Predictive value and cost-effectiveness analysis of a rapid polymerase chain reaction for preoperative detection of nasal carriage of Staphylococcus aureus


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 health technology that motivated this study was the rapid polymerase chain reaction (PCR) used by the LightCycler assay (Roche Diagnostics, Indianapolis) for nasal carriage detection of Staphylococcus aureus (S. aureus) in the preoperative setting.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
Nasal swabs from consecutive patients scheduled for a cardiothoracic surgery were included.

Setting
The setting was tertiary care (a hospital). The economic study was carried out in Cleveland (OH), USA.

Dates to which data relate
The dates to which the effectiveness evidence for diagnostic test characteristics related were not reported. The costs used included references from 2001-2002. The price year was not stated.

Source of effectiveness data
The effectiveness data were derived from a single study and estimates based on opinion.

Link between effectiveness and cost data
The costs used were derived partially from the study institution and partially from published references, but they do not appear to have been derived from the same sample of patients as that used in the study.

Study sample
A trained nurse obtained consecutive nasal specimens with cotton tipped swabs from 293 patients attending the cardiothoracic preoperative clinic in a semester. Two nasal samples were obtained from each patient, one for PCR and the other for culture. The study did not report any sample size calculations. It was also not stated whether there were any patients who met the inclusion criteria but were not included.
Study design
This was a diagnostic cohort study that was performed in one tertiary care centre. It was not reported whether both tests were performed independently or were assessed in a blinded manner. Both tests were performed on all 293 patients. Discordant results were determined as positive or negative by a third test, using a peptic nucleic acid fluorescence in situ hybridisation assay. In effect, this was used as the 'gold' standard.

Analysis of effectiveness
The primary aims of the cross-sectional study were to determine the operating characteristics (sensitivity and specificity) of PCRs and predictive values for the prevalence detected, as well as other possible prevalence using Bayes theorem.

Effectiveness results
The prevalence of S. aureus carriage was 28% (67 patients). PCR was 97.0% sensitive and 97.1% specific for the detection of S. aureus on nasal swabs. At that prevalence, the positive predictive value (PPV) of PCR was 92.86% and the negative predictive value (NPV) was 98.82%.

PPVs and NPVs were determined for different prevalence of nasal carriage. For example, at a prevalence of 10%, the PPV was 78.8% and the NPV was 99.7%, while at a prevalence of 50%, the PPV was 97.1% and the NPV was 97.0%.

There were 10 discordant specimens between PCR and culture that were tested by in situ hybridisation.

Clinical conclusions
Rapid real-time PCR is an accurate method for identifying S. aureus carriers, with NPVs greater than 97% for prevalence up to 50%.

Modelling
A simple decision analytic model was developed, using Data TreeAge software (version 4.0), to compare the five strategies in terms of their costs and the length of time until adequate treatment.

Measure of benefits used in the economic analysis
The measure of benefit used was the length of delay until initiation of adequate treatment between the strategies. This was calculated as 3 minus the delay (in days) to make the decision to initiate mupirocin therapy. The authors chose this measure as 3 days was the longest time expected for culture results to be reported.

Direct costs
The hospital costs were included in the analysis. These consisted of individual PCR samples, cultures and a 5-day treatment course of mupirocin. The quantities and the costs were not reported separately, but the authors stated that cost components included current market prices of materials and labour costs of personnel time associated with specimen collection, preparation, and interpretation or reporting. In the case of PCR, they included the FastStart DNA kit, primers, reagents and other materials to process a sample, as well as labour costs. Due to the short-term horizon of the study, discounting of the future costs was appropriately not considered. The cost data were obtained from published references, while the costs of strategies were derived by modelling, using the diagnostic test characteristics data. The quantity/cost boundary considered was that of a hospital which currently has PCR and culture technology in place. For that reason, capital costs and depreciation related to PCR and culture equipment were not included. The price year was not reported and references ranged from 2001-2002.

Statistical analysis of costs
The costs were considered as deterministic estimates and no statistical analysis was performed.
Indirect Costs
The indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
The authors stated that one-way sensitivity analyses were performed for all variables. Those reported were for PCR and culture costs, time to perform PCR, and carriage of S. aureus prevalence. A two-way sensitivity analysis was reported to have been undertaken (simultaneously varying the proportion of positive cultures available at days one and two), but the results of this analysis were not reported. The range of costs were halved or doubled from the baseline value, but other ranges selected were not described in detail.

