Comparative evaluation of colorimetric microtiter plate systems for detection of herpes simplex virus in cerebrospinal fluid

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 studied was definitive laboratory diagnosis of Herpes simplex virus (HSV) in cerebrospinal fluid (CSF). Four colorimetric microtiter plate systems: Prime Capture system (from ViroMed laboratories, Inc.), Quanti- PATH system (from CPG, Inc.), GEN-ETI-K system (from Incstar Corp.), and Mayo Clinic by PCR ELISA (Boehringer Mannheim Corp.) were compared with conventional Southern blotting for the detection of HSV polymerase chain reaction (PCR) products resulting from clinical CSF specimens.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with encephalitis and meningitis.

Setting
The setting was a molecular microbiology laboratory. The economic study was conducted at the Mayo Clinic, Rochester, Minnesota, USA.

Dates to which data relate
Dates to which data relate were not reported. Resources and prices were based on information for 1996.

Source of effectiveness data
Effectiveness data were derived from a single retrospective study.

Link between effectiveness and cost data
Costing was undertaken retrospectively on the same sample of specimens as that used in the effectiveness study. However, the cost analysis was performed for the Mayo MTP system and the conventional Southern blotting method only.

Study sample
No power calculations were reported. Eighty-six clinical CSF specimens were selected retrospectively for the study. The method of sample selection was not described in detail.
Study design
The study was a retrospective within-group comparison study in which subjects served as their own controls. The clinical CSF specimens were submitted to the Molecular microbiology laboratory for the diagnosis of HSV CNS disease by PCR. The PCR products were tested using the conventional Southern blotting and the four MTP systems. The period of observation was not reported.

Analysis of effectiveness
All specimens included in the initial study sample were taken into account in the effectiveness study. The primary outcome measures used in the analysis were the sensitivity and specificity of each alternative and the turnaround time for amplicon identification for each alternative.

Effectiveness results
The effectiveness results were as follows:

Of the 86 CSF specimens tested, 54 were HSV DNA positive and 32 were HSV DNA negative by conventional Southern blotting methods.

Compared with Southern blotting, the sensitivity and specificity for each MTP system were as follows:

PrimeCapture system, sensitivity 63.0% and specificity 100%;
Quanti-PATH system, sensitivity 98.2% and specificity 96.9%;
GEN-ETI-K system, sensitivity 98.2% and specificity 100.0%; and
Mayo system, sensitivity 100.0% and specificity 96.9%.

Southern blotting, followed by probe hybridisation, required a minimum of 15 hours for amplicon identification. All four MTP systems needed a test time of less than 4 hours for completion of the identification of the HSV amplicon. All four MTP systems had turnaround times 12 to 24 hours less than for Southern blotting.

Clinical conclusions
Substitution of MTP systems for Southern blotting improved turnaround time and did not compromise test sensitivity.

Measure of benefits used in the economic analysis
The authors did not develop a summary benefit measure and health outcomes were left disaggregated. Thus, a cost-consequences analysis (CCA) was performed.

Direct costs
The cost analysis compared Southern blotting versus the Mayo MTP system. Direct costs were determined on an annualised basis and an estimated annual volume of 3,040 procedures. The cost/resource boundary adopted in the study was not stated. Direct costs included the costs for test kits, materials, reagents, and equipment and laboratory personnel salaries. Eight percent was added to each direct cost to cover utilities. Variable allied health effort (hands-on time) was calculated per specimen. Fixed effort (specimen processing, buffer preparation, maintenance, bench cleaning, and data entry) was calculated on a per-day basis. Each procedure was outlined on a flowchart and timed by laboratory personnel. Costs and quantities were not reported separately. Discounting was not necessary as costs were incurred over a short time frame. The price year was not explicitly stated but is likely to have been 1996.

Statistical analysis of costs
No statistical analysis of costs was carried out.
Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Please refer to the effectiveness results above.

Cost results
The total annual cost of Southern blotting was $176,472,000 and the total annual cost of the Mayo MTP system was $173,128,000.

Annual costs were similar for the Mayo assay and the conventional Southern blotting methods.

Synthesis of costs and benefits
Not applicable as a cost-consequences analysis was conducted.

Authors' conclusions
The authors concluded that colorimetric MTP systems were likely to improve test turnaround times and patient care at no additional cost.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used, namely the conventional Southern blotting. The use of Southern blotting as the basic comparator was supported by the literature. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a retrospective within-group comparison study in which each CSF specimen served as its own control. This study design was appropriate for the study question as no external comparison group was required. The sample was unselected and appears to have been representative of the study population. The outcomes measures are likely to be valid. Limited data on effectiveness were reported and no statistical analysis was reported. The size of the sample population was small (n=86) and no evidence was provided that the initial study sample was appropriate for the study question. These issues should be considered when estimating the internal validity of the study.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences analysis (see validity of effectiveness comments above).

Validity of estimate of costs
The perspective adopted was not stated, but it is likely to have been that of the hospital. Few details on cost data were
reported. No statistical analysis on costs was carried out. Costs and quantities were not reported separately and the price year and period of follow-up were not clearly specified. These issues affect the reproducibility of the economic analysis in other settings. Discounting was not relevant and was not performed. The cost analysis was only conducted to compare two diagnostic systems.

Other issues
The issue of generalisability to other settings was not addressed and the authors did not compare their findings with those from other studies. Sensitivity analyses were not conducted and the overall external validity of the analysis was low. The results do not seem to have been presented selectively. The authors did not report further limitations of their study.

Implications of the study
MTP systems may be adapted for automation, which is a compelling requirement for PCR testing, which, in many laboratories, is expanding at a rapid rate. For the authors, these factors make the implementation of this technology in routine diagnostic testing a fundamental goal in their laboratory.

Source of funding
None stated.

Bibliographic details

PubMedID
9705419

Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Blotting, Southern /methods; Cerebrospinal Fluid /virology; Colorimetry /economics /instrumentation /methods; Costs and Cost Analysis; DNA, Viral /cerebrospinal fluid; Enzyme-Linked Immunosorbent Assay /methods; Herpes Simplex /cerebrospinal fluid /diagnosis; Humans; Polymerase Chain Reaction /economics /instrumentation /methods; Reproducibility of Results; Sensitivity and Specificity; Simplexvirus /genetics /isolation & purification; Time Factors

AccessionNumber
21998001257

Date bibliographic record published
31/01/2004

Date abstract record published
31/01/2004