Screening for genital chlamydial infection

Epidemiological, social, diagnostic and economic evaluation of population screening for genital chlamydial infection

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Executive summary

Health Technology Assessment 2007; Vol. 11: No. 8

Health Technology Assessment
NHS R&D HTA Programme
www.hta.ac.uk

Executive summary

Background

Screening for genital chlamydial infection is being introduced across England in a National Chlamydia Screening Programme. This opportunistic programme, whose main focus is young women attending contraceptive clinics, is planned to cover all primary care trusts by March 2007. The organisation and focus of the screening programme were based on recommendations of an Expert Advisory Group to the Chief Medical Officer, which summarised the available evidence in 1998. The Expert Advisory Group also identified gaps in the evidence about the cost-effectiveness of chlamydia screening, the performance of new diagnostic techniques, methods for reaching the sexual partners of infected people, and possible criteria for targeting screening. These questions have been addressed in this multidisciplinary project, the Chlamydia Screening Studies (ClaSS) project, through a variety of research methods.

Objectives

The objectives of the report were to address the areas raised by the Expert Advisory Group as part of their work in the proposed National Chlamydia Screening Programme. These were categorised as follows.

- Chlamydia screening survey: to establish the prevalence of genital chlamydia in men and women in the general population.
- Social research: to determine the social, emotional and psychological effects of screening and partner notification for genital chlamydia.
- Laboratory studies: to find the best test and specimen to use for screening for genital chlamydial infection in men and women.
- Partner notification: to establish the most effective methods of accessing partners of infected patients for the diagnosis and treatment of genital chlamydial infection.
- Case–control study: to find the most cost-effective criteria for targeted screening and which outcomes should be measured.
- Economic evaluation: to determine how to maximise the cost-effectiveness of screening for genital chlamydial infection in non-genitourinary medicine (GUM) clinic settings.

Methods

Design

A multicentre multidisciplinary series of linked studies was conducted. The core study was a cross-sectional population-based chlamydia screening survey. Adult men and women were invited by post to collect self-taken urine and (for women) vulvovaginal swab specimens at home, and to post these to a laboratory for testing for *Chlamydia trachomatis*. People with positive tests provided a confirmatory specimen after receiving results and a third specimen 6 weeks after treatment.

Questionnaires about anxiety, depression and self-esteem were sent before, at and after screening to random samples of survey participants testing negative. In-depth semi-structured interviews were also conducted during screening and partner notification with participants, non-participants and staff.

All specimens were used in laboratory evaluations of the performance of different diagnostic tests on individual specimens. Male urine and female vulvovaginal swab specimens were used to examine pooling groups of four and eight specimens. Specimen stability in female urine and vulvovaginal swab specimens was assessed from GUM clinic attenders not involved in ClaSS.

After receiving results and treatment at their general practice, chlamydia-positive cases were invited into a randomised controlled trial (RCT) comparing partner notification carried out by the practice nurse with referral to a specialist health adviser at a GUM clinic. Positive cases and two matched negative controls per case were asked to complete a detailed risk factor questionnaire before receiving their results.

A systematic review of economic evaluations of chlamydia screening was conducted, as were time and motion studies in laboratories and patient cost questionnaires. In addition, primary data were collected on costs of screening invitations, reminders, consultations and telephone follow-up. Finally, a dynamic model of chlamydia transmission was developed using discrete event simulation. The primary data were then used to determine the cost-effectiveness of proactive chlamydia screening. ▶

Setting
The study was conducted among the general population in the Bristol and Birmingham areas of the UK.

Participants
In total, 19,773 men and women aged 16–39 years randomly selected from 27 general practice lists were eligible.

Interventions
The invitation was sent to men and women to collect a specimen of early-morning first catch urine and for women to take a first catch urine specimen and a vulvovaginal swab at home and post specimens to a laboratory to be tested for *C. trachomatis*. Specimens were tested by enzyme immunoassay (EIA) and/or nucleic acid amplification tests (NAATs). Practice nurse-led partner notification, including a sexual history and patient referral, was carried out with ongoing support from a health adviser or by specialist referral to a sexual health adviser and partner notification at a GUM clinic. Health advisers conducted telephone follow-up for both.

Main outcome measures
For the chlamydia screening survey, the main outcome measures were coverage of the postal screening invitation, uptake of chlamydia screening and chlamydia prevalence. From a social research perspective, the outcome measures were the qualitative data about the emotional effects of chlamydia screening, anxiety, depression and self-esteem scores before and after screening. In the laboratory studies, performance characteristics of diagnostic tests for *C. trachomatis* on self-taken first catch urine and vulvovaginal swab specimens were used. When considering partner notification, the number of people with at least one sexual partner treated and cost of partner notification were the main outcome measures. Odds ratios for associations between risk factors and chlamydia were considered for case–control study aspects. The economic evaluation considered the health service and patient costs of chlamydia screening at 2005 and cost per major outcome averted in 2003 (costs were in UK pounds).

