A cost-effectiveness analysis of caspofungin vs liposomal amphotericin B for treatment of suspected fungal infections in the UK

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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 study evaluated caspofungin at a dose of 70 mg on day 1 and 50 mg once daily thereafter, compared with liposomal amphotericin B (L-Amb) at a dose of 3 mg/kg per day, for the treatment of fungal infections in febrile neutropenic adults.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical UK cohort with a suspected or proven fungal infection. The patients had an average weight of 77 kg. The majority (74%) suffered from acute leukaemia while the remainder had various other cancers.

Setting
The setting was inpatient care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data related to one randomised controlled trial (Walsh et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). The costs for resource outlays were derived from current UK referenced sources and indexed to 2005.

Source of effectiveness data
The model input parameters included baseline infection, treatment efficacy, continuation and discontinuation of treatment, complications, survival and mortality. Survival data at 1 and 5 years were included. Complications included nephrotoxicity and other adverse events such as chills, nausea, vomiting and dyspnoea.

Modelling
A decision-tree model was developed for the analysis. The tree branches were fully explained, data sources were reported clearly, and the few assumptions necessary were justified on the basis of peer-reviewed publications.

Sources searched to identify primary studies
The probabilities that the patient had a successful outcome, or died, were based on the results from a randomised
controlled trial (Walsh et al. 2004) that compared caspofungin with L-Amb therapies for efficacy and safety. Survival data at 1 and 5 years were obtained from UK National Statistics from 1998 to 2001 and other published trial data.

Methods used to judge relevance and validity, and for extracting data
Specific details of the methods used to source peer-reviewed literature and other national publications used in the study were not stated. The authors appear to have used the most up-to-date sources available; however, no details on how they were identified and selected were reported.

Measure of benefits used in the economic analysis
The summary measure of benefit used was the quality-adjusted life-years (QALYs). The utility values used to weight life-years lost were based on a catalogue of preference scores recorded in 1997 to 2000 from the CEA Registry at the Harvard School of Public Health (http://www.hsph.harvard.edu). The methods by which these utility values were elicited, or from whom, were not specified. The QALYs were discounted at a rate of 3.5%, in accordance with UK guidelines.

Direct costs
The direct costs from the NHS perspective were included. These comprised drug costs, hospitalisation costs and associated drug costs relating to adverse events. Resource use was based on UK reference sources and guidelines and, for drug use for adverse events, based on expert opinion. Costs for nephrotoxicity were included as proxy costs within extended hospitalisation stays. The costs were undiscounted and were indexed to 2005 UK pounds sterling. The inflation index used was not specified. Drug costs per day, cost per adverse event and the per diem cost for hospital stays were used and summarised as average total direct costs.

Statistical analysis of costs
The data were treated deterministically.

Indirect Costs
Productivity costs were not included.

Currency
UK pounds sterling (£). The exchange rate to US dollars ($) was also provided: 1 = $1.80.

Sensitivity analysis
A probabilistic sensitivity analysis was used to investigate uncertainty in the model outcomes. Distributions were allocated to data inputs in the model and random values were repeatedly sampled in simulations to reflect the data variability. The results were summarised in an overall outcome value with 95% confidence intervals (CIs). Cost-effectiveness acceptability curves were created to illustrate the findings at different levels of willingness-to-pay for an additional unit of QALY. Variation in the dose level of L-Amb was also tested in a one-way sensitivity analysis.

Estimated benefits used in the economic analysis
Treatment with caspofungin was found to save 0.55 additional life-years (95% CI: 0.10 to 0.97) or, adjusting for quality-of-life preferences, 0.40 additional QALYs (95% CI: -0.13 to 0.97) per patient treated compared with L-Amb.

Cost results
Average total direct costs were £9,763 (95% CI: £6,955 to 12,577) with caspofungin compared with £11,795 (95% CI: £8,902 to 14,724) for L-Amb.
Antifungal drug costs were approximately half of the average total direct costs for both agents but were significantly lower for caspofungin compared with L-Amb.

