The impact of natural history parameters on the cost-effectiveness of Chlamydia trachomatis screening strategies

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The study examined seven strategies for the screening of Chlamydia trachomatis in women aged 15 to 29 years. The strategies were:

- no screening;
- biennial (i.e. every other year) screening for all women;
- biennial screening followed by a single repeat test within 3 to 6 months after a positive test result;
- biennial screening followed by a shift to semiannual screening (i.e. every 6 months) for those with a positive test result;
- annual screening for all women;
- annual screening followed by a single repeat test within 3 to 6 months after a positive test result; and
- annual screening followed by a shift to semiannual screening for those with a positive test result.

In all screening strategies, detected infection was treated with antibiotics. Testing was performed using urine-based nucleic acid amplification tests (NAATs). The seven strategies could be targeted at three different age groups: 15 to 19 years, 15 to 24 years and 15 to 29 years.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of non-pregnant, disease-free, sexually active 15-year-old females. The target age of screening was determined by the three age groups highlighted.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The clinical data were derived from studies published between 1979 and 2004. The resources and costs came from sources published between 1996 and 2003. The price year was 2000.
Source of effectiveness data
The clinical and epidemiological data used in the decision model were the probabilities of:

- acute chlamydial infection
- persistent acute chlamydial infection
- acute pelvic inflammatory disease (PID)
- PID sequelae (chronic pelvic pain and ectopic pregnancy)
- tubal infertility

- accuracy (sensitivity and specificity) of NAAT
- effectiveness of treatment for acute infection
- compliance with azithromycin
- azithromycin-related side-effects
- effectiveness of treatment for acute PID

Modelling
A published Markov model with a lifetime horizon and 6-month cycles was used in the current analysis. No further details of the decision model were reported and readers were referred to the primary publication.

Sources searched to identify primary studies
There were few details on the sources of the clinical data as they had fully described in the published model. It was stated only that new prevalence data came from the National Longitudinal Study of Adolescent Health (Add Health Study). Information on the other sources used in the earlier publication was not given.

Methods used to judge relevance and validity, and for extracting data
The method used to derive the clinical data was not described.

Measure of benefits used in the economic analysis
The summary benefit measures that were combined with the costs were the life-years and quality-adjusted life-years (QALYs). Both measures were estimated using the modelling framework. The utility weights used to adjust survival were obtained from the literature and were calculated using the Health Utility Index. Both benefits were discounted at an annual rate of 3%.

Direct costs
The analysis of the costs was performed from a societal perspective. It included the direct medical costs associated with NAAT, the treatment of acute urogenital chlamydial infection, the treatment of azithromycin-related side-effects, and the treatment of acute PID and its sequelae. The unit costs and the quantities of resources used were not presented separately. Costs and patterns of resource consumption were derived from published studies. Drug costs came from average wholesale prices. Medicare reimbursement rates were used for some items. Discounting was relevant, given that long-term costs were evaluated, and an annual discount rate of 3% was applied. The price year was 2000.

Statistical analysis of costs
The costs and quantities appear to have been treated deterministically.

Indirect Costs
Productivity costs (i.e. time costs reflecting the value of lost workdays due to screening, treatment and disease) were incorporated in the analysis. This was appropriate for the societal perspective adopted. The unit costs were given separately from the quantities of resources used. The costs and quantities of resources used were derived from the US Labor Bureau of Labor Statistics. As in the analysis of the direct costs, the price year was 2000 and an annual discount rate of 3% was applied.

Currency
US dollars ($).
Sensitivity analysis
A one-way deterministic sensitivity analysis was carried out on all model inputs using published ranges of values. Two-way sensitivity analyses on key epidemiological inputs were also performed. In a further analysis, the impact of simultaneous variations in the probability of persistent infection and the relative risk of re-infection was also tested.

Estimated benefits used in the economic analysis
The QALYs associated with no screening were 27.3020.

Screening increased mean QALYs per patient by 0.0035 to 0.0209, depending on the screening strategy (data for single strategies not reported).

Cost results
The lifetime costs associated with no screening were $268.

Screening increased total costs per patient by $24 to $134, depending on the screening strategy (data for single strategies not reported).

Synthesis of costs and benefits
Incremental cost-utility ratios and incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the alternative strategies.

