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
Targeted oral ganciclovir prophylaxis was assessed. This comprised a proposed 14-week course of 3 g orally daily, with the dose adjusted for renal function, in addition to standard immunosuppression (corticosteroids, azathioprine, and either tacrolimus or cyclosporine for the first 3 months post surgery).

Type of intervention
Secondary prevention of symptomatic cytomegalovirus (CMV) in liver transplant patients.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised liver transplant recipients. All patients entering the study setting and undergoing a liver transplant were included.

Setting
The setting was secondary care. The economic study was carried out at the Birmingham Liver Unit, UK.

Dates to which data relate
The effectiveness and resource use data were collected between August 2001 and August 2002. A price year was not explicitly reported, but it seems to have been 1997.

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

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The authors recruited all patients receiving liver transplantation in the study setting between the dates of the study (n=120). There was no report that power calculations were carried out to estimate the influence of chance on the results. Thirty-six patients were D+/R+, 22 were D+/R-, 39 were D-/R+ and 24 were D-/R-. There were 9 early deaths, 4 of the long-term (survival > 3 months) survivors did not receive prophylaxis, and 1 patient experienced a possible allergic reaction to the first dose of ganciclovir.
Study design
The authors designed a prospective cohort analysis with patient groups defined by the donor and recipient's seropositivity. This design allowed the authors to distinguish those types of patient in whom prophylaxis is most effective. The analysis was based at a single centre. The intended length of follow-up was not reported, although the mean actual follow-up was 13.8 months (range: 8 - 20).

Analysis of effectiveness
The patients were analysed according to their seropositivity and duration of prophylaxis. The primary outcomes were:

whether or not CMV disease occurred;
the timing of disease relative to the transplant; and
the tolerance of and compliance with the prophylaxis protocol.

Effectiveness results
For the 45 patients who were long-term survivors and received prophylaxis, the mean duration of prophylaxis was 82 days. Only 20% of patients took ganciclovir for the planned 98 days.

Of the 49 long-term survivors, 7 suffered symptomatic CMV. All symptomatic patients were D+/R- (7 out of 22; 32% of the D+/R- cohort).

Of the 7 symptomatic patients, 5 had not received prophylaxis according to the proposed protocol, 2 did not receive prophylaxis (CMV began at 38 and 45 days post transplant), and 3 had early cessation (1 at 1 month and 2 at 2 months).

The authors noted that protocol violations were disproportionately represented in the D+/R- group. There was also a difference in the duration of prophylaxis, with D+/R+ and D+/R- groups receiving ganciclovir for a median duration of 90 and 73 days, respectively.

Oral ganciclovir was well tolerated, cessation of treatment being necessary in only 3 patients. Patient compliance appears to have been good, but prophylaxis was stopped earlier than planned in a significant proportion of cases.

Clinical conclusions
The authors concluded that targeted prophylaxis led to a reduction in the incidence of CMV disease from 9.5 to 5.8%. They observed that the incidence in CMV disease in the D+/R- group was not clearly reduced by the implementation of the targeted strategy, but they believed this was related to the failure of medical staff to comply with the newly introduced protocol which occurred more frequently in the D+/R- group.

Measure of benefits used in the economic analysis
The authors estimated the number of deaths prevented as a summary measure of health benefit.

Direct costs
The authors estimated the cost of CMV management by estimating the cost of ganciclovir prophylaxis and the cost of treating symptomatic CMV disease. The quantities were estimated from actual drug usage during the clinical study (August 2001 - August 2002), while the unit costs of the drugs were taken from the Monthly Index of Medical Specialities, May 2000. Inpatient care and additional treatment costs were reported to include the cost per day of hospital accommodation, the cost of diagnostic tests and additional drug costs. The authors aimed to make direct comparisons with projected costs calculated in 1997 and, therefore, made use of costing figures that were applied to the 1997 CMV audit. Thus, it would appear that 1997 became the price year, although it was unclear whether more recent costs were deflated to this level (however, the authors reported that the cost of ganciclovir was unchanged between 1997 and 2002). Discounting was not required as the costs were measured during 1 year.
Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not reported.

