infertility following PID	0.2	Rates from Hu et al (2004).
G	Probability of infertile couple seeking diagnosis of infertility	0.835	Assume 100% of couples that seek medical help for infertility have diagnostic tests.

Diagram reference	Description	Value	Assumptions and sources
H	Probability of treatment for tubal infertility if help sought	1.0	It is assumes that 100% of couples that seek medical help for infertility and have diagnostic tests have fertility treatment.
I	Development and treatment of chronic pelvic pain following PID	0.18	Rates from Hu et al (2004).
J	Development of ectopic pregnancy following PID	0.09	Rates from Hu et al (2004).
K	Probability of Chlamydia being untreated without the intervention	1.0	Norman et al (2004).

Table 3. Associated outcomes (monetary values in £2007/08) associated with Chlamydia

Diagram reference	Description	Value	Assumptions and sources
a	Chlamydia treatment	£10.97	Cost of treatment: http://cks.library.nhs.uk/chlamydia_uncomplicated_genital
b	The cost of treating Epididymitis	£10.97	Cost of treatment: http://cks.library.nhs.uk/chlamydia_uncomplicated_genital Assume that 100% of cases are treated.
c	QALYs associated with Epididymitis	0.009	7 day duration QALYs calculated using HUI utility weights and durations from Stratton et al, 2000.
d	The cost of treating PID	£9.11	Rates from Chesson et al, (2008). Assumes that the only primary complication a female with Chlamydia can develop is pelvic inflammatory disease (PID) and that following treatment of Chlamydia the probability of PID attributable to Chlamydia is 0.04 of females with Chlamydia (Chesson et al, 2008). Cost of treatment http://www.cks.nhs.uk/pelvic_inflammatory_disease Assumes that 100% of cases are treated.
e	The QALYs associated with PID	0.01726	10 day duration. QALYs calculated using HUI utility weights and durations from Stratton et al (2000).
f	Cost of treatment for tubal infertility	£4,606	It is assumes that 100% of couples that have tubal infertility seek medical help for infertility and have diagnostic tests have fertility treatment. Fertility treatment costs from NICE CG11 Infertility costing template. Assume an average of 2 NHS funded cycles per couple. Uses weighted average cost of different types of treatment.

Diagram reference	Description	Value	Assumptions and sources
g	The QALYs associated with tubal infertility	12.3	15 year duration. QALYs calculated using HUI utility weights and durations from Stratton et al (2000).
h	Treatment costs of chronic pelvic pain	£370	Rates from Hu et al (2004). Cost of treatment http://www.cks.nhs.uk/pelvic_inflammatory_disease
i	QALYs associated with chronic pelvic pain	6.0	Duration is 10 years. QALYs calculated using HUI utility weights and durations from Stratton et al (2000).
j	Treatment costs of ectopic pregnancy	£418	NHS National Tariff 2008 http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_081096
k	QALYs associated with ectopic pregnancy	0.09	Duration is 31 days. QALYs for ectopic pregnancy were calculated as an average of in and outpatients – 0.053 and 0.059 respectively. QALYs calculated using HUI utility weights and durations from Stratton et al (2000).

Effectiveness evidence

A literature review was undertaken by Bazian to identify evidence on the cost-effectiveness of *Chlamydia* screening programs. Further details are available on the evidence methods page of the ***H.E.L.P.*** website.

The review of the evidence on the cost-effectiveness of opportunistic screening for *Chlamydia trachomatis* identified a number of studies. Table 4 provides the following details of the studies identified:

- Population, intervention and model
- Perspective, discounting, inflation, cost year
- Utility/benefit
- Unit costs
- Efficiency

Table 5 provide a quality assessment of the effectiveness and cost-effectiveness studies. Further details are available on the quality appraisal methods page.

The following criteria were applied to select effectiveness evidence for undertaking the economic analysis:

- Location. Studies from the UK were preferred over studies from other locations.
- Population. Studies applied to the general population were preferred over studies applied to restricted population groups (e.g. pregnant women; individuals from specific communities/nationalities).
- Counterfactual. Studies for which the counterfactual intervention was 'usual care' or 'do nothing' in a UK setting were preferred over studies for which the counterfactual was different from 'usual care' or 'do nothing'.
- Method. Studies using more rigorous design methods (e.g. randomised control trials or quasi experimental designs with regression models controlling for confounders) were preferred over studies using less rigorous design methods (e.g. before-after studies or simple correlation analysis).