When L-Amb dosage was lowered to 1 mg/kg from 3 mg/kg, the cost-difference between caspofungin and L-Amb was 1,453 (-3,179 to 6,093).

**Synthesis of costs and benefits**

Based on the cost-effectiveness acceptability curve generated, the probability that caspofungin would be cost-effective in comparison with L-Amb was at least 78% at any level of willingness-to-pay.

At the generally accepted maximum willingness-to-pay threshold of 20,000 or 30,000 per QALY saved, there was a 95% probability that caspofungin was cost-effective.

**Authors' conclusions**

The model showed caspofungin to be economically superior to liposomal amphotericin B (L-Amb), both in terms of cost-savings and higher quality-adjusted life-year (QALY) gains. The authors stated that their findings were well below the threshold of 30,000 per QALY often used by the National Institute of Clinical Effectiveness in the UK.

**CRD COMMENTARY - Selection of comparators**

The interventions represented two antifungal drugs that are currently approved in the UK. The authors provided justification for their choice and the exclusion of other older interventions. You should decide if these treatment options are widely used in your own setting.

**Validity of estimate of measure of effectiveness**

The clinical effectiveness data on successful resolution of infection were derived from one randomised controlled trial. Potentially, this is the highest quality of evidence for use in modelling analyses; however, the reader would need to assess the methods and quality of this study separately (Walsh et al. 2004). The authors discussed the quality and some limitations of the study in detail, such as the relevance to only average-weight individuals, and the potential for different drug doses in natural settings. However, as no review of the literature was reported to have been conducted, it was not clear whether this single randomised controlled trial represented the only, and best, evidence available.

**Validity of estimate of measure of benefit**

The authors chose a longer-term health benefit and commonly used generic outcome measure (i.e. QALYs) to fully capture health-related quality of life and survival benefits. Although this was the first time an economic evaluation had been undertaken on these two antifungal drugs and it was not possible for the authors to discuss their results in relation to other studies, use of this outcome measure will facilitate comparisons of their results with future studies. The utility values used in the analysis were clearly referenced. As the 95% CI for the mean incremental QALY gained was wide and spanned 1, there is considerable uncertainty as to whether caspofungin is superior to L-Amb.

**Validity of estimate of costs**

All relevant costs from the perspective of the UK NHS appear to have been included in the analysis. However, the time horizon of the model was not clear, and it was also unclear whether the costs were discounted (as the QALYs were). The resource units and costs were taken from public pharmaceutical listings and from the literature. The costs and probabilities of health events were reported separately and clearly.

**Other issues**

The authors approached the analysis in a thorough manner, with careful attention to model structure and multivariate sensitivity analyses to test how the results may change with movements in the cost or effectiveness estimates used. A clear conclusion was reached regarding which option was the most efficient choice and the likelihood of the reliability of the model. The authors did not discuss issues of generalisability to other settings or different population groups. However, they did discuss the limitations and strengths of their study.
**Implications of the study**
Although the authors did not suggest areas for further research, these may include research on the effectiveness of antifungal treatments in more naturalistic settings or on different patient groups to support the authors' conclusions.

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**Bibliographic details**

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**Other publications of related interest**
Because readers are likely to encounter and assess individual publications, NHS EED abstracts reflect the original publication as it is written, as a stand-alone paper. Where NHS EED abstractors are able to identify positively that a publication is significantly linked to or informed by other publications, these will be referenced in the text of the abstract and their bibliographic details recorded here for information.


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Amphotericin B /administration & dosage /adverse effects /therapeutic use; Antifungal Agents /administration & dosage /adverse effects /therapeutic use; Cost-Benefit Analysis; Double-Blind Method; Echinocandins; Great Britain; Humans; Length of Stay /economics; Liposomes; Mycoses /drug therapy; Peptides, Cyclic /adverse effects /therapeutic use; Quality-Adjusted Life Years

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