Results

Screening invitations reached 73% (14,382/19,773) of eligible people. Overall, 4731 men and women participated in the cross-sectional screening survey. Uptake rates were 39.5% [95% confidence interval (CI) 37.7 to 40.8%] in women and 29.5% (95% CI 28.0 to 31.0%) in men. Uptake was lower in more deprived areas. There were 219 people with positive chlamydia results. Prevalence in 16–24-year-olds was 6.2% (95% CI 4.9 to 7.8%) in women and 5.3% (95% CI 4.4 to 6.3%) in men. Chlamydia prevalence was not strongly associated with any demographic or practice level factors. The number of new partners in the past 12 months was the strongest predictor of infection. During the screening study an estimated 68.8% (95% CI 67.3 to 69.9%) of 16–24-year-old patients had attended their own general practice (75% of women and 60% of men).

Being invited to post home-collected specimens to a laboratory was well accepted by those who took part and did not adversely affect anxiety, depression or self-esteem. Reasons for not taking part in screening included low perception of personal risk or relevance, and not wanting to take responsibility for their own or their partner's health. Some women found taking a vulvovaginal swab unpleasant and this put some off from participating in screening.

The sensitivities of PCE EIA with negative grey-zone testing on male first catch urine and female vulvovaginal swab specimens were 75.0% (24/32, 95% CI 56.9 to 88.5%) and 66.4% (97/146, 95% CI 58.2 to 74.0%). Testing male urine using Cobas polymerase chain reaction (PCR) identified all positive specimens (32/32, 95% CI 89.1 to 100%). The relative sensitivities of female urine and vulvovaginal swabs were 91.8% (134/146, 95% CI 86.1 to 95.7) and 97.3% (142/146, 95% CI 93.1 to 99.2%), respectively. Inhibition was present by Cobas PCR in 2% (19/1003) of male urine, 13% (192/1476) of female urine and 16% (232/1269) vulvovaginal swab specimens, and by Becton Dickinson strand displacement amplification (SDA) in 7% (85/1269) female urine specimens and one swab. Compared with individual testing (£137.35 per positive urine, £104.10 per swab), pooling urine specimens in groups of four required 50% (969/1936) of the number of tests and cost £70.93 per positive, but missed 8.5% (9/106) of positive specimens; pooling swab specimens in groups of four required 60% (637/1062) of the tests and cost £42.66 but missed 5.3% (4/76) of positive specimens. The performance of Cobas PCR on female urine and vulvovaginal swab specimens stored at room temperature for 24 and 48 hours was equivalent.

A total of 140 people (74% of those eligible) participated in the randomised trial. Of patients referred to the GUM clinic, 31% (21/68) did not attend. In intention-to-treat analysis, compared ▶

with referral, the practice nurse strategy resulted in 12.4% (95% CI –3.7 to 28.6%) more patients with at least one partner treated and 22.0% (95% CI 6.1 to 37.8%) more patients with all partners treated. The strategies cost the same (£34.48 per index case for the practice nurse strategy and £34.55 for specialist referral) and qualitative research showed that patients preferred to be seen at their practice.

A total of 148 chlamydia-positive cases and 246 negative controls took part in the case–control study (response rate 69%). Among cases, 68.6% (70/102, 95% CI 58.7 to 77.5%) of women and 73.9% (34/46, 95% CI 58.9 to 85.7%) of men were asymptomatic. The case–control study did not identify any additional independent factors that would help to target screening.

The health service and patient costs (2005 prices) of home-based postal chlamydia screening were £21.47 (95% CI £19.91 to 25.99) per screening invitation and £28.56 (95% CI £22.10 to 30.43) per accepted screening offer. About 30% of the costs were incurred by the patient. Most published economic evaluations of chlamydia screening suggest that both population-based and opportunistic screening are cost-effective but use static models, which do not capture the effects of interaction between individuals, and use estimates of the incidence of chlamydial complications that may be overestimated. In a transmission dynamic model using discrete event simulation in a population of 50,000 with 60 runs over 15,000 simulated days, the incremental cost-effectiveness ratio comparing screening women only annually with no screening at 8 years was £29,000 per major outcome averted, and for screening men and women annually compared with no screening £27,000 per major outcome averted (with uptake in women 39%, uptake in men 29% and risk of pelvic inflammatory disease in women with chlamydia 8.9% by the age of 35 years). Results were sensitive to uptake and incidence of sequelae. The cost of screening men and women annually by 8 years with 60% uptake in women and 40% in men was £17,000 per major outcome averted, with pelvic inflammatory disease incidence 25% £6800, and with 60% uptake in men and women and 25% pelvic inflammatory disease £3700 per major outcome averted.

