A comparison of cost-effectiveness of three protocols for diagnosis and treatment of gonococcal and chlamydial infections in women in Africa

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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
Diagnostic techniques and treatments for gonococcal and chlamydial infections were compared. The diagnostic techniques were 'gold' standard (GS) methods, syndromic management (SM; treatment provided for the most likely organisms responsible for the observed signs and symptoms), and either community-wide or targeted mass treatment (MS). The GS methods were stated to be laboratory diagnostic techniques such as ligase chain reaction (LCR) and polymerase chain reaction (PCR). The two treatments were azithromycin and doxycycline.

Type of intervention
Primary prevention and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 1 million hypothetical South African women of reproductive age (15 - 45 years).

Setting
The setting was the community. The economic study was carried out in South Africa due to the high prevalence of sexually transmitted diseases (STDs) and the relative availability of data in the literature.

Dates to which data relate
The effectiveness data were obtained from studies published between 1986 and 2002. The costs were estimated from studies published between 1995 and 2002, and were inflated to 2002 prices. Resource use was determined within a decision analytic model.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A decision tree model was created to estimate the cost-effectiveness of the three protocols, using 10,000 Monte Carlo simulations. The model was created with DATA (version 3.0; TreeAge Software), Microsoft Excel (version 7.0) and Crystal Ball 2000 (Decisioneering).

Outcomes assessed in the review
The review assessed the following probabilities for inclusion in the model:
the prevalence of N. gonorrhoea (NG) (low-risk population);
the prevalence of C. trachomatis (CT) (low-risk population);
the relative risk of CT, given NG-positive;
the percentage of women having symptoms, given NG- or CT-positive;
the percentage of non-STD vaginal discharge;
the percentage of women seeking treatment for NG or CT infection (among women who are symptomatic);
the percentage of NG- or CT-positive, but symptom-negative, women seeking care for other services or complaints in the last month;
the probability of treatment efficacy with doxycycline (imperfect compliance);
the probability of treatment efficacy with azithromycin (single dose);
the probability of spontaneous cure of NG or CT;
the probability of MT coverage;
the sensitivity and specificity of SM;
the sensitivity and specificity of GS treatment (culture and PCR or LCR of endocervical specimens).

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

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Where it was not possible to find reliable data for South Africa, the authors used data relating to sub-Saharan Africa or used estimates from other STD models.

**Number of primary studies included**
Thirty-three primary studies were included in the review.

**Methods of combining primary studies**
Where the authors observed differences in estimates they used one of three methods to derive a single estimate. They chose preferred data from relatively larger and more recent studies, estimated a median representative value, or counted on the general estimates used in published STD models.

**Investigation of differences between primary studies**
Results of the review
The following probabilities were estimated for the model:

the prevalence of NG (low-risk population) was 0.04 (range: 0.03 - 0.08);
the prevalence of CT (low-risk population) was 0.08 (range: 0.05 - 0.16);
the relative risk of CT, given NG-positive, was 2.00 (range: 1.25 - 4.00);
the percentage of women having symptoms, given NG or CT positive, was 0.35 (range: 0.10 - 0.64);
the percentage of non-STD vaginal discharge was 0.17 (range: 0.05 - 0.35);
the percentage of women seeking treatment for NG or CT infection (among women who are symptomatic) was 0.70 (range: 0.11 - 0.77);
the percentage of NG- or CT-positive, but symptom-negative, women seeking care for other services or complaints in the last month was 0.15 (range: 0.08 - 0.25);
the probability of treatment efficacy with doxycycline (imperfect compliance) was 0.86 (range: 0.80 - 0.90);
the probability of treatment efficacy with azithromycin (single dose) was 0.96 (range: 0.94 - 0.98);
the probability of spontaneous cure of NG or CT was 0.25 (range: 0.15 - 0.50);
the probability of MT coverage was 0.85 (range: 0.75 - 0.90);
the sensitivity of SM was 0.70 (range: 0.12 - 0.89) and the specificity was 0.55 (range: 0.30 - 0.94);
the sensitivity and specificity of GS treatment (culture and PCR or LCR of endocervical specimens) were both 0.95 (range: 0.90 - 0.99).

Measure of benefits used in the economic analysis
The summary measure of benefit was the number of women cured with treatment. The number of overtreated women was also calculated for each strategy.

Direct costs
The costing was carried out from the perspective of the health care system. It focused on the costs of treating STDs, drugs to treat NG or CT infection, personnel and diagnostic tests. The authors focused on the incremental costs of the protocols. The costs were obtained from a review of the literature and were annualised. The costs were estimated from studies published between 1995 and 2002, and were inflated to 2002 prices using the US Consumer Price Index. The unit costs were reported separately. Resource use was determined within a decision analytic model. Discounting was not reported. It was not possible to assess whether discounting was necessary since a time horizon for the model was not reported, although the authors did suggest that the horizon was "limited".

