SCREENING

The cost effectiveness of opportunistic chlamydia screening in England

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An appendix can be found on our website http://sti.bmj.com.

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Background/aim: The National Chlamydia Screening Programme (NCSP) is being implemented in England. This study aims to estimate the cost effectiveness of (a) the NCSP strategy (annual screening offer to men and women aged under 25 years) and (b) alternative screening strategies.
Methods: A stochastic, individual based, dynamic sexual network model was combined with a cost effectiveness model to estimate the complications and associated costs of chlamydial infection. The model was constructed and parameterised from the perspective of the National Health Service (NHS) (England), including the direct costs of infection, complications and screening. Unit costs were derived from standard data sources and published studies. The average and incremental cost effectiveness ratio (cost per major outcome averted or quality adjusted life year (QALY) gained) of chlamydia screening strategies targeting women and/or men of different age groups was estimated. Sensitivity analyses were done to explore model uncertainty.
Results: All screening strategies modelled are likely to cost the NHS money and improve health. If pelvic inflammatory disease (PID) progression is less than 10% then screening at any level is unlikely to be cost effective. However, if PID progression is 10% or higher the NCSP strategy compared to no screening appears to be cost effective. The incremental cost effectiveness analysis suggests that screening men and women aged under 20 years is the most beneficial strategy that falls below accepted thresholds. There is a high degree of uncertainty in the findings.
Conclusions: Offering an annual screening test to men and women aged under 20 years may be the most cost effective strategy (that is, under accepted thresholds) if PID progression is 10% or higher.

The prevalence of genital chlamydial infection is 3–10% in women under 25 years old in England.[1] Since many cases are asymptomatic, chlamydia screening is a way of identifying undiagnosed infection so that individuals and their partners can be treated. Earlier treatment prevents complications and reduces onward transmission. The National Chlamydia Screening Programme (NCSP) is currently being implemented in England.[2 3] However, questions remain regarding its cost effectiveness and that of alternative screening strategies. A transmission dynamic model of chlamydial infection in a sexually active population was used previously to estimate the impact of different screening strategies on chlamydia prevalence.[4 5] These results were used in this analysis to estimate the complications from untreated chlamydial infection, and the costs associated with acute infection, clinical complications, and screening activities. A cost effectiveness analysis was performed to compare different screening strategies, in the context of limited resources.

METHODS

Transmission dynamic model

A stochastic, individual based, dynamic sexual network model was developed to simulate sexual behaviour and chlamydia transmission in England. The full methodology is explained elsewhere, including details of the extensive fitting process used to model sexual behaviour and chlamydia epidemiology realistically.[4] The model simulated a heterosexual population of 20 000 men and 20 000 women aged 16–44. The rate of sexual partner change was highest in the youngest cohorts and decreased with age. Infection in the model was transmitted within discordant partnerships, assuming no acquired immunity to chlamydia. Symptomatic infection was assumed to have a shorter average duration than asymptomatic infection (1 month vs 6 months), because of active treatment seeking. Without screening effective partner notification (notification plus treatment of infected partners) was assumed to be 20%. The overall chlamydia prevalence in the model was 3.2% among all individuals, highest in 16–19 year olds and decreasing with age.[4]

Three opportunistic screening strategies were modelled, targeting different age groups (<20, <25, <30, <35, <40 years old):

- *Strategy 1* Offer an annual screen to women
- *Strategy 2* Offer an annual screen to women and if they have changed their partner in the last 6 months
- *Strategy 3* Offer an annual screen to women and men.

It was assumed that 85% of the population attended a healthcare site annually.[5] Of those eligible for screening, a proportion (50% at baseline) accepted the screen. Thus, under strategy 1 the minimum interval between screens was 1 year. Once eligible, individuals attend approximately twice a year, but accept 50% of the time, hence the average time between screens was 2 years. Each subsequent screening offer was assumed to be independent of previous offers or acceptances.

Evidence from a recent study indicated that women have a greater risk of infection and reinfection if they have acquired a new partner.[6] Strategy 2 extends screening eligibility based on sexual behaviour, to target those at highest risk. The NCSP

Abbreviations: CER, cost effectiveness ratio; EP, ectopic pregnancy; ICER, incremental cost effectiveness ratio; MO, major outcome; MOA, major outcomes averted; NCSP, National Chlamydia Screening Programme; PID, pelvic inflammatory disease; PN, partner notification; QALY, quality adjusted life year; TFI, tubal factor infertility