There were 5 non-dominated strategies: no screening, biennial screening in the 15 to 24 year age group, biennial screening followed by a shift to semiannual screening for those who test positive in the 15 to 24 and 15 to 29 year age groups, and annual screening followed by a shift to semiannual screening for those who test positive in the 15 to 29 year age group.

The most efficient strategy was to screen all sexually active women aged 15 to 29 years annually and to re-screen those who tested positive every 6 months. This strategy produced the highest number of QALYs and had an incremental cost per QALY gained of $7,180 compared with the next best strategy. The remaining three non-dominated strategies had an incremental cost per QALY gained ranging from $5,660 to $6,770, compared with the next best strategies.

In the cost-effectiveness framework, the incremental cost-effectiveness ratios ranged from $236,700 to $303,000. The high figures in comparison with the cost-utility ratios highlighted the low mortality but high morbidity associated with the disease.

The results of the sensitivity analysis showed that the most influential parameters were screening test costs, yearly probability of acquiring an acute chlamydial infection, the risk of developing acute PID, the risk of developing long-term complications, and the yearly decline in the risk of acute chlamydial infection after 25 years of age. In particular, screening became cost-saving over no screening when the screening test cost was lower than $4.50 (it was $13 in the base-case analysis) or when the annual risk of acquiring Chlamydia trachomatis exceeded 14% (4% in the base-case analysis). The incremental cost per QALY gained with screening exceeded the threshold of $50,000 when the risk of developing PID was lower than 6% (base-case value 30%) or the risk of developing complications was less than 15% of the base-case value.

Some key findings of the two-way sensitivity analysis were as follows. Over the plausible range of values for persistence and relative risk of re-infection, the strategy of annual screening in women aged 15 to 29 years with semiannual screening for those who test positive remained the most cost-effective strategy. When it was assumed that the relative risk for re-infection was high, screening strategies that targeted the age group 15 to 29 years and allowed for women with a history of positive test to be screened on a semiannual basis dominated most other strategies.

Authors' conclusions
The routine annual screening of women aged 15 to 29 years followed by selective targeting of those with documented infection for semiannual screening was a cost-effective strategy. The analysis highlighted key epidemiological data requiring further investigation, such as the clinical significance of asymptomatic compared with symptomatic infection and the relative contribution of persistent versus repeated infection to repeat test positivity. The most influential natural history parameter was the risk of developing pelvic inflammatory disease (PID) for women with acute Chlamydia trachomatis.

CRD COMMENTARY - Selection of comparators
The choice of the comparators, which was based on the screening strategies under examination in a previous study, appears to have been appropriate in that a wide range of possible options was considered. The baseline strategy of no screening was also included. You should decide whether these represent valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data were derived from published studies. However, as for the modelling section, no information on the sources used was given in the current publication. For example, no details of a review of the literature were reported. Thus, the reader should refer to the primary publication if attempting to judge the validity of the clinical data.

Validity of estimate of measure of benefit
Both benefit measures (life-years and QALYs) were appropriately modelled and discounted. Health-related utility weights were reported and were based on standard questionnaires, although no details were provided of the studies from which these data were taken. These measures are appropriate given the impact of the interventions on quality of life and survival. They can also be easily compared with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs was consistent with the perspective adopted in the study. Only the major cost categories were reported and a breakdown of the cost items was not given. Similarly, details on resource consumption and unit costs were provided for only a few items. Again, more information should be available in the primary analysis. The year of the costs was reported, which has important implications for the generalisability of the study results. Statistical analyses were not performed but the impact of varying some key cost estimates was investigated in the sensitivity analysis.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. However, they did acknowledge some limitations of their analysis, such as the use of data from uncertain sources requiring further examination and validation. The use of a deterministic sensitivity analysis explored the issue of variability in the data and implicitly addressed the issue of the external validity of the study results, but the issue of the generalisability of the study findings to other settings was not explicitly discussed. It was also noted that the decision model did not consider the transmission of chlamydia infections to newborns or sexual partners. The inclusion of these aspects would have further favoured the screening strategies.

Implications of the study
The study results support the implementation of routine screening, a conclusion similar to that achieved in the previous economic evaluation. Further studies should investigate the validity of some assumptions concerning the determination of the risk for PID associated with asymptomatic and symptomatic acute infection, the relative contribution of persistence versus re-infection to repeat test positivity rates, and the risk of chlamydial infection in women over the age of 25 years.

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Bibliographic details
Other publications of related interest
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