Statistical analysis of costs
A total of 10,000 Monte Carlo simulations were run using triangular distributions with upper and lower extremes for parameter estimates.
Indirect Costs
Some indirect costs were included when estimating the personnel costs. The costs to the patient were not included.

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were used to assess the impact of different costs and probabilities. Multivariate analyses were used to assess the robustness of the cost-effectiveness estimates to changes in the underlying assumptions.

Estimated benefits used in the economic analysis
When treated with doxycycline, the number of women cured was 33,601 (range: 9,127 - 83,990) under the GS protocol, 20,295 (range: 2,208 - 64,272) under SM, and 100,958 (range: 56,129 - 167,608) under MT.

When treated with azithromycin, the number of women cured was 37,796 (range: 9,739 - 94,001) under the GS protocol, 22,826 (range: 2,432 - 74,655) under SM, and 113,577 (range: 63,739 - 186,626) under MT.

The number of overtreated women was 4,668 for the GS strategy, 34,618 for the SM strategy, and 691,381 for the MT strategy.

Cost results
The total cost of treatment with doxycycline was $3,231,252 (range: 745,089 - 7,051,323) under the GS protocol, $1,293,520 (range: 215,643 - 2,858,974) under SM, and $5,833,336 (range: 5,265,966 - 6,291,881) under MT.

The total cost of treatment with azithromycin was $3,295,595 (range: 778,357 - 7,357,010) under the GS protocol, $1,555,913 (range: 331,990 - 3,562,442) under SM, and $9,583,337 (range: 8,651,230 - 10,336,661) under MT.

The total costs of the GS protocol and SM were sensitive to the percentage of women seeking STD treatment and the prevalence of non-STD vaginal discharge. The total cost of MT was sensitive to the coverage rates.

Synthesis of costs and benefits
Average cost-effectiveness ratios were calculated. These compared the costs and effects of each strategy with "do nothing".

The total cost per NG or CT cured with doxycycline treatment was $99 (range: 39 - 337) under the GS protocol, $73 (range: 22 - 535) under SM, and $60 (range: 36 - 99) under MT.

The total cost per NG or CT cured with azithromycin treatment was $92 (range: 39 - 313) under the GS protocol, $78 (range: 25 - 428) under SM, and $87 (range: 53 - 143) under MT.

Authors' conclusions
The optimal diagnostic and treatment protocol depended on the specific characteristics of the relevant population. The authors pointed out the populations in which each of the protocols would be optimal. They suggested that "as it becomes clear that solutions are complex and multifaceted, different combinations of intervention protocols are being supported".

CRD COMMENTARY - Selection of comparators
The authors compared GS, SM and MT strategies. These alternatives were justified through a discussion of the relative
merits and problems associated with each. GS use of laboratory diagnostic techniques seemed to be standard practice.

**Validity of estimate of measure of effectiveness**
The authors reported that they carried out an extensive review of the literature, but they did not claim that this was systematic. Three different methods were used to combine the estimates from the primary studies. These were choosing a preferred point estimate from a larger or more recent study, estimating a median value, or using estimates from published models. The authors clearly showed which references were used in estimating a specific parameter value, but their summary estimate did not adopt a weighting method to reflect differences in sample size. The authors carried out sensitivity analyses to estimate the impact of differences between the primary studies.

**Validity of estimate of measure of benefit**
The number of women cured with treatment was the summary measure of health benefit. This estimate was obtained through the decision model, which was appropriate for the clinical question posed.

**Validity of estimate of costs**
The costing was carried out from the perspective of the health care system. The analysis seems to have included all the costs relevant to this perspective. Although the authors provided a range for the costs, they did not estimate any confidence intervals. This makes it more difficult to assess whether changes in cost may alter the principle results and conclusions. Since the ranges for total cost and cost per NG or CT cured overlap between diagnostic protocols and treatment, omissions in cost may well affect the results. The authors discussed, for instance, that including the cost of HIV/AIDS infections might impact on the results. The unit costs were reported separately from the quantities.

**Other issues**
The authors made appropriate comparisons of their results with those from other studies. The issue of generalisability was addressed. In particular, the model structure could be used and repopulated to estimate the costs and effects in potentially any situation. There was an explicit discussion of the generalisability of the analysis to the male population. The authors explained that they only presented the results for the multivariate analyses. However, they did highlight areas of similarity and difference with the results that were not reported. The authors' conclusions accurately reflected the scope of the study. A number of limitations, which focused on omissions from the model, were presented. For example, the costs incurred by individuals and households, and the possibility of reinfection.

**Implications of the study**
The authors recommended that the chosen diagnostic and treatment protocol should depend on the specific population under consideration. In addition, a "thorough analysis of how the algorithm functions in specific well-defined circumstances is essential in making the final decision about whether to use syndromic management". The need for further research was clearly evident in these recommendations.

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