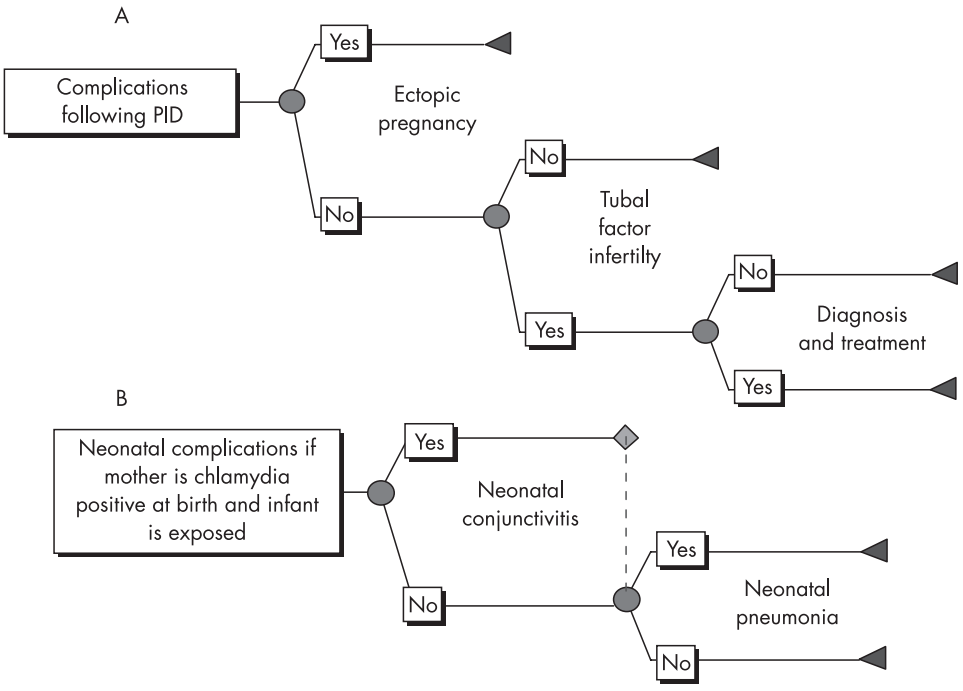

Figure 1 Flow of complications in (A) women with pelvic inflammatory disease (PID), and (B) neonates exposed to infected mothers.

recommendation of an annual screen for men and women under 25 years old[2] (strategy 3) was chosen as the baseline screening strategy for sensitivity analyses. Results of the sensitivity analyses performed on screening effectiveness have been reported previously.[5] The probability of accepting a screen when offered was changed for both men and women from 50% (baseline) to 10%, 30%, and 70%. An additional, pessimistic scenario of 10% of women and 1.4% of men accepting was also modelled, which roughly approximates the number of screens performed in men and women in the NCSP in 2004–5.[7] The efficacy of partner notification (PN) and treatment with screening introduction was changed from 20% to 50% (applied to partners of those screened and those actively seeking treatment). A final scenario examined the cost effectiveness when individuals only accepted a screen once, since evidence suggested that acceptance declines after the first screen acceptance.[8]

Cost effectiveness model

A cost effectiveness model was constructed in Excel to estimate the costs of acute infection, the number of complications and their associated costs, and the costs of interventions under different screening strategies compared to no screening. The number of female and neonatal complications was modelled using a decision tree (Precision Tree, Palisade software) (fig 1).

Only symptomatic pelvic inflammatory disease (PID) was modelled, as there is evidence from Westrom *et al* that the severity of PID symptoms is directly related to the probability of further complications such as ectopic pregnancy (EP) and tubal factor infertility (TFI).[9] Furthermore, the causal link between undetected asymptomatic PID and TFI is weak. There is conflicting evidence about the proportion of chlamydia cases that result in PID.[10–12] Therefore, three scenarios were run for no screening and each screening strategy with a PID progression probability of 1%, 10%, and 30%. To determine which assumption may be closest to the actual value, the number of cases of PID estimated by the model (no screening) was compared to an estimate of the annual incidence of PID in 16–44 year olds of between 1500 and 2400 per 100 000 women, from a GP based study.[13] This included all clinical diagnoses of PID from any cause, and also those who might have been misdiagnosed (none of these cases were confirmed laproscopically).

The dynamic model output the incident cases of symptomatic and asymptomatic chlamydial infection in men and women, and acute complications (symptomatic PID in women and epididymitis in men), by year for each simulation. These cases in women were then used to estimate the number of cases of EP, TFI, neonatal conjunctivitis, and neonatal pneumonia. The probabilities of complications are given in table 1 and supporting evidence in the appendix (available at http://sti.bmj.com/supplemental). Because of the stochastic nature of infection within the dynamic model, each simulation of the dynamic model resulted in a different number of cases of

Table 1 Risk of developing complications following acute chlamydial infection

Complication	Probability (sample size)	Probability applied to:	Distribution type	Reference
Symptomatic PID (women)	1%, 10%, 30%	Asymptomatic chlamydial infection	Scenario analysis*	Assumption
Ectopic pregnancy (women)	7.6% (1309)†	Symptomatic PID	Beta	Weström *et al*[9]
Tubal factor infertility (women)	10.8% (1309)†	Symptomatic PID (exclude those with EP)	Beta	Weström *et al*[9]
Neonatal conjunctivitis	14.8% (1055)‡	Infected women giving birth vaginally	Beta	Rosenman *et al*[18]
Neonatal pneumonia	7.0% (597)‡	Infected women giving birth vaginally	Beta	Rosenman *et al*[18]
Epididymitis (men)	2%	Asymptomatic chlamydial infection	Fixed	Assumption based on work by Welte *et al*[19 20]

PID, pelvic inflammatory disease, EP, ectopic pregnancy. *All screening strategies were run with all three probabilities. †Based on the number of women trying to conceive, after a laparoscopically diagnosed PID case, the total denotes the total number followed up. ‡The total is the number of infants exposed at birth.

