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 an artificial system for albumin dialysis (Molecular Adsorbent Recirculating System, MARS), in addition to standard medical therapy (SMT), for patients with cirrhosis who developed a super-imposed acute liver injury.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 65 years, who presented with cirrhosis and a super-imposed acute liver injury leading to decompensation and severe hyperbilirubinaemia (serum total bilirubin greater than 20 mg/dL). Patients were excluded for hepatobiliary obstruction, inability to undergo the extracorporeal treatment because of active bleeding or sepsis causing haemodynamic instability, co-morbid conditions associated with a poor outcome, and extensive surgery in the month before admission. Patients with coma of non-hepatic origin, patients who were pregnant, and patients with hepatorenal syndrome (Type I and Type II) were also excluded. The exclusion criteria were obtained from the original effectiveness paper (Heemann et al., see Other Publications of Related Interest).

Setting
The setting was secondary care. The effectiveness study was carried out in Germany, but was then applied to US cost data.

Dates to which data relate
The effectiveness data were derived from a study published in 2002, while the costs were estimated from a study published in 2001. The price year was not reported.

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

Link between effectiveness and cost data
The average costs for events were derived from a costing study in the USA. These were then applied to differences in events derived from the effectiveness study conducted in Germany.

Study sample
The following information was obtained from the published economic evaluation and the original clinical paper.

Power calculations, if performed, were not reported. Of an initial sample of 46 patients, 24 patients fulfilled the inclusion criteria. The reasons for exclusion were bilirubin levels (n=14), hepatorenal syndrome (n=4), acute liver failure (n=1), refractory gastrointestinal bleeding (n=1), fungal sepsis with haemodynamic instability (n=1) and refusal (n=1). There were 12 patients in each group. The mean age was 48 years in the MARS group and 57 years in the control group. There were 6 females in the MARS group and 4 females in the control group.

Study design
The following information was obtained from the published economic evaluation and the original clinical paper.

This was a prospective, randomised clinical trial that was carried out at the Liver Transplant Centers of the Universities of Essen and Rostock in Germany. Randomisation was conducted using a ratio of 1:1 (treatment:control) in blocks of 6 patients. A set of blind envelopes was provided to each hospital. The length of follow-up was 30 days or patient death. Only 15 patients completed the final assessment. Seven patients died, one discontinued MARS treatment due to catheter-related problems, and one patient withdrew after improvement.

Analysis of effectiveness
The basis of the analysis of the clinical study was intention to treat, but a per protocol analysis was also conducted. There were several health outcomes reported in the original clinical paper. This published economic evaluation reported the number of complications in each arm of the trial. These included in-hospital deaths, worsening of hepatic encephalopathy (Grade 4), worsening of renal function, new formation of ascites, variceal bleed, severe hypotension, developing electrolyte disorders and coagulopathy. The two groups were comparable in terms of their baseline characteristics.

Effectiveness results
There was 1 in-hospital death in the SMT-MARS group and 6 in the SMT group.

There were no cases of worsening of hepatic encephalopathy in the SMT-MARS group, but there were 3 cases in the SMT group.

There was 1 case of worsening of renal function in the SMT-MARS group and 7 cases in the SMT group.

There were no cases of new formation of ascites in the SMT-MARS group, but there was 1 case in the SMT group.

There were no cases of variceal bleed in the SMT-MARS group, but there was 1 case in the SMT group.

There were 2 cases of severe hypotension in the SMT-MARS group and 3 cases in the SMT group.

There were 4 cases of developing electrolyte disorders in the SMT-MARS group and 10 cases in the SMT group.

There were 4 cases of coagulopathy in the SMT-MARS group and 3 cases in the SMT group.

Clinical conclusions
The effectiveness study showed that MARS led to improved survival, renal function and hyperbilirubinaemia in comparison with standard care. The new procedure proved to be safe.

