Diagnosis and management of pharyngitis in a pediatric population based on cost-effectiveness and projected health outcomes

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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 compared six management strategies for Group A haemolytic streptococcal (GAS) pharyngitis.

Strategy 1 was to use antibiotics to treat all patients with pharyngitis without testing.

Strategy 2 was to observe all patients without providing testing or treatment.

Strategy 3 was to test all patients with pharyngitis using a rapid antigen test, then to treat those with positive test results with antibiotics.

Strategy 4 was to test all patients with pharyngitis with a throat culture, then to treat all patients with positive test results with antibiotics.

Strategy 5 was to test all patients with pharyngitis with a rapid antigen test, use a culture test for all negative results, and treat patients with positive test results with antibiotics.

Strategy 6 was the use a clinical scoring system to triage in order to decide on the diagnostic or treatment approach. This strategy implied that patients with a low score were disregarded, patients with an intermediate score were tested and those with positive results received antibiotic treatment, and patients with a high score were treated without being tested.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-utility analysis.

Study population
This was a modelling study. The target population comprised children and adolescents who presented to the physician with pharyngitis. No further inclusion or exclusion criteria were reported.

Setting
Although the setting was not explicitly stated, it appears to have been primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness evidence was taken from studies published between 1961 and 2004. The resource use data in relation to productivity losses were taken from sources published in 2003. The cost data were taken from sources published between 1990 and 2005. All costs were reported for the price year 2003.
**Source of effectiveness data**
The effectiveness data were derived from a review and synthesis of published data, augmented by authors’ assumptions.

**Modelling**
The authors constructed a decision tree to model the overall costs and utility for each of the six strategies. The time horizon was unclear.

**Outcomes assessed in the review**
The following input parameters were used in the model:

- the probability of developing peritonsillar abscess (PTA);
- the probability of developing acute rheumatic fever (ARF);
- the probability of a side effect of antibiotics (mild, severe and death);
- the effectiveness of antibiotic treatment;
- the incidence of GAS in the general population;
- the incidence of having a score of 0 or 1, 2, 3 or 4 according to the modified Gentor scoring system;
- the incidence of a clinical score of 2, 3 or 4;
- the sensitivity and specificity of culture; and
- the sensitivity and specificity of the rapid test.

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

**Sources searched to identify primary studies**
The authors searched PubMed for primary studies. References in the bibliographies of the reviewed articles were also checked.

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

**Methods used to judge relevance and validity, and for extracting data**
The validity of the primary studies does not appear to have been assessed.

**Number of primary studies included**
Overall, the authors used 15 primary studies as sources of effectiveness evidence.

**Methods of combining primary studies**
The primary studies do not appear to have been combined.
Investigation of differences between primary studies
The authors do not appear to have investigated differences between the primary studies.

Results of the review
The probability reaction to antibiotics was 0.02 (95% confidence interval, CI: 0.007 to 0.04) for mild reaction and 0.0064 (95% CI: 0.0025 to 0.0075) for severe reaction.

The probability of death due to antibiotics was 0.00001 (95% CI: 0.000005 to 0.000015).

The effectiveness of antibiotic treatment was 0.80 (95% CI: 0.70 to 0.90).

The incidence of GAS in the general population was 0.26.

The incidence of having a score according to the modified Gentor scoring system was 0.05 (95% CI: 0.02 to 0.10) for score of 0 or 1, 0.2045 (95% CI: 0.1203 to 0.2888) for score 2, 0.2754 (95% CI: 0.2227 to 0.3280) for score 3 and 0.6778 (95% CI: 0.5812 to 0.7743) for score 4.

The incidence of a clinical score was 0.14 (95% CI: 0.1192 to 0.1761) for score 2, 0.4631 (95% CI: 0.4231 to 0.5031) for score 3 and 0.151 (95% CI: 0.1223 to 0.1798) for score 4.

The sensitivity of culture was 0.834 (95% CI: 0.77 to 0.93) and the specificity was 0.99 (95% CI: 0.95 to 0.995).

The sensitivity of the rapid test was 0.891 (95% CI: 0.80 to 0.95) and the specificity was 0.95 (95% CI: 0.90 to 0.99).

Methods used to derive estimates of effectiveness
The authors made assumptions to derive some estimates of effectiveness.