Table 4. Cost-effectiveness of opportunistic screening for *Chlamydia trachomatis* identified a number of studies

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
Low et al, 2007; UK ▪ cost study	Cost study based on chlamydial screening in non-GUM settings: adult men and women invited to collect urine and (for women) vulvovaginal swab specimens at home and mail these to a laboratory. Amplified enzyme immunoassay (PCE EIA) and two nucleic acid amplification tests used. Chlamydia positive and two negative controls completed a risk factor questionnaire. Chlamydia positive were invited to participate in a RCT of partner notification strategies (not reported here). 19,773 women and men aged 16 to 39 years randomly selected from 27 GP practice lists - invitations apparently reached 73% of these (14,382/19,773). 4,731 participated in surveys.	▪ Service and patient cost perspective ▪ Adjusted for inflation ▪ Discounting 1.5% and 3.5% ▪ Cost year: GBP2005	NS	£21.47 per screening invitation £28.56 per accepted offer	ICER(GBP2003): £27,000/major outcome averted at 8 years when annual screening of men and women was compared with no screening in the base case. This fell to £3,700/major outcome averted if estimated screening uptake and pelvic inflammatory disease incidence were increased.

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
Low et al, 2007; UK ▪ cost modelling study	Cost study simulating a single round of home-based population screening for Chlamydia. Decision-tree diagram to describe flow of patients from initial screening invitation to treatment. Unit cost of each component of screening was applied to number of people passing through each stage, including costs of treating partners. Patient costs were derived through questionnaires to patients.	▪ Healthcare and patient perspectives ▪ Cost year: GBP2005	NS	Average cost to health service (including cost of running the study) was £14.65 per individual screening invitation. Cost per person screened: £21.74 Patient/user cost: £6.82 per patient (which includes average out-of-pocket expense per patient for all modes of transport and opportunity cost - time lost at work)	
Low et al, 2007; UK ▪ cost modelling study	HTA-economic evaluation of active screening for Chlamydia using a transmission dynamic model: Individual based discrete event simulation. Main features: ageing and replacement, partnership formation and dissolution, chlamydia transmission and progression, testing and treatment, sequelae associated with chlamydia (PID, epididymitis, infertility, ectopic pregnancy, neonatal complications, conjunctivitis, pneumonia). Data on long-term sequelae in women from Uppsala Women's Cohort Study.	▪ Unclear perspective ▪ Unclear whether adjusted for inflation ▪ 3.5% discounting ▪ Cost year: GBP2003	NS	Some of these unit costs were from the primary study conducted by this HTA group: ▪ Cost per screening invitation (including administration): £11.82 ▪ Planned screening test male: £7.82 ▪ Planned screening tests female: £6.94 ▪ Background screening test male: £6.66 ▪ Background screening test female: £6.31	ICER (£/major outcome avoided): ▪ Female only vs. no screening: £28,000/moa ▪ Male and female vs. no screening: £25,700/moa

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
	Model used primary data from studies conducted for this HTA (cross sectional study to estimate prevalence of chlamydia, evaluate test performance; a RCT of partner notification in primary care) Model included the following annual screening interventions: no screening, screening women only and screening men and women both within a defined age group. Virtual individuals with ages drawn from a uniform distribution between lower and upper limits. Initial population is evenly distributed in aged between 12 and 62 years and is assumed to be 50% female.			▪ Treatment of index case including PN: £30.16 ▪ Treatment of partners: £22.60 ▪ Infertility: £428 ▪ Ectopic pregnancy: £2319 ▪ PID: £2846 ▪ Epididymitis: £790 ▪ Neonatal complications: £708 *Total costs* ▪ No screening: £1,720,000 ▪ Female only screening: 2,154,000 ▪ Male and female screening: 2,561,000	
Adams, 2004; UK ▪ cost study	UK based cost study. Opportunistic screening in women aged 16 to 24 years and partner notification in GUM clinics, family planning clinics, antenatal clinics, termination of pregnancy clinics, GP cinics. Costs include treatment and partner management (azithromycin, 1g single dose or doxycycline).	▪ Health sector ▪ Cost year: GBP2001	NS	Average cost with partner management: ▪ £14.88 per screening offer ▪ £21.83 per testing episode ▪ £38.38 per positive episode	

