One-year, single-center cost analysis of mycophenolate mofetil versus azathioprine following cadaveric renal transplantation

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 mycophenolate mofetil (MMF) in the prophylaxis of organ rejection, following renal transplantation.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The patients were recipients of primary allogeneic renal transplantation at a university clinic.

Setting
The setting was the community and secondary care. The economic study was conducted in Cincinnati, Ohio, USA.

Dates to which data relate
The effectiveness evidence and resource use data were collected between 1990 and 1996. The unit prices were from 1996.

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

Link between effectiveness and cost data
The resource use data were collected retrospectively using the same patient sample as that used in the effectiveness study.

Study sample
Power calculations were not performed to determine the sample size. The patients were identified from a retrospective review of patients' records in a university clinic. Only patients with complete records were included in the study. Forty-three patients receiving AZA and 33 patients receiving MMF were included in the study. No baseline characteristics were given.

Study design
The clinical data were derived from a retrospective cohort study of patients' records. The follow-up was one year for all
patients. The study participants were from one study centre.

**Analysis of effectiveness**
The primary outcomes were defined as mild rejection or infection, or moderate/severe rejection or infection. These outcomes were defined by the authors as follows.

Mild rejection: responsive to high-dose corticosteroids.

Moderate/severe rejection: requires inpatient hospitalisation.

Mild infection: treated as an outpatient.

Severe infection: requires hospitalisation.

The authors stated that the two groups were comparable in clinical and demographic characteristics, and that the analysis was undertaken without adjustment. However, no evidence for this was provided.

**Effectiveness results**
Four MMF patients developed 5 episodes of mild rejection, whilst 4 AZA patients experienced 4 mild rejections. Three patients in the MMF group developed 3 episodes of moderate-to-severe rejection, compared with 18 patients in the AZA group who had 22 similar events, (p<0.05). In the MMF group, 26 patients experienced 49 mild infections and 15 experienced 17 serious infections. In the AZA group, 27 patients had 43 mild infections and 15 patients had 21 severe infections.

**Clinical conclusions**
The MMF group experienced significantly more moderate-to-severe rejection events. There was no clear difference in infection rates.

**Modelling**
The clinical pathways of organ transplant and infection were constructed using a decision tree.

**Measure of benefits used in the economic analysis**
No summary measure of clinical benefit was derived. The analysis was therefore categorised as a cost-consequences study.

**Direct costs**
The authors stated that the perspective of the analysis was that of the health service. The authors included the inpatient costs that were recorded in the hospital accounting system. The outpatient costs included the cost of immunosuppressants and other medications, and were based on acquisition costs. The costs of home nursing were also included. The resource quantities and unit costs were not given. The resource use was generally obtained from actual data in the patient records, or from record linkage to other accounting systems. All the costs were adjusted to 1996 US dollars.

**Statistical analysis of costs**
The costs between the two groups were compared statistically, although the authors did not state how this was performed.
Indirect Costs
The indirect costs were not included in this study.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analysis was not carried out.

Estimated benefits used in the economic analysis
Not applicable.

Cost results
The average drug cost was $4,067 in the MMF group and $482 in the AZA group.

The costs of moderate/severe episodes were $8,662 in the MMF group and $24,000 in the AZA group, (p<0.0001).

Over the one-year follow-up period, AZA was associated with an average patient cost of $78,473 and MMF with an average patient cost of $69,610. This represented an average saving of $8,863 per patient.

Synthesis of costs and benefits
The costs and benefits were not synthesised in this cost-consequences analysis.

Authors' conclusions
The study indicated that compared with azathioprine (AZA), mycophenolate mofetil (MMF) reduced the overall cost to the health care system during the first year following renal transplantation.

CRD COMMENTARY - Selection of comparators
MMF was compared with AZA for use in conjunction with cyclosporine and corticosteroids in the first year following renal transplantation. The comparison seems to have been relevant, although clinical decision-makers should assess whether this comparator is appropriate in their own setting.

Validity of estimate of measure of effectiveness
The measure of effectiveness was derived from a retrospective assessment of mild or moderate/severe infections or rejections. The clinical outcome estimate was derived from a selected number of patients evaluated retrospectively. However, bias may enter an observational study at several stages. For example, the authors stated that the study arms were comparable, but they did not provide any information to support this statement. Further, the authors stated that they selected cases for the study based on the completeness of the patients' records, a criterion that may have resulted in selection bias. It was, therefore, difficult to assess the validity of the clinical estimate in this study.

There was also a problem with the measure of effectiveness in that it reflected not only health status, but also the institutional procedures relating to hospital admission. Also, the meaning of "responsive to high dose corticosteroids" in terms of health status was unclear.

Finally, the lack of statistical significance may have arisen from the small sample size, as no power calculations were carried out.
Validity of estimate of measure of benefit
No summary measure was used (see the commentary on effectiveness).

Validity of estimate of costs
The resource use data were identified from a retrospective review of patients' records. Some of the limitations to this approach were outlined above. The unit costs were derived from the acquisition costs and on hospital accounting data. This was a pragmatic approach to the costing of health care services, and may not reflect the true long-term marginal costs of services.

Other issues
The authors did not address the issue of generalisability in the paper. Little information was provided about the patient sample, so it is difficult to draw inferences to other patient populations. Further, the study was conducted in a single research centre, and the treatment patterns and costs in this centre may not reflect those of other settings.

Implications of the study
The authors stated that the use of MMF was associated with cost-savings. They suggested that more studies are needed to determine the long-term effect and benefits of MMF in transplantation.

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