Estimates of effectiveness and key assumptions
The authors assumed that the probability of developing PTA was 0.015 (95% CI: 0 to 0.03), and the probability of developing ARF was 0.00000656 (95% CI: 0 to 0.000328).

Although the authors' assumptions were not fully justified, they were referenced to the medical literature.

Measure of benefits used in the economic analysis
The authors used health utility (i.e. quality-adjusted life-days, QALDs) as the measure of benefit in the economic analysis. The utility values were taken from published studies. Utility values and relevant CIs were estimated using the General Health Policy Model and the Quality of Well-being Scale. The states assigned a utility value were PTA, ARF, death, mild and severe penicillin reaction, rheumatic heart disease, untreated GAS, after rapid test and after culture.

Direct costs
Health service costs were included in the analysis. These covered the costs of treating PTA and ARF, drugs (penicillin and cephalosporin), diagnostic tests (throat culture and rapid antigen test), death (approximation of medical costs incurred before death), mild and severe reaction to penicillin, rheumatic heart disease and follow-up by telephone call. The authors reported summary costs for the cost of treatments, whereas unit costs were only reported for drugs and diagnostic tests. The cost data were taken from published sources. All costs were appropriately adjusted for inflation and reported for the price year 2003. Discounting was also conducted.

Statistical analysis of costs
The cost data were reported as mean values with 95% CIs. Further statistical analysis of the costs was not undertaken.
Indirect Costs
Productivity losses were included in the analysis. Work time lost due to various conditions (e.g. GAS untreated, immediate treatment, delayed treatment, death, ARF, rheumatic heart disease, and mild and severe penicillin reaction) was multiplied by the equivalent parental wage. Hourly parental wages were taken from official published sources, while resource use was partly based on published studies and on authors' assumptions. No justification for these assumptions was provided. The costs and the quantities were reported separately. All costs were appropriately adjusted for inflation and reported for the price year 2003.

Currency
US dollars ($).

Sensitivity analysis
One-way sensitivity analyses were conducted on all model parameters to investigate the robustness of the results to changes in the input parameters. Tornado diagrams were also used to show the impact of the range of each variable on the model's results. The most influential parameters were further investigated in two- and three-way sensitivity analyses in order to determine threshold values for these parameters. The analysis was also performed from the health care payer perspective. CIs for costs and utilities for each strategy were calculated using a Monte Carlo simulation with 10,000 repetitions. The analyses were performed using DATA 3.5 for Healthcare for Windows (TreeAge Software, Williamstown, MA).

Estimated benefits used in the economic analysis
From a societal or health care payer perspective, penicillin treatment on Medicaid or private insurance reimbursement rates produced QALDs that ranged from 0.0512 when none of the patients received treatment to 0.3103 QALDs when all patients were treated. The rapid testing approach resulted in 0.0953 QALDs, testing all patients with culture resulted in 0.0930 QALDs, rapid test followed by culture for those with negative results resulted in 0.0998 QALDs, and clinical scoring resulted in 0.1257 QALDs.

From a societal perspective, cephalosporin treatment at private insurance or Medicaid reimbursement rates produced utility benefits that ranged from 0.0512 QALDs when none of the patients received treatment to 0.3072 QALDs when all patients were treated. The rapid testing approach resulted in 0.0926 QALDs, testing all patients using culture resulted in 0.0911 QALDs, rapid test followed by culture for those with negative results resulted in 0.0970 QALDs, and the clinical scoring strategy resulted in 0.1241 QALDs.

Cost results
The total costs per patient were reported.

When a societal perspective was adopted, the strategy of no treatment was the most costly, resulting in a cost of $79.1269 per patient. Clinical scoring resulted in lower costs when the treatment strategy with penicillin using private reimbursement was implemented. It resulted in a cost of $48.2950 per patient. When treatment (cephalosporin or penicillin) was administered using Medicaid reimbursement, the strategy that tested all patients with culture proved the least expensive, resulting in a cost of $40.7639 with penicillin and $37.0156 with cephalosporin.

From the health care payer perspective, the "no treatment" strategy was the least expensive strategy, resulting in a cost of $6.9189 per patient. The strategy of treating all patients was the most expensive, resulting in a cost that ranged from $43.5274 per patient with penicillin to $53.1723 per patient with cephalosporin.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was performed. This demonstrated that, from a societal perspective, testing reimbursed at Medicaid rates and treatment for all patients was dominated by clinical scoring, rapid test, culture, and rapid test followed by culture. Performing a throat culture on all patients was the dominant approach compared with all
other strategies.

