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 Chlamydia trachomatis in adolescent males were examined:

- universal screening with a urine-based nucleic acid amplification test (NAAT);
- selective screening (with a urine-based NAAT) of males with a positive urine leukocyte esterase (ULE) test; and
- no screening.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of male youths at high risk for chlamydia.

Setting
The setting was a juvenile justice detention facility. The economic study was conducted in Massachusetts, USA.

Dates to which data relate
The effectiveness and resource use data were partly gathered from February 2001 to February 2003 and partly derived from studies published between 1980 and 2002. The price year was 2002.

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

Link between effectiveness and cost data
The costing was not conducted on the same sample of patients as that included in the effectiveness study.

Study sample
Power calculations were not conducted. The sample comprised all males aged between 14 and 18 years who entered two Central Massachusetts detention facilities between February 2001 and February 2003. The individuals were required not to have voided in the last 1 hour and not to have used any antibiotics in the last 3 weeks. Of 835 initially identified
adolescents, 678 agreed to participate. Of these, only 594 were sexually experienced and were included in the final study sample. The mean age was 15.6 (+/- 0.9) years. The main reasons for those declined participation (157) were not interested (58%), recently tested (11%) and did not think he could have an infection (10%). The participants were comparable with non-participants in terms of their age, but racial and ethnic compositions were different. There were significantly more Hispanics and fewer white individuals among the participants.

**Study design**
This was a prospective case series in which a single group of adolescents was enrolled in the study, without a control group. The study was conducted at two detention centres, the Worcester and Westboro in Massachusetts. The participants were interviewed and underwent urine testing. Those testing positive were further contacted for treatment, regardless of whether they were still at the centre or had left the programme. Positive patients were also encouraged to refer their sexual partners for treatment. The length of follow-up was not reported. No patient was lost to the follow-up assessment.

**Analysis of effectiveness**
All of the patients included in the initial study sample were considered in the effectiveness study. The outcome measures used were the prevalence of chlamydia and the sensitivity and specificity of the ULE test. These were then entered into the decision model as probability values. The mean number of female sexual partners per infected male in the preceding 2 months and the proportion of asymptomatic infected males were also reported.

**Effectiveness results**
The prevalence of chlamydia was 4.8% (95% confidence interval, CI: 3.2 - 6.8).

The sensitivity the ULE test was 61.5% (95% CI: 40.6 - 79.8) and the specificity was 80.6% (95% CI: 77.4 - 83.9).

The mean number of female sexual partners per infected male in the preceding 2 months was 1.6.

The proportion of asymptomatic infected males was 84.6%.

**Clinical conclusions**
The probability values identified in the primary study were used in the decision model.

**Modelling**
A deterministic model, based on a decision tree, was constructed to assess the costs and benefits of the two screening strategies relative to no screening, in a cohort of 4,000 adolescent males at risk for chlamydia. The time horizon of the model was 10 years. The structure of the tree was reported in the paper. The model considered sequelae prevented and costs saved in infected males and female partners of index males.

**Outcomes assessed in the review**
The model inputs assessed in the review were the sensitivity and specificity of NAAT, and the probabilities of the following:

- chlamydia transmission from male to female,
- partner treatment,
- epididymitis,
- inpatient treatment of epididymitis,
pelvic inflammatory disease (PID),
the proportions of PID that are silent and overt,
inpatient treatment of PID,
chronic pelvic pain,
ectopic pregnancy,
infertility, and
infertile women seeking fertility services.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
MEDLINE was searched using the keywords "Chlamydia trachomatis", "ligase chain reaction", "LCR", "LCx", "strand displacement amplification", "SDA", "Becton Dickinsons" and "BDProbeTec". However, this search was performed only to identify relevant primary studies reporting estimates of the sensitivity and specificity of NAAT. The sources searched for other estimates were not reported.

**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**
Overall, 42 primary studies were used to derive the effectiveness evidence. However, only 19 studies were included in the meta-analysis.

**Methods of combining primary studies**
A meta-analysis was conducted to estimate the sensitivity and specificity of NAAT. Weighted average values were calculated. The methods used to combine other estimates from the primary studies were not reported.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The sensitivity of NAAT was 91.3% (range: 74.1 - 96.4) and the specificity was 99.1% (range: 96.9 - 100).

The probability values were:

65% (range: 58 - 68) for chlamydia transmission from male to female,

55% (range: 19 - 90) for partner treatment,
5.2% (range: 3 - 5.2) for epididymitis,
8.7% for inpatient treatment of epididymitis,
35% (range: 30 - 41) for PID,
60% for the proportion of PID that is silent and 40% for the proportion of PID that is overt,
12.1% (range: 5 - 25) for inpatient treatment of PID,
18% for chronic pelvic pain,
6% (range: 3.6 - 9.1) for ectopic pregnancy,
9% (range: 7.7 - 20) for infertility, and
22.4% for infertile women seeking fertility services.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the number of PID cases prevented with each screening strategy relative to no screening. Other model outputs were the number of cases of chronic pelvic pain, ectopic pregnancy, infertility in past and future female partners, and epididymitis in index males.

