Effect of routine use of a multiplex PCR for detection of vanA- and vanB-mediated enterococcal resistance on accuracy, costs and earlier reporting

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 multiplex polymerase chain reaction (MPCR) for the detection of vancomycin-resistant Enterococci (VRE) infections.

Type of intervention
Other: laboratory testing.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised specimens (rectal swabs and stool samples) from patients admitted to the hospital with a history of hospitalisation within the last 6 months or direct transfers from another hospital, those transferred into identified high-risk units, and those identified as VRE positive.

Setting
The setting was a microbiology laboratory. The economic study was conducted in Hamilton, ON, Canada.

Dates to which data relate
No dates for the effectiveness and resource use data were reported. The price year was 1999.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was conducted prospectively. The resource data came from the experiment and the average price was calculated for that time.

Study sample
Power calculations, if performed, were not reported. Consecutive specimens obtained from 204 patients (1,196 specimens), and sent for VRE surveillance testing to the study centre over a 17-week period, were included in the analysis. The 466 specimens that presented black colonies on BEAA/Vanco6 screen plates were further processed for CBT and MPCR, thus forming the final sample under study. There was only one group as it was a paired test (both diagnostic tests were tried on each specimen).
Study design
This was a diagnostic cohort study in which two diagnostic tools were tested on the same samples taken from a single group of patients. The study was conducted in a single centre. The same technologists performed both the CBT and MPCR. MPCR was performed Monday through Friday, while CBT was conducted on a daily basis. Specimens with discordant results for the two tests were also analysed. This analysis included:

- MPCR re-testing of specimens from reserved DNA;
- a review of patient clinical records to determine the VRE status of prior or subsequent VRE screening specimens from the same patient;
- examination of gel electrophoresis results by a second objective reviewer;
- testing by PCR for vanC1 and vanC2/C3 mediated resistance; and
- examination of the original screen plate to determine the amount of black growth present and used for PCR amplification.

Analysis of effectiveness
All specimens included in the sample were accounted for in the clinical analysis. The outcomes used in the effectiveness analysis were positive and negative results of specimen analysis (sensitivity and specificity) for both CBT and MPCR, and the average time taken to produce the test results from the receipt of specimens (the turnaround time).

Effectiveness results
CBT identified 208 specimens as positive. MPCR identified 215 positive specimens, of which 205 were also identified by CBT.

MPCR failed to identify 3 CBT positive specimens, thus the sensitivity of MPCR was 98.6% (205 out of 208).

MPCR identified 10 additional positive results not detected by CBT, giving a specificity of 96.1% (248 out of 258) for MPCR.

In terms of the turnaround time, the first results by MPCR became available between 12 and 24 hours after they were received in the laboratory. The average turnaround time was 62.3 hours. The majority of the CBT results were available between 84 and 96 hours (average: 99.7 hours) after being received.

The authors noted that about 15% of the MPCR results were delayed for 24 to 48 hours because of the lack of MPCR testing at weekends.

There was no test for statistical significance.

The final interpretation of the status of the 13 discordant specimens was that the CBT results were correct. Consequently, the CBT results were taken to be 100% reliable. The sensitivity and specificity of MPCR were derived by comparing its results with those of CBT, as specified above.

Clinical conclusions
The effectiveness analysis showed that MPCR provided a rapid and reliable assay to detect VRE infections.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis. Thus, a cost-consequences analysis was conducted.
Direct costs
Discounting was not applied due to the short time horizon of the study. The unit costs were not reported separately from the quantities of resources. The cost items included were the average cost of the test per specimen for CBT and per specimen (assuming 6 specimens processed per day) for MPCR. The costs included reagents and labour (technologist time). The cost/resource boundary adopted in the study was not reported. The quantities of resources were estimated from review of CBT and MPCR data, which were derived from the effectiveness study. The costs were calculated on the basis of the workload levels reported in the study (about 300 specimens per months). The price year was 1999.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Canadian dollars (Can$). The authors reported that Can$1 = US$ 0.65 in 1999.

Sensitivity analysis
No sensitivity analyses were conducted.

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

Cost results
The mean costs per specimen were $17.46 ($4.85 reagents and $12.61 labour) for CBT and $10.40 ($2.80 reagents and $7.60 labour) for MPCR.

Synthesis of costs and benefits
Not relevant as the costs and benefits were not combined.

Authors’ conclusions
Compared with the conventional biochemical test (CBT), multiplex polymerase chain reaction (MPCR) offered high sensitivity and specificity for the detection of vancomycin-resistant Enterococci (VRE) infection, a high turnaround and lower costs.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. CBT was selected as it represented the standard test for the detection of VRE infections. You should decide whether it represents a widely used test in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a single cohort of patients who were prospectively subjected to both diagnostic approaches. This prospective design was appropriate for the study question. The study sample was fairly representative of the study population. The results were not affected by confounding factors, as the same cohort of patients underwent both tests. Further, discordant results were subsequently analysed to determine the true status of the corresponding specimens. No statistical analyses were reported (if any were performed).
Validity of estimate of measure of benefit
The health outcomes were left disaggregated and the study was categorised as a cost-consequences analysis.

Validity of estimate of costs
The perspective adopted in the study was not reported, but it was presumably that of the microbiology laboratory. Only those costs strictly related to the diagnostic tests were included in the analysis. The unit costs were reported only for labour, while the quantities of resources used were not given. The costs and the quantities were treated deterministically since no statistical analyses were carried out. The cost estimates were specific to the study setting and no sensitivity analyses were conducted. The price year was reported.

Other issues
The authors did not compare their findings with those from other studies. In addition, the issue of the generalisability of the study results to other settings was not addressed. Thus, the external validity of the analysis was low. The study included patients at risk of VRE infection and this was reflected in the conclusions of the analysis.

Implications of the study
The authors noted some implications of their study. First, the turnaround time could be reduced if the laboratory would offer MPCR seven days a week. Second, two policies may reduce the occurrence of false positive and false negative results: weak bands on the gel could be considered equivocal and PCR repeated from the sub-plate. Third, an increase in workload volumes could further reduce the costs per specimen with MPCR. Consequently, the authors recommend the use of MPCR as a primary screening assay on presumptive Enterococci (black colonies on vancomycin screen plate).

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