Impact of an intravenous fluconazole restriction policy on patient outcomes

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 prescription guideline to substitute the use of intravenous fluconazole with oral fluconazole, in the treatment of patients with moderate to severe infections.

Type of intervention
Prescribing guideline.

Economic study type
Cost-effectiveness analysis (cost-consequences).

Study population
The study population comprised adult and paediatric patients in a university teaching hospital, who were receiving fluconazole for moderate to severe infections. This included patients with disseminated fungal disease or febrile neutropenia.

Setting
The setting was secondary care. The economic study was carried out at the University of California, San Francisco, USA.

Dates to which data relate
The data on the resource use, prices and patients' outcomes were obtained from the first 6 months of 1997 (comparator) and from 1998 (intervention).

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

Link between effectiveness and cost data
The costing was performed as part of the same study, which evaluated the clinical outcome retrospectively from routinely collected medical records.

Study sample
Power calculations were not used to determine the sample size. The analyses of the costs and the outcomes were conducted on different study samples. The cost study included adult and paediatric inpatients at the hospital who were receiving intravenous or oral fluconazole. The pre-guideline group consisted of patients receiving treatment between 1 January and 30 June 1997. Of these, 142 patients had received intravenous fluconazole, and it was not reported how many had received the oral form. The post-guideline group consisted of patients receiving treatment between 1 January
and 30 June 1998. Of these, 325 patients had received oral fluconazole, whereas 45 patients had used the intravenous form.

Patients on intravenous fluconazole in the cost study were also included in the outcome analysis if they satisfied a number of criteria for the administration of oral fluconazole. A total of 30 patients were selected. These were compared with 45 patients in the second study period (1998) who had used oral fluconazole.

Study design
This was an observational before-and-after study conducted in a single study centre. The duration of follow-up was not reported.

Analysis of effectiveness
The outcomes evaluated in the clinical evaluation were "success overall", "failure overall", "change to alternative antifungal" and death. The data for these outcomes were collected from a review of the patients' medical records. The authors identified a subgroup of patients using intravenous fluconazole in the pre-guideline group who, judging by their records, would have been eligible for oral fluconazole. This group was subsequently compared with a subgroup in the post-guideline group who used oral fluconazole. The rationale for selecting these subgroups for comparison was that the patients were similar in that they received, or could have received, fluconazole for moderate to severe fungal infection or febrile neutropenia. There was no explanation as to why only 44 of the 325 patients in the post-guideline group who used oral fluconazole were selected for comparison. Further, no explanation was provided as to why only 30 of the 142 patients on intravenous fluconazole in the pre-guideline group were selected for comparison. The two groups were shown to be similar at baseline in terms of their demographics. However, for the adult patients, there was a trend for those in the oral group to be older, (p=0.05).

Effectiveness results
Sixty-six per cent of patients on intravenous fluconazole in the pre-guideline group were categorised as "overall success", whereas 65.9% of those on oral fluconazole in the post-guideline group had the same outcome, (p=0.95). The authors stated that the number of deaths was similar both pre- and post-guideline, (p=0.31), but did not state the number of events.

Clinical conclusions
The authors claimed that this evaluation confirmed their hypothesis that intravenous and oral fluconazole have similar efficacy.

Measure of benefits used in the economic analysis
No summary measure of benefits was used in the economic analysis. The study was essentially a cost-minimisation evaluation as the effectiveness results were similar for the two treatments.

Direct costs
The authors stated that the economic analysis included all the patients included in the study, and the acquisition costs for oral and intravenous fluconazole. The costs were not discounted given the short timeframe of the analysis (less than 1 year). The total number of dispensed doses in both study periods was reported. The price year was not stated.

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
No indirect costs were included.

**Currency**
US dollars ($).

**Sensitivity analysis**
A sensitivity analysis was not conducted.

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

**Cost results**
The estimated annual savings following guideline implementation were $73,000. The authors stated that "intravenous fluconazole expenditure per patient-day dropped from $1.41 to 0.86 with guideline implementation".

**Synthesis of costs and benefits**
The costs and benefits were not combined.

**Authors' conclusions**
The authors concluded "a restriction policy for intravenous fluconazole results in significant cost-savings, with no significant decrease in successful outcomes or change in mortality".

**CRD COMMENTARY - Selection of comparators**
The cost analysis appears to have included all the patients being prescribed oral or intravenous fluconazole. The authors compared the total fluconazole budget divided by the number of patient days, before and after implementation of the programme. This seemed a relevant basis on which to compare the acquisition costs before and after guideline implementation. The authors did not, however, state the total number of patients included, and it was difficult to assess whether all the patients were included in the comparative analysis of the costs. The authors selected a subgroup of patients for the analysis of outcomes, and compared those receiving intravenous fluconazole before programme implementation, with those receiving oral fluconazole after programme implementation.

**Validity of estimate of measure of effectiveness**
The evaluation of the patients' outcomes should be treated with caution due to the potential biases associated with the study design chosen, which was a before-and-after study using different cohorts of patients. In addition, the reasons why some patients were excluded, and the characteristics of these excluded patients, were not provided. Although statistical analyses were conducted, the sample sizes were small. Any potential differences in study outcome would, therefore, have had to be very high in order for them to become significant in this analysis. The authors acknowledged that the appropriateness of the dose was not addressed, which may impact on success rates. Moreover, long-term relapse and reinfection were not assessed, although the restriction policy was not associated with a negative impact.

**Validity of estimate of measure of benefit**
The principal benefit was cost-minimisation since the economic analysis was based on the therapeutic equivalence of the intervention and the comparator.

**Validity of estimate of costs**
Only acquisition costs were included in the cost analysis, even though other costs, such as those for administration and complications, could have been relevant to this analysis. The authors did not report the unit costs or the price year, thus limiting the generalisability of the cost results. It was, therefore, difficult to assess the validity of the cost calculation provided in the paper.

**Other issues**
The results many need to be treated with caution given the limitations of the study. The results would benefit from validation in an experimental study with randomised patients. The authors compared their analysis with other studies with similar hypotheses and found comparable results. In addition, they identified the potential biases and confounding variables in their discussions. The authors also addressed the issue of generalisability in terms of wholesale prices (see Other Publications of Related Interest), although these would apply mostly to a US setting.

**Implications of the study**
The authors recommended that similar prescription guidelines be introduced at other medical centres, in order to reduce the costs with no decrease in clinical efficacy.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
11197590

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Oral; Adult; Aged; Cost-Benefit Analysis; Drug Utilization Review /economics /statistics & numerical data; Female; Fluconazole; Guideline Adherence /economics /statistics & numerical data; Humans; Injections, Intravenous; Male; Middle Aged; Organizational Policy; Treatment Outcome

**AccessionNumber**
22001000260

**Date bibliographic record published**
31/05/2002

**Date abstract record published**
31/05/2002