**Direct costs**
An annual discount rate of 3% was applied since the time horizon of the model was 10 years. The unit costs and the quantities of resources used were reported separately for most items. The health services included in the economic evaluation were the costs of screening and treatment, such as tests, visits, inpatient stay and medications. Cost-savings from sequelae prevented were also considered. The cost/resource boundary of the health care system was adopted. The resource use data were estimated on the basis of the authors' experience and probability values derived from the review of the literature. The costs came from several sources, such as Medicare reimbursement rates, local medical centres, Massachusetts state and published studies. Cost-to-charge ratios were applied when charge data were used. A time-and-motion study was conducted to estimate the labour costs associated with collecting urine specimens and performing the ULE test. All the costs were adjusted to 2002 values. The total costs were calculated using modelling.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate and bivariate sensitivity analyses were carried out to address variability in the data. A threshold analysis was conducted to determine the prevalence of chlamydia infection above which cost-savings were generated by each of the two screening strategies. Either the ranges used were derived from the literature, or confidence intervals were used.

**Estimated benefits used in the economic analysis**
Compared with no screening, in the hypothetical cohort of 4,000 males, selective screening prevented 62 cases of PID, 11 cases of chronic pelvic pain, 4 cases of ectopic pregnancy, 6 cases of infertility in past and future female partners, and 6 cases of epididymitis in index males. Compared with selective screening, universal screening prevented 37 cases of PID, 7 cases of chronic pelvic pain, 2 cases of ectopic pregnancy, 3 cases of infertility in past and future female partners, and 3 cases of epididymitis in index males.

Cost results
In the hypothetical cohort of 4,000 males, selective screening saved $59,000 in comparison with no screening and universal screening saved $29,000 in comparison with selective screening.

Synthesis of costs and benefits
An incremental analysis was performed to combine the costs and benefits of the screening strategies.

Selective screening dominated the option of no screening since it prevented more PID cases and was less costly. Universal screening dominated selective screening since it prevented more PID cases and was less costly.

The threshold analysis showed that universal screening was the most cost-effective strategy for chlamydia prevalence as low as 2.8% or higher. Selective screening remained cost-saving for a prevalence as low as 1.7%.

The sensitivity analysis revealed that the results of the model were sensitive to the cost of NAAT, the number of female partners, the rate of PID development, PID sequelae cost, and the sensitivity of the ULE test.

Selective screening became the most cost-saving strategy when the sensitivity and specificity of the ULE test were above 78% and 83%, respectively.

Authors’ conclusions
Universal chlamydia screening with the urine-based nucleic acid amplification test (NAAT) was a cost-effective strategy for the population of adolescent males entering detention.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. No screening was selected to reflect current practice, while the screening strategies under investigation both represented feasible strategies for adolescents at risk of chlamydia infection. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data derived from the literature. Some estimates were obtained from a well-conducted review of the literature, and the data were combined using a meta-analysis. However, other estimates came from primary studies that were identified selectively and were not described. Therefore, it was difficult to evaluate the validity of the sources used. Other data came from the authors’ experience in two detention centres. The information was based on case series and no control group was used. In addition, the descriptive nature of the study limited the validity of the data. However, the authors conducted extensive sensitivity analyses on all model inputs, which were varied within plausible ranges. This enhanced the validity of the estimates used in the decision tree.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the interventions considered in the study. Hence, it would be difficult to compare with the benefits of other health care interventions. The use of more generalisable measure would have been interesting. The benefits were not discounted. All model outputs were reported.
Validity of estimate of costs
The authors reported clearly the perspective adopted in the study and it would appear that all the relevant categories of costs were considered. The price year was reported, which makes reflation exercises in other settings easy. The source of the data was reported for each item, as well as the unit costs. The costs were treated deterministically but were varied in the sensitivity analysis, which identified the key variables. Discounting was relevant and was conducted. A cost-to-charge ratio was applied to estimate the true costs. Reimbursement rates were assumed to be appropriate proxies for costs.

Other issues
The authors compared their findings with those from other studies, and noted the differences between their study and other economic evaluations. The authors discussed the reasons for different conclusions reached in the other studies. In terms of the generalisability of the results to other settings, the authors noted that their analysis referred to a very specific population. Caution is therefore required when extrapolating the conclusions of the analysis to non-detained male adolescents. The authors stressed that their results depended on the estimates derived from the literature, which could vary across different settings. However, the conclusions of the study were robust, as shown in the sensitivity analysis.

Implications of the study
The study results suggested that screening detained males at risk of chlamydia infection should be conducted routinely. In addition, it represents a public health opportunity to reduce the adverse clinical outcomes and costs associated with sexually transmitted diseases.

Source of funding
Supported by the National Institute of Allergy and Infectious Diseases (grant number 5 K23 A101750), the Charles H Hood Foundation (Child Health Research Grant) and the University of Massachusetts Center for AIDS Research Clinical Investigation Core (AI42845).

Bibliographic details
PubMedID
14743071
DOI
10.1097/01.OLQ.0000109517.07062.FC
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM
MeSH
Adolescent; Adolescent Behavior; Adolescent Health Services /economics; Chlamydia Infections /epidemiology /prevention & control /urine; Chlamydia trachomatis /isolation & purification; Cost-Benefit Analysis; Decision Support Techniques; Decision Trees; Humans; Male; Mass Screening /economics /methods; Massachusetts /epidemiology; Prevalence; Prisoners; Urinalysis /economics /utilization