The clinical and economic consequences of screening young men for genital chlamydial infection

Ginocchio R H, Veenstra D L, Connell F A, Marrazzo J M

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
Three strategies for the screening of asymptomatic young men for chlamydial infection (CI) were examined. The strategies were:

- no screening;
- screening all men with a ligase chain reaction (LCR) assay of urine;
- testing all young men with a leukocyte esterase (LE) strip test of urine, followed by confirmatory LCR for positive individuals (LE-LCR).

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 asymptomatic men.

Setting
The setting is likely to have been primary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from a review of studies published between 1980 and 2002. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies.

Modelling
A decision tree model was constructed to determine the events and costs associated with the three screening strategies in a hypothetical cohort of asymptomatic men. A simplified version of the tree structure was presented. The model was populated with data derived from the literature. The time horizon of the model before the development of pelvic inflammatory disease (PID) was one year. Infertility was evaluated 10 years after contraction of CI, and ectopic pregnancy and chronic pelvic pain 5 years after.
Outcomes assessed in the review
The outcomes estimated from the literature were:

the sensitivity and specificity of LCR and LE;

the efficacy of treatment for CI and side effects;

in men, the prevalence of infection, the rates of patients returning for treatment, the spontaneous cure rate, the rate of symptoms/urethritis, the rate of patients seeking care for symptoms/urethritis, the rate of epididymitis, and the rate of patients seeking outpatient treatment for epididymitis;

in women, the rate of transmission from male to female partner, the rate of partner traced or treated, the rate of CI detected by routine screening, the rate of symptoms, and the rate of women seeking care for symptoms;

the rate of developed PID, the rate of silent PID, the rate of inpatient treatment, and the rate of surgery;

the rate of infertility, and the rates of clinical evaluation, laparoscopy, surgery and in vitro fertilisation;

the rate of ectopic pregnancy and the rates for medical management, outpatient or inpatient surgery;

the rate of chronic pelvic pain, and the rates of clinical evaluation and laparoscopy; and

the pregnancy rate, the live birth rate, and the rates of conjunctivitis, pneumonia, and the inpatient treatment of pneumonia.

Study designs and other criteria for inclusion in the review
It was not stated whether a review of the literature was undertaken. The design of the primary studies was not reported.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Forty-eight primary studies provided the evidence.

Methods of combining primary studies
The most plausible estimates of those derived from the literature were selected.

Investigation of differences between primary studies
Not stated.

Results of the review
The sensitivity of LE was 70% and the specificity was 80%.
The sensitivity of LCR was 92.7% and the specificity was 99.6%.
The efficacy of treatment for CI was 96% and the rate of CI treatment side effects was 13%.

In men:
the prevalence of infection was 5%,
the rate of patients returning for treatment was 75%,
the spontaneous cure rate was 10%,
the rate of symptoms/urethritis was 50%,
the rate of patients seeking care for symptoms/urethritis was 20%,
the rate of epididymitis was 1%, and
the rate of patients seeking outpatient treatment for epididymitis was 90%.

In women:
the rate of transmission from male to female partner was 100% (one female partner infected per year per each infected male),
the rate of partner traced or treated was 50%,
the rate of CI detected by routine screening was 5%,
the rate of symptoms was 20%, and
the rate of women seeking care for symptoms was 10%.

The rate of developed PID was 25%, the rate of silent PID was 60%, the rate of inpatient treatment was 12%, and the rate of surgery was 20%.

The rate of infertility was 15%, the rate of clinical evaluation was 45%, the rate of laparoscopy was 75%, the rate of surgery was 30%, and the rate of in vitro fertilisation was 12%.

The rate of ectopic pregnancy was 8%, the rate of medical management was 20%, and the rates of outpatient and inpatient surgery were 75% (outpatient) and 5% (inpatient), respectively.

The rate of chronic pelvic pain was 18%, the rate of clinical evaluation was 75%, and the rate of laparoscopy was 90%.

The pregnancy rate was 14%, the live birth rate was 58%, the rate of conjunctivitis was 23%, the rate of pneumonia was 15%, and the rate of inpatient treatment of pneumonia was 20%.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the number of PID cases prevented. The number of prevented cases of urethritis, epididymitis, infertility, ectopic pregnancy, chronic pelvic pain, neonatal conjunctivitis, and pneumonia were also assessed as model outputs. An annual rate of 3% was applied to discount future benefits (infertility, ectopic pregnancy, and chronic pelvic pain).
Direct costs
An annual discount rate of 3% was used as some costs were incurred over a long timeframe. The unit costs were presented separately from the quantities of resources used, although some costs were presented as macro-categories. The direct costs included in the economic evaluation were presented as base case, low (-10%) and high (+60%):

test costs;
clinical care (males), which included screening visits, return-for-treatment visit, symptoms/urethritis evaluation (return visit and initial visit), epididymitis evaluation (returning patient and initial visit);
clinical care (females), which included female partner traced or treated, symptom evaluation, routine screening, PID (inpatient treatment, outpatient treatment), infertility treatment, ectopic pregnancy treatment, chronic pelvic pain treatment;
clinical care (neonates), which included conjunctivitis treatment and pneumonia treatment.