Table 2 Estimated average costs of acute infection, complications and interventions

Condition	Baseline cost (£) (SD)
Acute conditions	
Symptomatically infected and actively seeking treatment for chlamydial infection	
Men	64 (6)
Women	61 (5)
Screened and infected (men/women)	31 (2)
Screened and *not* infected (men/women)	20 (2)
Do *not* accept screen offer (men/women)	6 (1)
Partner treatment	27 (2)
Complications	
Pelvic inflammatory disease	137 (46)
Epididymitis	142 (67)
Ectopic pregnancy	762 (329)
Tubal factor infertility	10798 (4279)
Neonatal conjunctivitis	41 (4)
Neonatal pneumonia	612 (555)

infection. The dynamic model was run 100 times for each scenario, and the average of these was input into the model to get base case results.

The model was constructed and parameterised from the perspective of the National Health Service in England, and included the direct costs of infection, complications, and screening. Unit costs were derived from standard data sources[14–16] and other published studies. Costs to the patient and wider society were not included in this analysis as recommended by the National Institute for Health and Clinical Excellence (NICE).[17] Estimates of the average costs of acute conditions, complications, and interventions are given in table 2 and further details including how they were derived are given in the appendix (see http://sti.bmj.com/supplemental). Costs estimated in previous time periods were inflated to 2004 pounds sterling (£) using the Hospital and Community Health Services Pay and Prices Index.[14] All costs and effects were discounted at an annual rate of 3.5% in the base case. Sensitivity analyses were done using no discount rate for costs and effects, and 6% for costs and effects, and 3.5% for costs and no discounting of effects.

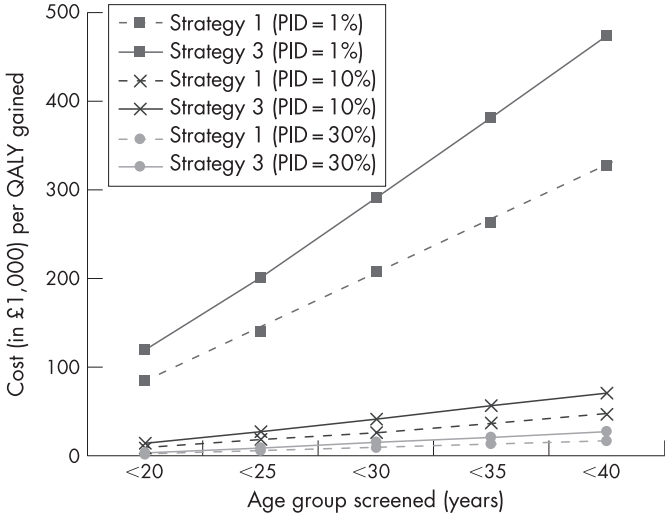

Figure 2 The average cost effectiveness of screening strategies 1 (offer women annual screen) and 3 (offer women and men annual screen) in different age groups compared to no screening, under different assumptions about pelvic inflammatory disease (PID) progression.

Two outcomes were considered in the analysis: the number of major outcomes averted (MOA) and quality adjusted life year (QALY) gained. The MOAs included cases of epididymitis, PID, EP, TFI, and neonatal conjunctivitis and neonatal pneumonia. Details of the QALY estimates for each condition are given in the appendix (on the *STI* website, see http://sti.bmj.com/supplemental).

The average cost effectiveness ratio (CER) was used to compare each strategy with no screening. The CER was calculated as: (difference in costs)/(difference in benefits), between screening and no screening, where the benefits are either MOAs or QALYs gained. However, as recommended by NICE, an incremental cost effectiveness ratio (ICER) analysis was also done to assess the relative cost effectiveness of alternative screening strategies.[17] The ICER was calculated by ranking the programmes in order of net costs, and the additional benefits and additional costs of each programme compared with the previous strategy (excluding dominated ones) were estimated. Programmes were dominated if they cost more than the previous strategy and resulted in fewer benefits. Both the CER and ICER were estimated separately for each assumption about the progression to PID.

The time horizon for analysing the effects of screening was 10 years. Chronic complications in women (EP, TFI) and the associated costs that occurred until a woman was 44 years old were also included.

A probabilistic multivariate sensitivity analysis was performed to assess the uncertainty of model assumptions using @Risk (version 4.5, Palisade Corporation) running within Excel (version 2000, Microsoft). For each dynamic model simulation result (100 total for each screening strategy), the economic model was run 100 times, and for each realisation a different value for input parameters was randomly sampled from their distributions (through Latin hypercube sampling). Details of the distributions are given in the tables and the appendix (see http://sti.bmj.com/supplemental). For the multivariate sensitivity analysis, PID progression was assumed to be 10%. The ICER was estimated for the costs and effects of no screening and the top four screening strategies.