Measure of benefits used in the economic analysis
The summary benefit measure was the number of survivors. This was derived directly from the effectiveness analysis.
Direct costs
Discounting was not applied because the timeframe of the analysis was very short (30 days). The unit costs were not presented separately from the quantities of resource use, but the cost for each complication was provided. The costs were not broken down and the perspective of the study was not reported. The cost analysis was based on another published study (Kim et al., see Other Publications of Related Interest), which identified the factors influencing the costs of hospital care for patients with AoCLF. These factors were death, variceal bleeding, hepatorenal syndrome, hepatic encephalopathy, ascites and human immunodeficiency virus infection. The incidence of these factors was derived from the effectiveness study.

The unit cost data were derived from the Healthcare Cost and Utilization Project, which is a national health care database containing data for inpatient hospital stay from over 900 hospitals in 19 US states. It was unclear whether costs or charges were used. In addition, the price year was not reported. The authors assumed that the pattern of complications observed in the study used to derive the costs was comparable to the pattern observed among the patients in the effectiveness analysis.

Statistical analysis of costs
No statistical tests of the costs were carried out.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not conducted.

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

Cost results
The total costs were $179,520 in the control group and $124,896 in the MARS group.

Synthesis of costs and benefits
The average cost per survivor was $35,904 in the control group. Since there were 11 survivors in the MARS group, up to $394,944 could have been spent to save all 11 lives. As the total costs in the MARS group were $124,896, then up to $270,048 would be saved if MARS was performed. As the total cost of the MARS procedure itself for the entire population was $227,500, then the cost per survivor in the MARS group was $32,036. This led to nearly $4,000 cost-savings in comparison with control patients.

Authors' conclusions
The use of Molecular Adsorbents Recirculating System (MARS) had a beneficial effect on the rate of complications and in-hospital death. This translated into reduced hospital costs and improved survival among patients with cirrhosis who developed a super-imposed acute liver injury.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The new intervention was appropriately compared with the standard care provided to patients with AoCLF. You should decide whether this represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness data were derived from a randomised clinical trial, which was appropriate for the study question. This paper contained few details of the study design. Reference was made to the original clinical paper (Heemann et al., see Other Publications of Related Interest). Consequently, it was not possible to judge the internal validity of the effectiveness data from this paper.

**Validity of estimate of measure of benefit**
The benefit measure, which was derived directly from the effectiveness analysis, was the number of survivors. Thus, there could be some problems when comparing it with the benefits of other health care interventions.

**Validity of estimate of costs**
The perspective of the study was not explicitly reported and the cost categories were not broken down. It would be useful to analyse the study used to derive the cost estimates. The price year, unit costs and the quantities of resource use were not provided. Only the cost per case of complications was reported. Overall, few details of the cost analysis were reported. Those reported were the source of the cost data and the number of complications. The authors stated that the primary study used for the costs did not consider the effect of duration of stay in the intensive care unit on the costs. However, the inclusion of such costs would favour the MARS group due to the lower rate of complications.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not address the issue of the transferability of the study results to other settings. Sensitivity analyses were not carried out. The authors calculated the cost per survivor in order to combine the costs and benefits of the MARS treatment in comparison with standard care. However, two points should be noted. First, the approach used to combine the costs and benefits was unusual. Second, the use of an incremental cost-effectiveness ratio would have been more interesting. The authors noted that a weakness of the study was that the effectiveness data were estimated in Germany and were then mixed with cost data taken from a US study.

**Implications of the study**
The main implication of the study was that the benefits of MARS might justify its higher costs in patients with AoCLF. However, further studies should be carried out to confirm the results of the present study.

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None stated.

**Bibliographic details**
Hassanein T, Oliver D, Stange J, Steiner C. Albumin dialysis in cirrhosis with superimposed acute liver injury: possible impact of albumin dialysis on hospitalization costs. Liver International 2003; 23(Supplement 3): 61-65

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**Other publications of related interest**

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