Real-time polymerase chain reaction detection of herpes simplex virus in cerebrospinal fluid and cost savings from earlier hospital discharge

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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
A diagnostic test for the detection of herpes simplex virus (HSV) in cerebrospinal fluid (CSF) was examined. The HSV polymerase chain reaction (PCR) assay used to rule out HSV encephalitis and carried out at the hospital laboratory (using SmartCycler II) was compared with the same test (using LightCycler) performed at a reference laboratory outside of the hospital.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing HSV testing. The patients were grouped into the following age categories: newborn (0 to 29 days), young child (30 days to 3 years), older child (4 to 17 years), and adult (18 years or older).

Setting
The setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered from May 1996 to January 2004. The price year was 2002.

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

Link between effectiveness and cost data
The costing was carried out on samples of patients that were different from those used in the effectiveness analysis.

Study sample
The authors stated that all eligible patients who had an HSV PCR performed on CSF between May 1996 and January 2004 were enrolled. This patient group was broken down into those who had the test performed in the hospital laboratory, on or after June 2003 (in-house test group), and those whose test was performed at an external laboratory (control group). A sample of 190 specimens (95 strains of HSV-1 and 95 strains of HSV-2) appears to have been used. No other details were given.
Study design
This was a diagnostic accuracy study that was carried out at a single institution, the Shands Hospital at the University of Florida in Gainesville, Florida. No follow-up was performed after hospital discharge.

Analysis of effectiveness
All of the patients included in the initial study sample were considered in the analysis of effectiveness. The primary outcome measure was the diagnostic accuracy of the test.

Effectiveness results
The in-house HSV PCR assay detected 95 of 95 strains of HSV-1 and 94 of 95 strains of HSV-2. One strain of HSV-2 was sequenced and found to differ by 2 base pairs from the probe. A probe with this sequence was included in the assay without loss of sensitivity.

These results were comparable to those observed at two reference laboratories to which the specimens were sent.

The authors stated that some significant improvements in diagnostic accuracy could be achieved using 2% dimethylsulfoxide rather than other additives.

Clinical conclusions
The effectiveness analysis showed that the same diagnostic accuracy was achieved at the hospital laboratory and at the reference laboratories.

Measure of benefits used in the economic analysis
The two interventions were equally accurate, thus a cost-minimisation analysis appears to have been performed.

Direct costs
The perspective of the hospital appears to have been chosen. The main category of costs was that associated with hospital stay, which was estimated on the basis of changes in turnaround time when using either the in-hospital or the external laboratory. In addition, the cost of developing and performing the test was also considered in a separate analysis. The unit cost of a hospital day was presented separately from the quantities of resources used.

Different cost calculations were made. In the period before the use of the in-hospital laboratory (pre-implementation period), the authors contacted all attending physicians in person 2 to 3 days after each PCR test was ordered and before the report of a result, in order to estimate whether the patient would have been discharged if the test results were known. In the post-implementation period (after the introduction of the in-hospital laboratory service), three types of analysis were performed. In the first analysis, all paediatric patients undergoing PCR were considered and one of the authors reviewed their hospital charts in order to estimate the hospital days saved (if any) as a result of the more rapid availability of the result. Adult cases were based on the experience of the attending physicians. Since this evaluation was in part subjective, a second analysis was performed by looking at the actual LOS in days for all patients who had the test performed. Finally, an analysis of LOS in matched pairs was carried out.

Discounting was not relevant as the costs per patient were incurred within a short time. The price year was 2002.

Statistical analysis of costs
The cost-differences were analysed using the chi-squared test.
**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were not carried out.

**Estimated benefits used in the economic analysis**
See the "Effectiveness Results-" section.

**Cost results**
In the pre-implementation period, attending physicians stated that 4 (of a total of 13) infants would have been discharged at the time they were told the HSV CSF PCR was (hypothetically) negative. In comparison with the time the patient was actually discharged, this would have resulted in a savings of 9 full days (2.25 days per patient) at a direct variable cost of $450 per day (approximately $4,050 throughout a 4-month period, or approximately $12,150 on an annual basis).

