Are follow-up throat cultures necessary when rapid antigen detection tests are negative for Group A streptococci?

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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 use of a diagnostic procedure, rapid antigen detection (RAD), for the detection of group A streptococcal (GAS) pharyngitis.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised children presenting to the practice with pharyngitis.

Setting
The setting was a private practice. The economic study was conducted at the Elmwood Pediatric Group, Rochester (NY), USA.

Dates to which data relate
The effectiveness and resource use data were gathered during January 1996 and October 1997 (period 1) and November 1997 and May 1999 (period 2). No price year was reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations to determine the sample size were not performed. A sample of eligible children presenting at the study centre from January 1996 through May 1999 were included in the study. Only patients with a negative RAD test were considered. In total, 11,427 RAD tests were performed during the overall study period. There were 4,847 tests conducted in period 1, of which 3,548 (73.2%) were negative. There were 6,580 tests performed in period 2, of which 4,837 (73.5%) were negative. No test was excluded from the initial sample.
Study design
This was a retrospective case-control study that was performed in a single centre. Patients in the intervention and control groups were enrolled during two different time periods. In period 1, RAD tests were not used for all patients with pharyngitis. However, in period 2, RAD tests were used as the primary test for GAS in all children presenting to the practice. About 98.2% of the patients were followed up with throat cultures after RAD.

Analysis of effectiveness
The analysis of effectiveness was limited to the patients followed up with throat cultures. The primary health outcome was the number of negative RAD tests, which were positive with the throat culture (rate of false-negative RAD test results).

Effectiveness results
The overall rate of false-negative RAD test results was 2.4% during the three-year period.

The age profile for these patients was as follows:

17% (34 children) for those under 5 years of age;
60.5% (121 children) for those in the 5 to 12-year age class;
and 17% (34 children) for those older than 12 years.

Fifty-five per cent were boys, and 5% (10 children) had repeat infections during the study period.

The rate of false-negative RAD test results was higher in period 1 (3.8%; 95% confidence interval, CI: 0.5 - 6.9) than in period 2 (1.4%, 95% CI: 0 - 4.2). The difference was statistically significant, (p=0.001).

The authors stated that, although different test kits were used during the study, no statistically significant difference was found in the number of false-negative results according to the kit used.

Clinical conclusions
The effectiveness analysis showed that the rate of false-positive results with the RAD test was small, and could challenge the use of LTC as the ‘gold’ standard for the detection of GAS infection. The use of the RAD test for all eligible patients would further reduce the rate of false-positive results.

Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used. A cost-consequences analysis was therefore carried out.

Direct costs
Discounting was not performed as the costs for each patient were incurred over a short period of time. The unit costs and the quantities of resources were not reported separately. The economic analysis included the costs to the private practice for unreimbursed culture verification, such as materials, labour, controls, culture result notification, calling in prescription to pharmacies, and overheads. It also included the costs to patients for treatment following a negative RAD test but positive throat culture, that is, the cost of penicillin treatment and the costs due to penicillin rashes and anaphylaxis. The costs of medical complications, which were inappropriately not followed with throat culture (such as acute rheumatic fever and suppurative complications), were also included in the analysis. The cost/resource boundary adopted in the analysis was unclear, but only the direct medical costs relevant to the private practice and the patient were included in the economic analysis. The cost data for most items were obtained from the study practice, with the exception of complications, the costs of which were estimated from a study published in 1999. All the costs were reported as yearly prices, assuming that 3,090 negative RAD tests were observed and 43 patients had a false-negative
test during period 2. The resource use was presumably estimated during the three-year period. No price year was reported.

Statistical analysis of costs
No statistical analysis of the costs was conducted.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The yearly costs for unreimbursed culture verification were $13,521.

The yearly costs for treating children after a negative RAD test but positive throat culture were $422.

The yearly costs for treating complications were $824.

Synthesis of costs and benefits
Irrelevant as a cost-consequences analysis was conducted.

Authors' conclusions
Culture confirmation of rapid antigen detection (RAD) test-negative results may be unnecessary in children with pharyngitis, due to the low rate of false-negative results when all patients are tested. The economic analysis showed that substantial cost-savings may be realised from eliminating follow-up throat cultures, as a confirmation of negative RAD test results, from the point of view of the private practice and the patient. The cost of complications for undetected infections was fairly low.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators. LTC represented the 'gold' standard for the diagnosis of GAS, while the RAD test was a simpler and faster procedure used in their setting. The RAD results were available in minutes instead of the 24 hours for throat culture. You should decide whether the comparators are widely used interventions in your own setting.

Validity of estimate of measure of effectiveness
The estimate of the effectiveness measure was derived from a retrospective case-control study, which appears to have been appropriate for the study question. However, the comparability of the study groups was not reported, and the demographics of the patients were not given. In addition, the effectiveness evidence was collected during two different
periods, and thus the possibility of external factors affecting the outcome results cannot be excluded, although the impact of using different test kits was assessed. Bias and confounding factors cannot be excluded due to the lack of randomisation. These issues tend to limit the internal validity of the analysis.

**Validity of estimate of measure of benefit**
No summary benefit measure was used in the economic analysis since a cost-consequences analysis was conducted.

**Validity of estimate of costs**
The cost/resource boundary of the analysis was unclear, although it appears likely that the authors took different perspectives. The unit costs were not reported separately from the quantities of resources and the price year was not given. This makes it difficult to reproduce the analysis in other contexts. Some of the cost data were derived from a published study. The costs were treated deterministically and no sensitivity analyses were performed.

**Other issues**
The authors did not compare their findings with those from other studies. In terms of the generalisability of the study results to other settings, the authors stated that the study results should be extrapolated with caution due to variations in disease prevalence, personnel experience and the RAD test used. The study enrolled children with pharyngitis, and this was reflected in the conclusions of the analysis.

**Implications of the study**
The main implication of the analysis is that throat culture confirmation of negative RAD test results for GAS infection is generally unnecessary. However, it may be of importance to some subpopulations of children with pharyngitis, such as those with a history of rheumatic fever or the family of patients with rheumatic fever.

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**Other publications of related interest**

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