Conclusions

Proactive screening for chlamydia in women and men under 25 years of age using home-collected specimens was feasible and acceptable, but the uptake of this method was lower than had been expected from an early pilot study.

The ClaSS project approach to screening included features that could enhance the uptake of opportunistic screening. Mixed models of chlamydia screening should be evaluated to see if they achieve higher consistent levels of screening uptake than either active or opportunistic screening alone.

Practice registers could be used by central chlamydia screening offices to optimise the process. Home-based specimen collection can be offered by post as an alternative to clinic-based screening.

The examination of risk factors for chlamydia in the prevalence and case–control studies did not find any factors, other than young age, that would help to target screening more easily. Men should be targeted more intensively for chlamydia screening, as prevalence in young men was the same as in young women. As nearly two-thirds of men aged 16–24 years (and three-quarters of women) attended their general practice in 1 year, this would be the best setting for opportunistic screening.

Chlamydia screening has the potential to increase inequalities in sexual health. Postal screening invitations were less likely to reach people in areas with high numbers of residents from non-white minority ethnic groups, and the uptake of the screening invitation was lower in more deprived areas. Women with the highest prevalence of infection were the most difficult to engage in screening. Even if chlamydia prevalence did not vary by gender, ethnic group or socioeconomic deprivation, introducing a screening programme that is less available and accessible, and less acceptable to people from vulnerable and disadvantaged groups, could create or widen existing inequalities. This applies to opportunistic as well as active screening.

Nurse-led partner notification, with support from specialist health advisers, could be considered for implementation within the National Chlamydia Screening Programme. Practice nurse-led partner notification was as effective a strategy for ensuring treatment of the sexual partners of people diagnosed with chlamydia in primary care as referral to a GUM clinic. The strategy was no more expensive than referral to a specialist GUM clinic and was

preferred by patients. The strategy could be extended to nurses in family planning clinics, youth sexual health clinics and NHS walk-in centres. Home-based specimen collection could be offered to eligible patients as an alternative to clinic-based screening; and can be given to individuals diagnosed with chlamydia to improve partner notification rates.

EIAs, even when used with strategies to enhance their performance, were inadequate for performing chlamydia screening using male urine and female vulvovaginal swab specimens.

Female vulvovaginal swab specimens are likely to become more popular for screening women using NAATs. They had high sensitivity and specificity, and lower levels of inhibition than with urine specimens. Women were, however, unfamiliar with this type of specimen. Some confused it with a cervical smear, and others said that it had put them off taking part in the study altogether. More education of the public about the benefits of vulvovaginal specimens should improve the acceptability of these types of specimen.

Pooling of specimens for screening is not recommended if resources to carry out individual testing are available. Pooling of self-taken urine and vulvovaginal swab specimens reduces costs and workload, but misses an appreciable proportion of positive tests.

Active chlamydia screening was not cost-effective, based on a model of chlamydia transmission that assumed realistic, but lower, screening uptake and disease progression rates than other models. However, these assumptions are thought to be more realistic for studying the asymptomatic population in whom chlamydia is diagnosed by NAATs.

Recommendations for research

There is still a need for a large multicentre RCT of chlamydia screening to determine whether reducing female reproductive tract morbidity and chlamydia transmission are realistic long-term goals. Existing RCTs have only evaluated population-based (proactive) screening with a maximum follow-up of 1 year. No RCT has demonstrated any impact on the population incidence and prevalence of infection. Any new RCT would have to include opportunistic screening as one of the interventions, because this is current practice in the National Chlamydia Screening Programme, and would have to measure long-term primary outcomes.

Further research on the mathematical modelling of interventions to control chlamydia and other sexually transmitted infections is required. In addition, studies are needed to determine the best ways of engaging young men in chlamydia screening. Other areas to be addressed include the risks of reinfection following screening and treatment, the appropriate screening interval, the uptake of repeat screening, the effects of chlamydia screening on inequalities in sexual health, the performance of female urine and vulvovaginal specimens for *C. trachomatis* diagnosis, the likelihood of progression of chlamydial infection, and issues surrounding quality of life and long-term consequences.

Publication

Low N, McCarthy A, Macleod J, Salisbury C, Campbell R, Roberts TE, *et al*. Epidemiological, social, diagnostic and economic evaluation of population screening for genital chlamydial infection. *Health Technol Assess* 2007;**11**(8).

NIHR Health Technology Assessment Programme

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The research reported in this monograph was commissioned by the HTA Programme as project number 97/32/31. The contractual start date was in August 2000. The draft report began editorial review in August 2005 and was accepted for publication in May 2006. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

ISSN 1366-5278

Published by Gray Publishing, Tunbridge Wells, Kent, on behalf of NCCHTA.
Printed on acid-free paper in the UK by St Edmundsbury Press Ltd, Bury St Edmunds, Suffolk.