RESULTS

PID progression

The assumption about the probability of progression to PID had a large impact on the results. The average annual incidence of predicted by the model was 58 (PID = 1%), 581 (PID = 10%), and 1750 (PID = 30%) per 100 000 women for a PID progression of 1%, 10%, and 30%, respectively. A study PID found 30% (42/140) of PID cases had evidence of ever being exposed to chlamydial infection.[25] If that is applied to the numbers seen in GP surgeries, then an estimated *maximum* of between 450 and 720 cases of PID per 100 000 annually seen in GP surgeries may be caused by chlamydia. This suggests an estimate of around 10% progression to PID is the most likely of the PID scenarios modelled.

Cost effectiveness

Under the baseline scenario without screening, in a model population of 40 000 sexually active individuals, there were on average 1392 major outcomes and 65 QALYs lost over 10 years (assuming a PID progression probability of 10%). For different PID progression probabilities there were on average 393 (1% PID) and 3529 (30% PID) MOs, corresponding to 10 and 156 QALYs lost, respectively.

The average cost effectiveness of different screening strategies (screening versus no screening) is presented in figure 2 and in tables 3–5 (results are ranked according to increasing costs). Strategy 1 was the least effective strategy, but most cost

Table 3 Cumulative major outcomes, quality adjusted life years lost, and costs expected over 10 years, the incremental cost per outcome for each screening strategy, and the average cost per outcome (compared to no screening) for each assumption about pelvic inflammatory disease (PID) progression: PID = 1%

	Total MO	Total QALYs lost	Total cost (£)	Incremental cost (£)/MOA	Incremental cost (£)/QALY gained	Average cost (£)/MOA	Average cost (£)/QALY gained
Baseline, no screening	393	10	108 408	–	–	–	–
Strategy 1 <20	256	6	430 991	2364	84 337	2364	84 337
Strategy 2 <20	222	5	670 680	7118	241 271	3305	116 693
Strategy 3 <20	201	5	739 267	3125	149,745	3284	119 562
Strategy 1 <25	215	5	811 689	Dominated	Dominated	3960	139 219
Strategy 1 <30	203	5	1 196 464	Dominated	Dominated	5754	207 198
Strategy 2 <25	171	4	1 378 328	21 573	736 387	5728	206 685
Strategy 3 <25	137	3	1 494 862	3474	157 304	5432	201 371
Strategy 1 <35	189	4	1 577 516	Dominated	Dominated	7204	262 845
Strategy 1 <40	185	4	1 959 279	Dominated	Dominated	8905	326 900
Strategy 2 <30	149	3	2 088 871	Dominated	Dominated	8122	296 053
Strategy 3 <30	114	3	2 253 126	32 374	1 544 567	7696	290 770
Strategy 2 <35	140	3	2 799 862	Dominated	Dominated	10 657	389 895
Strategy 3 <35	104	2	3 015 808	75 208	3 161 809	10 067	381 688
Strategy 2 <40	133	3	3 517 839	Dominated	Dominated	13 157	485 712
Strategy 3 <40	94	2	3 773 363	76 841	6 909 379	12 271	474 314

MO, major outcome; MOA, major outcomes averted. Values in the table are rounded for presentation. QALY, quality adjusted life years; All costs and effects are discounted at 3.5%. Results are presented in rank order of total costs, which include costs of infection, complications, and programme costs. Dominated means that the MOA or QALYs gained is less than the non-dominated strategy above it in the table.

effective (that is, lowest average cost per MOA or QALY gained). Strategies 2 and 3 yielded similar results and were less cost effective than strategy 1. Extending a strategy to include older ages resulted in smaller increases in health than costs, thereby increasing the CER. The average CER of the NCSP strategy under baseline assumptions and 10% PID progression was £27 269. None of the screening programmes modelled were cost saving.

Results of the incremental cost effectiveness analyses comparing alternative strategies are given in tables 3–5. A high ICER corresponds to a small increase in benefit over the screening programme above it but with a relatively large additional cost. The rank order of screening scenarios was the same in the incremental analysis for all assumptions about PID progression. If PID progression were 1%, the ICER was very high (over £80 000 per QALY gained) for any screening programme compared to no screening. For PID progression of 10% or higher, the incremental cost per QALY gained when strategies 1, 2, and 3 (aged under 20 years) were added was below £20 000–£30 000 per QALY gained. However, adding screening of older age groups resulted in high ICERs (over £50 000).

Sensitivity analyses

The sensitivity of the estimated cost effectiveness to the intervention assumptions given the NCSP strategy (strategy 3, <25 years) is presented in table 6. Low acceptance resulted in a higher CER compared to the baseline of 50% acceptance. Increasing the effective partner notification rate from 20% to 50% reduced the cost effectiveness ratio by about 10%. Offering men and women aged under 25 years a single screening test was more cost effective than continuous screening, mainly because of the much lower costs. The impact of changing the discount rate is given in table 7.

