High- versus low-dose fluconazole therapy for empiric treatment of suspected invasive candidiasis among high-risk patients in the intensive care unit: a cost-effectiveness analysis

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.

CRD summary
This study assessed the cost-effectiveness of low- versus high-dose antifungal therapy with fluconazole for patients with suspected or invasive candidiasis in an intensive care unit. The authors concluded that high-dose fluconazole was a relatively cost-effective option, and further clinical trials on its safety and efficacy were warranted. Overall, despite some limitations, a reasonably thorough account of this exploratory cost-effectiveness study was reported. The authors' conclusions reflect the scope of the analysis and should be considered in this context.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The objective was to assess the cost-effectiveness of high-dose versus low-dose fluconazole therapy for treatment of suspected or invasive candidiasis among patients in intensive care. Patients with suspected candidiasis were defined as non-neutropenic patients experiencing fever, hypothermia, or unexplained hypotension after receiving antibacterial therapy for three days.

Interventions
High-dose fluconazole was started at a loading dose of 1600mg followed by 800mg daily. This was compared with low-dose fluconazole which started at a loading dose of 800mg followed by 400mg daily. Antifungal therapy was given for 14 days.

Location/setting
USA/inpatient care.

Methods
Analytical approach:
A published decision analytic model was modified and used to synthesise the data (Golan, et al. 2005, see ‘Other Publications of Related Interest’ below for bibliographic details). The analysis was conducted over a lifetime horizon and the authors stated that a societal perspective was taken.

Effectiveness data:
The effectiveness data were obtained from published literature and expert clinical opinion. The main effectiveness parameter, efficacy of fluconazole therapy, was derived from four published randomised controlled trials, which compared fluconazole with amphotericin, and data from the decision model (Golan et al, 2005). Other outcomes included, fluconazole resistance, mortality, and toxicity related to the therapy.

Monetary benefit and utility valuations:
None.

Measure of benefit:
The measure of benefit was life-years saved (LYS).

Cost data:
The direct costs were intensive care unit and hospital ward days, antifungal drug costs and physician reimbursement. Drug costs were valued using generic acquisition costs in 2006. Other costs were derived from the published decision model (Golan et al, 2005). All costs were reported in US dollars ($) and a discount rate of 3% was reported.

Analysis of uncertainty:
One-way sensitivity analyses were undertaken on all base-case parameters. Threshold values were calculated at $50,000 and $100,000 per LYS. Two-way sensitivity analyses were also performed by simultaneously altering the values for Candida resistance to the two fluconazole doses. The results of the sensitivity analyses were presented in a tornado diagram.

Results
Results were presented for the entire cohort of patients and for only those patients who were confirmed to have invasive candidiasis.

For all patients, the cost of low-dose fluconazole was $20,984 compared with $21,978 for high-dose fluconazole.

For patients with confirmed invasive candidiasis, the costs of low-dose fluconazole was $22,175 compared with $28,047 for high-dose fluconazole.

For all patients, the discounted life-years was 78.06 for low-dose fluconazole compared with 78.18 for high-dose fluconazole.

For patients with invasive candidiasis, the life-years for low-dose fluconazole were 63.81 compared with 64.85 for high-dose fluconazole.

For all patients, the incremental cost per LYS was $55,526 and for those patients with invasive candidiasis it was $16,778.

One-way sensitivity analyses indicated that the model results were reasonably robust to wide variations in most parameters. The results of the one-way analysis were given narratively and presented using a tornado diagram. Using a willingness to pay threshold of $50,000 a number of parameters significantly influenced the incremental cost-effectiveness ratio (ICER) raising it over the threshold. At a willingness-to-pay threshold of $100,000 only the age of intensive care unit survivors put the value of the ICER over the threshold.

Authors' conclusions
The authors concluded that high-dose fluconazole antifungal therapy should reduce mortality associated with invasive candidiasis at a reasonable cost. They suggested that their results justified a clinical trial for the testing of high-dose fluconazole for the treatment of candidaemia in non-neutropenic patients.

CRD commentary
Interventions:
The two treatment options and their associated potential toxicities were fully described. However, it was not clear whether these were the only two relevant comparators, therefore it is possible that not all relevant comparators were included.

Effectiveness/benefits:
The methods used to identify and select the published literature were not reported. It is therefore not possible to determine if the model was populated with the best available evidence. The limited information presented makes any assessment of the validity of the effectiveness data difficult. Readers should refer to the original trials referenced by the authors to further assess their validity.

Costs:
The authors stated that a societal perspective was taken. Differential costs were considered, so any costs that were expected to be identical in the two groups, which included productivity costs, were omitted. It is not clear whether this
was a reasonable assumption. The analysis was conducted over a lifetime horizon and discounting of costs to reflect their present value may have been performed. A discount rate was reported in the tables of model inputs, but it was not clear whether this was applied to both costs and benefits. The sources of costs were given along with some resource use data.

Analysis and results:
The analyses were reasonably well reported and the authors explicitly described the assumptions made and the analytical steps taken. The results of the one and two-way sensitivity analyses were well-reported and illustrated. The use of probabilistic sensitivity analysis may addressed the parameter uncertainty in a more comprehensive manner. It is not clear why such an analysis was not undertaken and, given that an assessment of the validity of the effectiveness data was not possible, this analysis may have strengthened the findings. Some limitations were discussed by the authors including the potential reduced generalisability due to other hospitals having different candidiasis prevalence, treatment protocols relating to fluconazole, and rates of fluconazole resistance. The authors appear to have reasonably reported most of the important information.

Concluding remarks:
Overall, despite some limitations, a reasonably thorough account of this exploratory cost-effectiveness study was reported. The authors’ conclusions reflect the scope of the analysis and should be considered in this context.

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Other publications of related interest


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