The turnaround time was an average of 5.2 (+/- 7.2) days (median 4.1; 95% confidence interval, CI: 4.5 to 5.9) before in-house testing and 1.5 (+/- 1.0) days (95% CI: 1.3 to 1.7) when performed in-house.

The results of the analysis in the post-implementation period were as follows. Of 32 infants, 5 were thought to have been discharged an average of 2.1 (+/- 0.55) (95% CI: 1.4 to 2.8) days per patient sooner than if the PCR test had been sent to the reference laboratory (10.5 total hospital days). Of 23 children aged 30 days to 3 years, 4 were thought to have been discharged an average of 2.9 (+/- 0.75) (95% CI: 1.7 to 4.1) days sooner (11.5 days total). Two older children and one adult were judged to have been discharged 2.5, 2.5 and 2 days sooner, respectively. In total, 29 hospital days were estimated to have been saved throughout a 6.3-month period. This corresponds to 55.2 days saved over 1 year, or approximately $27,011 (assuming a direct variable hospital cost of $450 per day for low-intensity neonatal intensive care unit, $502 per day for paediatrics, and $609 per day for adults).

The second analysis of the actual observed LOS showed that a total of 42.1 days were saved throughout the first 7 months of implementation. This projected to an annualised total of 70.2 days. Using the above cost per day estimates, the 70.2-day total shorter LOS would result in annual direct variable cost-savings of approximately $31,590. When these results were broken down by age group, they showed that the shorter LOS was statistically significant only for newborns. Thus, the observed cost-savings were similar to those assessed using the authors' estimates of reduced LOS.

When the lower cost of the in-house test in comparison with the reference laboratory cost was included, an additional annual savings of approximately $11,000 was achieved. Thus, the total saving amounted to $42,590 in the first year, which was greater than the cost of the instrument ($29,000) plus the estimated $8,000 in test development costs (mostly technologists- time).

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was not relevant as a cost-minimisation analysis was carried out.

**Authors' conclusions**
The in-hospital polymerase chain reaction (PCR) assay for herpes simplex virus (HSV) was as sensitive as the national reference laboratories. Cost-savings were achieved through decreased length of stay (LOS) and reduced cost per test. These savings completely offset the capital and development costs within a year.
CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators (i.e. the same diagnostic test performed at the hospital laboratory or at an external reference laboratory). You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness analysis used a diagnostic study with historical controls, which was appropriate, although limited data on the study sample were provided. In effect, the assessment of the efficacy of the in-hospital service appears to have been a secondary aim of the analysis. The sequence of diagnostic tests was not reported, but the authors stated that the external laboratories were blinded and, thus, might not have been aware of the results of the in-hospital laboratory. However, in general, the comparison between the in-hospital and external laboratories was not carried out in a transparent fashion.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-minimisation analysis was performed. Please refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The perspective adopted in the analysis of the costs was unclear, but only the costs of hospital stay and tests were included. The unit costs were provided, as were data on quantities of resources, which were estimated using different approaches. The information on the unit costs and quantities of resources enhances the possibility of replicating the analysis in other settings. Statistical analyses were carried out to test the statistical significance of cost-differences. However, the cost estimates were specific to the study setting and the use of different cost estimates was not investigated. The price year was reported, which means that reflation exercises in other settings will be possible.

Other issues
The authors stated that other studies have reported cost-savings associated with in-house test reporting. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. This limits the external validity of the analysis. In general, the analysis focused on costs more than on effectiveness, and few details of the comparison between the two groups were given. The study referred to hospitals requiring laboratory tests for HSV and this was reflected in the authors' conclusions.

Implications of the study
The study results support the development of an in-hospital laboratory for the analysis of HSV specimens.

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