Table 4 Cumulative major outcomes, quality adjusted life years lost, and costs expected over 10 years, the incremental cost per outcome for each screening strategy, and the average cost per outcome (compared to no screening) for each assumption about pelvic inflammatory disease (PID) progression: PID = 10%

	Total MO	Total QALYs lost	Total cost (£)	Incremental cost (£)/MOA	Incremental cost (£)/QALY gained	Average cost (£)/MOA	Average cost (£)/QALY gained
Baseline, no screening	1392	65	310 695	–	–	–	–
Strategy 1 <20	883	39	553 352	477	9204	477	9204
Strategy 2 <20	736	31	771 367	1484	29 416	703	13 640
Strategy 3 <20	673	29	832 498	959	24 103	726	14 371
Strategy 1 <25	739	32	918 213	Dominated	Dominated	930	18 476
Strategy 1 <30	645	28	1 283 628	16 415	978 039	1303	26 459
Strategy 2 <25	584	24	1 462,494	2928	44 109	1426	28 212
Strategy 3 <25	468	19	1 556 572	807	19 352	1348	27 269
Strategy 1 <35	633	28	1 666 599	Dominated	Dominated	1788	36 849
Strategy 1 <40	610	28	2 048 769	Dominated	Dominated	2224	46 404
Strategy 2 <30	491	20	2 157 585	Dominated	Dominated	2051	41 470
Strategy 3 <30	400	17	2 308 023	11 059	302 328	2013	41 461
Strategy 2 <35	460	20	2 869 275	Dominated	Dominated	2745	56 481
Strategy 3 <35	363	16	3 064 432	20 479	747 964	2676	55 987
Strategy 2 <40	444	20	3 582 115	Dominated	Dominated	3453	71 953
Strategy 3 <40	343	15	3 828 432	39 230	1 938 410	3355	70 952

MO, major outcome; MOA, major outcomes averted. Values in the table are rounded for presentation. QALY, quality adjusted life years; All costs and effects are discounted at 3.5%. Results are presented in rank order of total costs, which include costs of infection, complications, and programme costs. Dominated means that the MOA or QALYs gained is less than the non-dominated strategy above it in the table.

Table 5 Cumulative major outcomes, quality adjusted life years lost, and costs expected over 10 years, the incremental cost per outcome for each screening strategy, and the average cost per outcome (compared to no screening) for each assumption about pelvic inflammatory disease (PID) progression: PID = 30%

	Total MO	Total QALYs lost	Total cost (£)	Incremental cost (£)/MOA	Incremental cost (£)/QALY gained	Average cost (£)/MOA	Average cost (£)/QALY gained
Baseline, no screening	3529	156	709 068	–	–	–	–
Strategy 1 <20	2216	92	796 042	66	1364	66	1364
Strategy 2 <20	1878	75	974 854	529	10 402	161	3283
Strategy 3 <20	1676	66	1 008 678	168	3845	162	3338
Strategy 1 <25	1799	75	1 110 924	Dominated	Dominated	232	4960
Strategy 1 <30	1641	70	1 466 413	13 279	Dominated	401	8799
Strategy 2 <25	1397	55	1 600 015	546	53 317	418	8834
Strategy 3 <25	1195	46	1 682 280	407	8961	417	8845
Strategy 1 <35	1574	68	1 842 956	Dominated	Dominated	580	12 987
Strategy 1 <40	1508	66	2 213 265	Dominated	Dominated	744	16 829
Strategy 2 <30	1200	48	2 277 375	Dominated	Dominated	673	14 589
Strategy 3 <30	1018	41	2 419 181	4181	149 930	681	14 877
Strategy 2 <35	1138	47	2 991 631	Dominated	Dominated	955	21 068
Strategy 3 <35	909	38	3 163 011	6835	238 076	937	20 783
Strategy 2 <40	1071	46	3 696 199	Dominated	Dominated	1215	27 228
Strategy 3 <40	852	37	3 921 645	13 304	714 049	1200	26 966

MO, major outcome; MOA, major outcomes averted. Values in the table are rounded for presentation. QALY, quality adjusted life years; All costs and effects are discounted at 3.5%. Results are presented in rank order of total costs, which include costs of infection, complications, and programme costs. Dominated means that the MOA or QALYs gained is less than the non-dominated strategy above it in the table.

Uncertainty analysis

Figure 3 illustrates the range of likely results from the probabilistic sensitivity analysis on the ICER (PID progression = 10%). There is considerable uncertainty, even in the no screening scenario, particularly in the QALYs lost from chlamydia (the spread in the horizontal axis is greater than in the vertical). It is clear from figure 3 that strategy 1 (<20 years) results in large incremental QALY gains and has a high probability of falling below £20 000 per QALY gained (at 10% PID progression). Moving to strategy 2 (<20 years) results in almost half the points lying above the £30 000 per QALY gained line. Including men (strategy 3, <20 years) results in small additions to the cost of the programme and small additional benefits over strategy 2, and about half of the simulations fall below £20 000 per QALY gained. Increasing the programme further (strategy 1, <30 years), would result in large additional costs and few additional benefits, with nearly all results falling above £30 000 per QALY gained.

DISCUSSION

Estimates of the costs and cost effectiveness of different chlamydia screening strategies including the current strategy recommended by the NCSP (strategy 3, annual screening offer to women and men aged under 25 years) are presented. None of the screening strategies modelled were cost saving, but all resulted in better health and fewer major outcomes.