From a societal perspective, testing reimbursed at private insurance rates and treatment for all patients, or the rapid test followed by culture testing, were dominated. It was reported that moving from the scoring approach to the rapid test strategy, which had lower morbidity rates, would incur a cost of $32,132.01 per QALY. The analysis was based on the assumption that a strategy is preferred when it results in better health outcomes and incurs a cost of less than $200,000 per QALY. To move from the rapid test option to the option of culture for all patients would result in a cost of $1,677,492.39 per QALY, while to move to the no testing option would result in a cost of $233,034.71 per QALY.

From the health care payer perspective, the rapid test option for all patients had the best cost-utility.

Tornado diagrams demonstrated that the incidences of PTA and ARF after untreated GAS pharyngitis were the most influential parameters.

The one-way sensitivity analyses demonstrated that the results were most sensitive to the cost of throat culture. If its cost was below $17.3 then throat culture for all patients demonstrated the best cost-utility.

Two-way sensitivity analyses investigated the impact of the cost of throat culture and the cost of a rapid test. These demonstrated that when the cost of both tests was low, rapid test followed by culture became the preferred strategy.

From a societal perspective, cephalosporin resulted in lower costs and morbidity rates in the clinical scoring, rapid test, culture for all patients, and rapid test followed by culture strategies.

The Monte Carlo analysis demonstrated that the "no treatment" option incurred higher costs, (p<0.05), compared with scoring, rapid test, culture for all, and rapid test followed by culture.

Providing treatment for all patients resulted in higher morbidity compared with all other options, (p<0.05), while the no treatment strategy resulted in lower morbidity, (p<0.05).

Authors' conclusions
From a health care payer perspective, the "no testing and no treatment" strategy resulted in the lowest morbidity and lower costs. The rapid antigen testing approach had the best cost-utility ratio. From a societal perspective, observing patients with pharyngitis resulted in the lowest morbidity rate while the approach of testing all patients using throat culture demonstrated a better cost-utility ratio.

CRD COMMENTARY - Selection of comparators
An innovative feature of the study was that it used a no-testing and no-treatment scenario as the comparator. This allowed the active value of the remaining strategies to be evaluated. All strategies were chosen with reference to current clinical practice in the authors' setting. You should decide if this represents valid technology in your own setting.

Validity of estimate of measure of effectiveness
A systematic review was not undertaken. The designs of the studies included were not discussed, the validity of the studies was not evaluated, and differences between the primary studies were not been investigated. The authors appear to have used data from the available studies selectively. However, extensive sensitivity analyses were performed on all model parameters, using ranges that appear to have been appropriate. Sensitivity analyses improved both the internal validity of the study and the generalisability of its findings. The authors' assumptions were not clearly justified, although they were made with reference to the medical literature.

Validity of estimate of measure of benefit
The authors used health utility (QALDs) as the measure of benefit in the economic analysis. The utility values were taken from the literature. The valuation tool and values assigned to each condition were reported.
Validity of estimate of costs
The costs were analysed from both a societal perspective and that of a health care payer. It appears that all the relevant costs have been included in the analysis. However, the costs and the quantities were not reported separately which will hinder the reworking of the analysis in other settings. The costs were derived from published sources. Some estimates of parental work time lost were based on authors' assumptions, although the authors provided no justification for their assumptions. Although the costs were treated deterministically, extensive sensitivity analyses were conducted to assess the robustness of the estimates used. The ranges applied in the sensitivity analyses appear to have been appropriate. Adjustments for inflation, discounting, and the price year were all reported.

Other issues
The authors compared their findings with those from other studies and mainly attributed differences in the results to differing study methodologies. The issue of the generalisability of the results to other settings was not directly addressed, although extensive sensitivity analyses were performed. These enhance the generalisability of the study findings. The authors do not appear to have presented their results selectively. The study involved patients presenting at a general practice with pharyngitis and this was reflected in the authors' conclusions. As a limitation to the study, the authors acknowledged that their assumptions about the incidence of PTA and ARF may not reflect true incidence rates.

Implications of the study
The authors appeared somewhat reluctant to make recommendations for changes in policy or practice, owing to the lack of accurate estimates around the probability of developing ARF and PTA when GAS pharyngitis remains untreated. They recommend that future research should provide rigorous estimates on these parameters.

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Other publications of related interest
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