The cost/resource boundary of the study was that of the health care payer. Resource use was estimated from published data that reflected standard patterns of care. The costs were estimated from Medicaid maximum allowable fee schedules. This included resource-based relative value reimbursement schedule for physician and surgeon reimbursement, the prospective payment system for hospital fees, the prospective payment system for ambulatory surgical centre reimbursement, the clinical diagnostic laboratory fee schedule, and the maximum allowable cost prescription fee schedule. The 1999 Drug Topics Red Book was used for prescriptions not covered under W A Medicaid. The price year was 2000.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were conducted on all model inputs to assess the robustness of the estimated costs and effectiveness of the alternative screening strategies. The ranges used were obtained from the literature, or by varying from -10% to +60% of the cost estimates. Two-way sensitivity analyses on the prevalence of infection and the cost of the LCR assay were also conducted. Several alternative scenarios were considered. For example, the inclusion of the indirect costs, additional CI sequelae, the exclusion of costs of clinic visits associated with screening in a traditional health care setting, and an alternative source of the costs.

Estimated benefits used in the economic analysis
In a cohort of 100,000 men screened, the number of PID cases was 522 with no screening, 280 with LE-LCR, and 176 with LCR. The corresponding figures (in order: no screening, LE-LCR, LE) for the other outcomes were:

2,500, 1,283, and 762 for urethritis;
43, 23, and 14 for epididymitis;
58, 31, and 20 for infertility;
36, 19, and 12 for ectopic pregnancy;
81, 43, and 27 for chronic pelvic pain;
42, 22, and 14 for conjunctivitis; and
27, 15, and 9 for pneumonia.

Therefore, the number of PID cases prevented was 242 with LE-LCR over no screening, 346 with LCR over no screening, and 104 with LCR over LE-LCR.

Cost results
The cost per male was $7.44 with no screening, $36.58 with LE-LCR, and $59.20 with LCR.

The cost of screening itself was the main category of cost for LE-LCR and LCR.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the alternative screening strategies.

The incremental cost per PID case prevented was $12,041 with LE-LCR over no screening, and $21,750 with LCR over LE-LCR.

Both the estimated costs and effectiveness were robust to variations investigated in the sensitivity analysis, unless the base-case estimates were varied substantially.

The relative ranking of the strategies did not change when the indirect costs were included.

The inclusion of additional CI sequelae substantially increased the costs associated with no screening, while the increase in the costs of the two screening strategies was negligible. LE-LCR became cost-saving over no screening at a prevalence of 41% or more, while LCR was cost-saving over LE-LCR at a prevalence of 44% or more (the prevalence in the base-case was 5%).

The exclusion of costs of clinic visits associated with screening in a traditional health care setting favoured the two screening strategies. LE-LCR became cost-saving over no screening at a prevalence of 23%, but LCR did not become cost-saving over LE-LCR until a prevalence of 62% was reached.

Authors’ conclusions
Screening all men with a leukocyte esterase (LE) strip test, followed by confirmatory testing with ligase chain reaction (LCR), was a cost-effective strategy in comparison with no screening. A strategy of screening all men with LCR detected more cases of pelvic inflammatory disease (PID), but the additional cost was substantial.

CRD COMMENTARY - Selection of comparators
The choice of the comparators appears to have been appropriate, as it covered all possible screening strategies for the detection of CI in asymptomatic men. No intervention was compared with two screening strategies, a traditional and low-cost approach and a more sophisticated, expensive and accurate strategy. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a synthesis of completed studies. It was not stated whether a review of the literature was undertaken and no information on the design of the primary studies was provided. The methods used to
extract and then combine the primary estimates were not described. Thus, it is difficult to assess the validity of the estimates used in the model. However, the issue of uncertainty was investigated in the sensitivity analyses, which were carried out on all estimates.

**Validity of estimate of measure of benefit**
The benefit measure was specific to the disease considered in the study. It would therefore be difficult to compare it with the benefits of other health care interventions. The benefit measure was obtained using a modelling approach and discounting was applied to those model outputs that were assessed over a long timeframe. The key structure of the tree was provided. The authors noted that some outcomes related to CI were not accounted for in the model.

**Validity of estimate of costs**
The authors stated explicitly which perspective was adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. A breakdown of the cost items was provided, but some costs were presented as macro-categories. The source of the data and the price year were reported, which will simplify reflation exercises in other settings. The costs were treated deterministically in the base-case, but key cost estimates were varied in the sensitivity analysis in order to address the issue of uncertainty. Similarly, alternative sources of the costs and different cost scenarios were considered. The total costs were obtained using the same modelling approach as that used to estimate the benefits. The authors noted that the costs considered in the model were likely to have been lower than those paid by private health plans.

**Other issues**
The authors compared their findings with those from other studies, showing that, in general, similar results were obtained. Possible explanations for some of the differences observed were provided. The issue of the generalisability of the study results to other settings was not explicitly addressed, although sensitivity analyses were conducted. This enhances the external validity of the analysis. The authors noted some limitations of their study, which were mainly related to the data used in the decision model. However, extensive sensitivity analyses were carried out to deal with the issue of uncertainty.

**Implications of the study**
The results supported the strategy of LE-LCR in terms of cost-effectiveness, although LCR was the most effective alternative. The authors suggested that, if the cost of LCR testing decreased sufficiently (or in populations with high prevalence of CI), the LCR option could become the preferred screening strategy.

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