The most influential parameter was the probability of cases progressing to PID. Most other cost effectiveness studies of chlamydia screening have used an estimate of around 25–30% progression to PID (including both symptomatic and asymptomatic PID).[26] However, a recent study by van Valkengoed *et al* based on Dutch data concluded that the risk of PID after a

Table 6 Sensitivity of the estimated average cost effectiveness of screening to the choice of intervention parameter

PID rate	Scenario	Net MOA	Net QALY	Net costs (£)	Cost (£)/MOA	Cost (£)/QALY gained
1%	Screening baseline	255	7	1 386 454	5432	201 371
	Acceptance = F, 10%; M,1.4%	70	2	1 290 587	18 308	643 037
	Acceptance = 10%	117	3	1 315 002	11 240	407 440
	Acceptance = 30%	220	6	1 356 937	6182	231 433
	Acceptance = 70%	275	7	1 404 474	5101	190 166
	PN = 50%	286	8	1 415 138	4953	186 321
	Screen only once	187	5	530 449	2830	104 007
10%	Screening baseline	924	46	1 245 877	1348	27 269
	Acceptance = F, 10%; M, 1.4%	302	15	1 241 250	4106	83 717
	Acceptance = 10%	443	22	1 245 655	2809	57 445
	Acceptance = 30%	807	40	1 234 664	1530	30 869
	Acceptance = 70%	989	49	1 256 063	1270	25 633
	PN = 50%	1021	50	1 257 727	1232	24 966
	Screen only once	677	34	429 762	635	12 814
30%	Screening baseline	2334	110	973 212	417	8845
	Acceptance = F, 10%; M, 1.4%	762	35	1 156 289	1518	33 241
	Acceptance = 10%	1121	51	1 115 870	995	21 676
	Acceptance = 30%	2030	95	1 005 087	495	10 605
	Acceptance = 70%	2481	117	969 306	391	8320
	PN = 50%	2599	122	960 098	369	7899
	Screen only once	1735	81	227 799	131	2826

NSCP, National Chlamydia Screening Programme; PID, pelvic inflammatory disease; MOA, major outcomes averted; QALY, quality adjusted life years; PN, partner notification, F, female; M, male. Under baseline assumptions, screening acceptance is 50%, PN is 20%, and screening is offered annually.
The baseline is the NSCP strategy (strategy 3, annual screen offer to men and women under 25 years old) compared to no screening.

Table 7 Sensitivity of the results to the discount rate for costs and effects, NCSP strategy (strategy 3, annual screening offer to men and women aged under 25 years compared with no screening).

PID rate	Discount rate effects (%)	Discount rate costs (%)	Net MOA	Net QALY	Net costs (£)	Cost (£)/MOA	Cost (£)/QALY gained
1%	0	0	321	11	1 644 897	5118	144 924
	3.5	3.5	255	7	1 386 454	5432	201 371
	0.0	3.5	321	11	1 383 644	4305	121 907
	6	6	219	5	1 236 641	5641	243 833
10%	0	0	1187	81	1 406 086	1185	17 265
	3.5	3.5	924	46	1 245 877	1348	27 269
	0.0	3.5	1187	81	1 220 846	1029	14 991
	6	6	786	32	1 131 554	1439	35 620
30%	0	0	2996	197	959 671	320	4872
	3.5	3.5	2334	110	973 212	417	8845
	0.0	3.5	2996	197	911 004	304	4625
	6	6	1987	76	922 869	464	12 081

NSCP, National Chlamydia Screening Programme; PID, pelvic inflammatory disease; MOA, major outcomes averted; QALY, quality adjusted life years.

chlamydial infection is likely to be less than 1%.[12] Another study by Morré *et al* followed up 30 asymptomatically infected women and none developed PID after 1 year of follow up.[11] If 30% of women with asymptomatic chlamydial infection progress to PID, we would expect a much higher reported incidence of PID in general practice than is observed. Although some cases may be undiagnosed, the number of reported cases of PID in general practice is likely to be a reasonable upper bound on the number of cases caused by chlamydial infection, since this is PID from all causes including misdiagnosis.[13] In fact the number of reported cases is inconsistent with progression greater than about 10%. This has major implications for the results of the cost effectiveness analysis (tables 3-5).

If we were to consider solely the NCSP strategy compared to no screening, the average cost effectiveness ratio is about £27 000 when PID progression is 10%. NICE suggest that programmes with an ICER of greater than £20 000–£30 000 per QALY gained are unlikely to be accepted on cost effectiveness grounds.[17] Therefore, the NCSP strategy appears to be acceptable on cost effectiveness grounds if we ignore other screening strategies. However, NICE recommends that the incremental cost effectiveness ratio of alternative strategies is also explored.[17] This indicates that the NCSP strategy involves a relatively high expected cost compared to the additional expected benefits. If PID progression were 10% or higher, then the full incremental analysis suggests that screening men and women aged under 20 years should be recommended. If only 1% of infected women develop PID, then none of the screening strategies appeared to be acceptable on cost effectiveness grounds.