Estimated benefits used in the economic analysis
The effectiveness of the various strategies was 1.01 days for culture-guided therapy, 2.5 days for PCR-guided therapy, and 3 days for treat-PCR, treat-culture, and universal therapy. The incremental effectiveness of PCR-guided therapy compared with culture-guided therapy was 1.49 days quicker, while that of treat-PCR, treat-culture, and universal therapy were equal at 0.5 days quicker.

Cost results
The costs of the various strategies were $22.60 for culture-guided therapy, $25.10 for PCR-guided therapy, $28.60 for treat-PCR, $37.40 for treat-culture, and $49.40 for universal therapy.

The incremental cost of each strategy compared with the next most expensive was $2.50 for PCR-guided therapy compared with culture-guided therapy, and $3.50 for treat-PCR, $8.80 for treat-culture, and $20.80 for universal therapy.

Synthesis of costs and benefits
Two strategies (treat-culture and universal therapy) were dominated, as they were more costly and equally effective than their comparator. The incremental cost-effectiveness ratio of PCR-guided therapy was $1.64 per additional day gained compared with culture-guided therapy. The treat-PCR strategy had an incremental cost-effectiveness ratio of $6.98 per additional day gained compared with PCR-guided therapy.

In one-way sensitivity analyses, if the cost of PCR fell below $8.25, both PCR-related strategies dominated the culture-guided strategy. If the cost exceeded $19.62, both PCR-related strategies were dominated by the culture-guided treatment and treat-culture strategies. If the cost of culture exceeded $10.75, the culture-guided strategy became more expensive than PCR-guided treatment. If PCR results took more than 1.2 days, the culture-guided and treat-PCR strategies dominated PCR-guided treatment. Universal preoperative treatment became less costly than PCR and culture strategies if nasal carriage prevalence was more than 83%.

Authors' conclusions
Although culture-guided therapy was the least costly strategy, rapid real-time polymerase chain reaction (PCR) avoided delay in the initiation of treatment, and it was a rapid and cost-effective method for identifying individuals who do not need preoperative mupirocin treatment. A drawback of PCR strategies is that susceptibility testing is not available, which could be important in an unusual setting with high resistance.

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the diagnostic and treatment strategies evaluated. Broth enrichment was excluded because of its additional necessary costs and time but, as the authors stated, it could be relevant in settings where there is more time between preoperative assessment and surgery. You should judge if the comparators used are relevant in your own setting.

**Validity of estimate of measure of effectiveness**
In terms of the cross-sectional study design, the authors did not report whether both PCR and culture were performed independently or were assessed in a blinded manner. No sample size or power calculations were reported. Otherwise, the study appears to have been well conducted.

**Validity of estimate of measure of benefit**
The benefit measure selected was delay in starting treatment up to a maximum of 3 days (i.e. when culture results are available). You should judge if this benefit measure is relevant in your setting.

**Validity of estimate of costs**
The relevant cost categories appear to have been included given the perspective of the study. The quantities and the unit costs were not reported separately, thus limited extrapolation exercises to other settings. The price date was not reported, which could limit future inflation exercises in other settings. The authors did not include the costs of equipment and depreciation, but stated that the study results were valid for hospitals which currently have PCR and culture technology in place. Although the ranges selected were not explicitly justified, the ranges evaluated appear to have been reasonable.

**Other issues**
The authors stated that a two-way sensitivity analysis was undertaken, but it was not reported in the paper. Generalisability was addressed in terms of the important assumption of excluding equipment capital costs, with the authors stating that the current trend is towards increased use of molecular techniques. The authors stated that the results should also be applicable to other patient groups, not only those in cardiac surgery. The authors did not report their results selectively and their conclusions reflected the scope of the analysis.

**Implications of the study**
The authors proposed screening all patients for nasal carriage of S. aureus by rapid PCR preoperatively, using the results to target therapy. Owing to a potential increase in antimicrobial resistance, there is no reason to use antibiotics without prior testing for carriage. As the authors also stated, the interpretation of the incremental cost-effectiveness ratios used is subject to debate, and it depends on the acceptability of delaying treatment for a few days. These results should be interpreted with caution, as although topical mupirocin is effective in eradicating S. aureus nasal carriage, there is little evidence for this and further prospective research on the reduction of postoperative infection is needed. For institutions in which PCR technology is not available, the choice will be between culture-guided therapy (if cost is the major concern) and treat-culture (if time delay is the major concern).

**Source of funding**
None stated.

**Bibliographic details**