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
Townshend, 2000; UK ▪ cost study	Selective opportunistic screening in women - age not specified. Three different types of screening were considered as an intervention. Each with a different level of effectiveness in terms of its probability of encountering an infective instead of a susceptible. Men and women aged 12 to 40 years. Dynamic model of three different potential screening policies (random screening, cyclical screening, screening at a partnership change). Each screening with a different level of effectiveness in terms of its probability of encountering an infective instead of a susceptible. Model assumes infective partner tracing system is implemented alongside the screening so that when an infective is detected their immediate sexual partners are tested. For infectives in any of the disease stages, the number of individuals receiving an initial screening test in a month is multiplied by the probability of a true positive to give the number receiving a confirmatory test. This then multiplied by the probability of a true	▪ Health sector ▪ 6% discounting ▪ Unclear cost year	NS	Costs were derived from several literature sources: Screening ▪ First test: £12.41 ▪ Re-test: £10.56 Treatment ▪ Epidydimitis: £210 ▪ PID: £350 ▪ Ectopic pregnancy: £4,300 ▪ Infertility (female): £2,100 ▪ Conjunctivitis: £35 ▪ Pneumonia: £760 ▪ Other symptomatic infection: £9 ▪ Chlamydia detected by screening: £9	

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
	positive to give number receiving treatment, which is then multiplied by the probability of the treatment being successful to give the number who recover from that particular disease stage in a month.				
Dryden, 1994; UK ▪ cost study	Cost study: screening of urine samples collected in general practice urine samples vs. no screening.	▪ Health sector ▪ Unclear discounting ▪ Unclear whether adjusted for inflation ▪ Cost year unclear	NS	▪ £7.84 test including time, overheads etc. ▪ £25.00 positive test follow-up ▪ £8.00 doxycycline (7 days treatment 100mg 12 hourly) ▪ £64.26 cost of contact tracing per index case	Cost per case cured: £245 (authors state that the cost of missing a diagnosis of chlamydia was not included because there were too many variables to consider)

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
Norman et al, 2004; UK	Screening for Chlamydia in primary and secondary care vs. no screening. Decision model: model probabilities were generated for a hypothetical sample of 250 women in each age group in each setting. Model analysed a series of possible events associated with screening and not screening for chlamydia. Major sequelae defined as PID, chronic pelvic pain, ectopic pregnancy, infertility, male urethritis, epididymitis, infantile conjunctivitis and infantile pneumonia. Baseline probabilities used in mode were based on data from both analysis of this cohort of women and from published literature. Model estimates costs of screening 3,750 women (i.e. 250 women in each age group and in each of the four sample populations). Prevalence estimated in 2,817 women; acceptability determined in 484 women.	▪ Health sector ▪ Unclear whether adjusted for inflation ▪ 5% discounting for future costs; 3% discounting for future benefits ▪ Cost year: GBP2001	NS	▪ LCR test (includes testing and nurse time): £12 ▪ Test positive patient follow up (30 mins nurse time): £6 ▪ Antibiotic treatment: £9 Female sequelae ▪ PID: £190 ▪ Chronic pelvic pain: £111 ▪ Ectopic pregnancy: £2,530 ▪ Infertility: £4,540 Neonatal sequelae ▪ Conjunctivitis: £8 ▪ Pneumonia: £303 Male sequelae ▪ Epididymitis: £15 ▪ Urethritis: £15	ICER (net cost per major sequelae averted): Universal screening vs. no screening: £651 Selective screening by age vs. universal screening: Under 20 years: £258 Under 25 years: £344 Under 30 years: £513 Selective screening by clinical setting v universal screening: Family planning clinic: £694 Antenatal clinic: £1,196 Colposcopy clinic: £621 Abortion clinic: £433

Table 5. Quality assessment for economic studies

Study reference	QA for economic studies						Score	Grading (++ 4-6; + 3; -0-2)
	All costs of intervention included?	Market values used for costs?	Perspective reported?	Sensitivity analysis?	Reports base year adopted?	Effectiveness data from RCT or MA?		
Low et al, 2007; UK	Yes	Yes	Yes	Yes	Yes	No	5	++
Adams, 2004; UK	Yes	No	Yes	Yes	Yes	No	4	++
Townshend, 2000; UK	Yes	Don't know	Yes	Yes	No	Don't know	3	+
Dryden, 1994; UK	Don't know	Don't know	Yes	No	No	No	1	-
Norman et al, 2004; UK	Yes	Don't know	Yes	Yes	Yes	No	4	++

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