The sensitivity analyses highlighted how the current strategy could be made more cost effective. Increased acceptance rates result in more favourable cost effectiveness results compared to baseline (table 6). The high CER for low acceptance occurs from the costs not only for those who accept screening but who also do *not* accept a screen,[27] in addition to the costs of complications. Efforts could be made to raise awareness about chlamydia and the benefits of regularly obtaining a screen to improve acceptance rates. Additionally, results from the third year of the NCSP indicate that 33% of partners were treated,[3] which is higher than our baseline assumption of 20% and would make screening more cost effective. Finally, the model used in this analysis was fitted to data from a review of chlamydia prevalence studies in women, but no equivalent data were available on male prevalence.[1] New evidence from the NCSP and surveillance from STI clinics suggest that the peak prevalence is in men aged 20–25.[3 28] Future analyses could

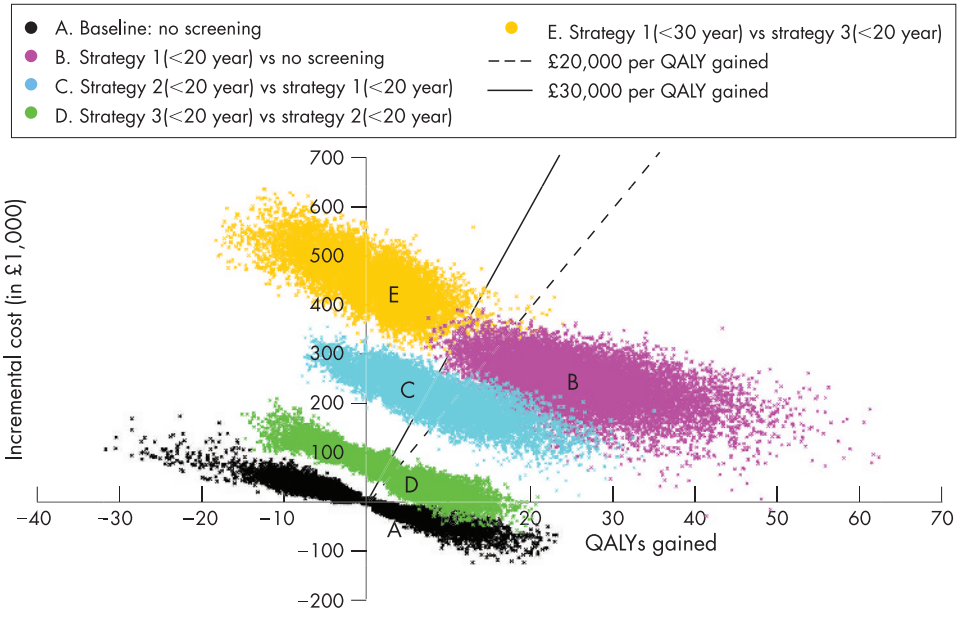

Figure 3 Multivariate sensitivity analysis of the estimated incremental costs and quality adjusted life year (QALY) gain for the most cost effective screening programmes, assuming pelvic inflammatory disease progression of 10%.

include new data to reflect these changes, which may in turn impact on the results.

A few papers have estimated the cost effectiveness of chlamydia screening using dynamic models[20 29 30]; however, most studies have used static models, which are incapable of including population level effects.[26 31] Welte *et al*[20] used an appropriate dynamic model similar to ours to examine the cost effectiveness of screening in the Netherlands. They estimated that screening might be cost saving after 10 years. The disparity in these results from ours is likely to be due to three key differences in their assumptions in both their dynamic and cost effectiveness models. Firstly, they assumed a high proportion of individuals being treated as symptomatic cases before screening introduction (~40% compared with under 5% in our model[4]), thereby effectively removing them from developing complications. Secondly, they assumed a high probability of PID progression (25%). Thirdly, costs for most complications were much higher than those assumed in our model. For example, they assumed that 25% of PID cases will be admitted to hospital inpatient care, including an 11 day hospital stay, yielding an average estimated cost that was over six times higher than ours. The costs of other complications (EP, TFI, neonatal complications, epididymitis) were also higher than our estimates.

The screening costs in the current analysis were taken from a chlamydia screening pilot study.[27 32] The initial set-up costs of a national chlamydia screening programme are likely to include costs not modelled in this analysis, including training costs, computerisation costs, personnel, etc. Therefore this analysis may underestimate the true costs of a screening programme, thereby making screening appear more favourable than it may be. Additionally, in accordance with the NICE guidelines, in this study only the direct medical and screening costs were examined. Another large population based chlamydia screening study is being conducted which includes an analysis of patient costs.[33] These could be included in further analyses, along with other societal costs. Finally, costs associated with false positive or false negative tests were not considered in this analysis. False positive tests result in costs due to treatment and partner follow-up. If chlamydia prevalence declines, the probability of false positive results increases. Individuals with false positive tests may incur psychological and social costs associated with disclosure of diagnosis to sex partners and stigma attached to STIs, with no compensating benefit resulting from treatment gained by those infected.[34–37] Therefore, there may be QALY loss from screening itself, which should be further investigated.