Currency
UK pounds sterling (£).

Sensitivity analysis
No sensitivity analyses were carried out.

Estimated benefits used in the economic analysis
The authors assumed that targeted prophylaxis prevented 2 deaths, based on the results from another study.

Cost results
The cost of ganciclovir prophylaxis for the 12-month period from August 2001 was 124,849. The cost of management of the symptomatic infection was 42,860. Therefore, the total cost of management of CMV was 167,709.

When compared with the cost of treatment without a targeted strategy, as estimated in another study (59,641), the incremental cost of the targeted strategy was reported to be 108,068.

Synthesis of costs and benefits
The cost per life-year saved, assuming a life expectancy following transplant of 20 years, was 2,702.

Authors’ conclusions
Targeted cytomegalovirus (CMV) prophylaxis with oral ganciclovir reduces the incidence and severity of symptomatic infection. It would appear to be a cost-effective means of improving outcomes following liver transplantation.

CRD COMMENTARY - Selection of comparators
There was no comparison technology; the authors carried out an audit following the introduction of targeted oral ganciclovir prophylaxis as a patient management strategy. Following an earlier study, which had predicted that this targeted strategy would prevent most symptomatic infection, the authors introduced this protocol into their setting. After a 1-year period they carried out the audit to establish compliance and the effect on CMV prevention.

Validity of estimate of measure of effectiveness
A prospective cohort analysis was carried out. This design made sense in the context of the aims and objectives expressed and the recent introduction of the new protocol in the authors’ setting. Although a randomised study helps to reduce potential biases in the study sample, randomisation would not have been possible in this instance as the groups were defined by the seropositivity of the donor and recipient. The study sample comprised patients receiving a liver transplant and so reflected the study population. The authors presented extensive data at the patient level, thus enabling the reader to fully understand the results.

Validity of estimate of measure of benefit
The estimation of benefits was an assumption based on results from the authors' earlier study. The authors might have looked for further evidence on life expectancy following liver transplant to support their assumption.

**Validity of estimate of costs**

The authors did not report the perspective from which the costing was carried out. Nevertheless, the costs incorporated suggested that the perspective of the health care provider was adopted. Although no indirect costs were estimated, they might have been relevant to the study as the absence of CMV disease may speed a patient's recovery and return them to productive work sooner. The authors could have provided more information on the component parts of the costing analysis and carried out some sensitivity analyses to help identify the main cost-drivers. The costs were reported separately from the quantities, thus enhancing the reproducibility of the study in other settings. The resource use quantities were taken from a single setting, while the prices were taken from the authors' setting. No statistical, sensitivity or any other kind of analysis of the quantities or prices was conducted. No other sources of resource quantities or prices were used. The price year was not stated clearly, hence impeding any future reflation exercises. Discounting was not necessary as the costs were incurred during a short time (less than 2 years).

**Other issues**

The authors made some appropriate comparisons between their own results and those of other authors. These suggested that the impact of prophylaxis "appears inferior" to the impact observed by others. Possible reasons for this difference were discussed. The authors did not address the impact of generalisability but, given the nature of the study as an audit of clinical practice in the authors' setting, it is doubtful that they intended the results to be transferable to alternative settings. Lessons concerning clinical effectiveness and compliance might well, however, be applicable to other pragmatic situations. The results were presented in details and the conclusions reflected those results well. No limitations were discussed.

**Implications of the study**

The authors did not make any recommendations for policy or practice following their study, nor did they make any suggestions for further work. They did, however, report that their experience "highlights the difficulties experienced in achieving compliance with clinical protocols in real practice compared with the compliance achieved during performance of sponsored supervised clinical trials".

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**Other publications of related interest**


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