In this analysis two outcomes were used: MOAs and QALYs gained. MOAs are an intermediate outcome, and it is difficult to compare results with other health interventions. However, only one other cost effectiveness study has used QALYs for chlamydia screening.[26 38] Hu *et al* also used the Institute of Medicine values,[21 38] as these are the only estimates currently available. The QALY estimates could be improved in future studies to better understand the health loss from chlamydial infection, complications, and screening.

This study used a dynamic model to estimate the likely cost effectiveness of chlamydia screening strategies. Results can be used to inform decisions about which screening strategies may be the most beneficial in the context of limited healthcare resources. It suggests that offering an annual screen to men and women under 25 years of age result in ICERs above the normally accepted levels when compared with screening only those aged under 20 years (although this strategy may be deemed cost effective when compared with ''no screening''). Results suggest that increasing screening acceptance and effective partner notification may yield a more favourable cost effectiveness ratio owing to greater benefits without a large relative increase in costs. Since one of the greatest uncertainties that impacts on the results is the probability of progression to PID, future work should focus on understanding its natural history. Monitoring the incidence of PID as screening is introduced nationally should be a research priority.

Key messages

- All chlamydia screening strategies modelled are likely to improve health and cost money.
- Screening men and women aged under 25 years (NCSP strategy) appears to be cost effective compared to no screening; results suggest that a less inclusive strategy may be more acceptable on cost effectiveness grounds.
- The results depend largely on the assumed progression from chlamydial infection to PID, which is likely to be lower than that used previously in cost effectiveness studies.
- A realistic model of infection, disease progression, and costs can be used to estimate the likely cost effectiveness of a national chlamydia screening programme which in turn can be used to advise public health policy decisions.

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Contributors: EJA was the primary author, constructed the cost effectiveness model and analysed and interpreted the results. KMET coded changes to the dynamic simulation model, helped interpret the results, and revised the manuscript. WJE assisted with model development, interpretation of results and revised the manuscript.

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COMMENTARY

Adams *et al* cast doubt on the cost-effectiveness of opportunistic chlamydia screening, as implemented in the English National Chlamydia Screening Programme.[1] A recent economic evaluation of a proactive postal screening approach has shown that this is also unlikely to be a cost-effective approach.[2] These two studies, using state-of-the-art individual-based transmission dynamic network models,[2 3] contrast sharply with almost all other published evaluations. Their results contradict not only those using an inappropriate modelling approach,[4] but also more recent studies that used dynamic modelling and found screening to be cost effective[5] or even cost saving.[6 7]

Adams *et al*'s study is an important contribution to the debate about the appropriateness of chlamydia screening programmes.[8] They clearly show that a chlamydia screening intervention can appear cost effective or not, depending on the assumption made about the probability of endocervical chlamydia progressing to pelvic inflammatory disease. They concluded that opportunistic screening was not cost effective if the progression rate was below 10% and that available epidemiological data were incompatible with a higher progression rate. The recent economic evaluations using individual-based dynamic modelling that found screening to be cost saving used figures of 20% to 25%.[6 7]

Decision makers such as the National Institute for Health and Clinical Excellence (NICE) use the incremental cost-effectiveness ratio (ICER) for decision making. In this case, the ICER refers to the additional cost per additional unit of benefit of screening compared to the alternative of no screening. Unfortunately, Adams *et al* misleadingly refer to the results of their main evaluation and the sensitivity analysis as *average* cost-effectiveness ratios (average CERs). Their definition, ''(difference in costs)/(difference in benefits) between screening and no screening'' is, however, the standard definition for the ICER.[1 9] The standard unit of benefit is the quality adjusted life-year (QALY) which is a single measure summarising health improvements resulting from changes in both quality and quantity of life. The only QALY estimates for chlamydia and its complications were derived from an expert panel meeting rather than primary research,[10] so their validity is not known.[4] Most economic evaluations of chlamydia screening have therefore estimated the costs of screening per major outcome averted, typically including pelvic inflammatory disease, ectopic pregnancy, tubal infertility and neonatal complications.[2 5–7] Such studies can be compared among themselves, but are less useful for decision making because there are no agreed thresholds for cost-effectiveness measured in ''natural units'' such as these.

Adams *et al* used both measures of cost-effectiveness. They estimated that the current strategy being implemented in the National Chlamydia Screening Programme in England had an ICER of £27 269 per QALY gained and £1348 per major outcome averted, compared to no screening, assuming about 40% of sexually active women and men under 25 years would be screened every year, and that 10% of untreated chlamydia cases result in pelvic inflammatory disease. They suggest that such a programme could be accepted on cost-effectiveness grounds because the ICER was below £30,000 per QALY. In fact, NICE guidance states that ''Above a most plausible ICER of £20,000/QALY, judgements about the acceptability of the technology as an effective use of NHS resources are more likely to make more explicit reference to factors including: the degree of uncertainty around the calculation of the ICERs …'' (section 6.2.6.10; page 33).[11] Given the considerable uncertainty about the QALY estimates used by Adams *et al* this ICER, in QALY terms, exceeds the acceptable threshold approved by NICE and should be subjected to