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 compared a drug regimen of voriconazole with conventional amphotericin B for the initial treatment of the severe infectious disease, invasive aspergillosis. Voriconazole is a newer antifungal agent with fewer toxic side-effects than the standard practice of amphotericin B. Comparisons were made between using voriconazole as first-line therapy and, in the case of treatment failure or toxicity, switching to amphotericin B as second-line therapy, and initial treatment by the conventional agent amphotericin B followed by voriconazole if necessary. Doses of each agent used were based on patients weighing 65 kg, in accordance with manufacturer-recommended doses.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population included hospital patients with proven or probable invasive aspergillosis. The patients were assumed to be 65 kg. No other details of the study population were given.

Setting
The setting was inpatient care. The economic study was undertaken in Geneva, Switzerland.

Dates to which data relate
The effectiveness data related to efficacy data from the Global Comparative Aspergillosis (GCA) study reported in various publications between 1998 and 2005. The resource use and cost data related to studies published in 1998 and 2001. The price year was 2004.

Source of effectiveness data
The clinical data used in the economic evaluation included:

the probability of switching because of a lack of response;

the probability of switching because of renal toxicity, as defined by acute renal failure (serum creatinine level increase of more than 100% or absolute values over 177 micro mol/L); and

survival at 12 weeks.
Modelling
A decision tree was used to model the cost-effectiveness of the two treatment protocols over a 12-week time period.

Sources searched to identify primary studies
Four publications provided clinical data for the cost-effectiveness analysis, of which three were reports on the GCA study (Wingard et al. 2004, Herbrecht et al. 2002 and Wenzel et al. 2005, see 'Other Publications of Related Interest' below for bibliographic details). The GCA study was reported to be the largest prospective study on invasive aspergillosis.

Methods used to judge relevance and validity, and for extracting data
A systematic review of the literature was not reported in the paper. The only justification given for the sources selected was the size of the GCA study.

Measure of benefits used in the economic analysis
The measure of benefit was the number of lives saved at 12 weeks. This was taken directly from the GCA study.

Direct costs
Direct costs to the hospital were included in the analysis. The costs included covered hospitalisation costs (medical ward and intensive care unit), drug acquisition costs, and toxicity-induced costs for acute renal failure. The hospitalisation costs were based on estimates of local, average patient costs per day, and were derived from local hospital estimates. The costs of renal toxicity were derived from the findings of another study (Bates et al. 2001, see 'Other Publications of Related Interest' below for bibliographic details). The resource quantities and the costs were not reported separately. Discounting was not relevant since the costs were incurred within 1 year.

Statistical analysis of costs
The data were deterministic.

Indirect Costs
Productivity costs were not included.

Currency
Swiss francs (CHF). The costs of renal toxicity from a previous study (Bates et al. 2001) were converted to CHF using 2004 purchasing power parities from the Organisation for Economic Co-operation and Development.

Sensitivity analysis
The authors handled parameter uncertainty using simple one-way sensitivity analyses. The parameters included patient weight, duration of voriconazole intravenous treatment after switching from amphotericin B, daily costs for hospital resources and intensive care unit, cost estimates per case of acute renal failure, and different incident rates for renal failure. The ranges of estimates used in these analyses were presented graphically in the paper. No rationale was provided for how these ranges were determined, although they appear to have been sufficiently wide. Structural uncertainty in the model was not investigated, nor was variability in data tested for different settings or patient profiles.

Estimated benefits used in the economic analysis
The estimated number of lives saved at 12 weeks was not reported. The 12-week survival rate was 70.8% with voriconazole and 57.9% with amphotericin B.
Cost results
The total treatment costs were CHF 37,878 per patient for voriconazole and CHF 49,861 for amphotericin B.

Synthesis of costs and benefits
The incremental cost-effectiveness ratios were not reported since first-line voriconazole was dominant (i.e. more effective and less costly than amphotericin B).

The voriconazole regimen had lower costs and higher benefits, making it the dominant option over amphotericin B.

The authors also reported average cost-effectiveness ratios. The average cost per life-year gained was presented separately for each treatment, and was CHF 53,500 for voriconazole and CHF 86,115 for traditional amphotericin B (2004).

The results from the sensitivity analyses showed no impact on the overall results.

Authors' conclusions
First-line voriconazole is clearly the dominant strategy compared with amphotericin B for the initial treatment of invasive aspergillosis. No economic benefits arose from using the traditional approach of starting with amphotericin B and switching only to voriconazole in the event of renal failure or non-response. The authors also concluded that these findings were stable when challenged with different data estimates in their sensitivity analyses.

CRD COMMENTARY - Selection of comparators
The selection of amphotericin B as the comparator option reflected usual care in the authors' setting and was justified as standard practice. You should decide whether this represents usual care in your own setting.

Validity of estimate of measure of effectiveness
The parameters of survival, non-response to treatment and incidence of acute renal failure were derived from published research, primarily one study that was the largest prospective study on invasive aspergillosis (the GCA study). The authors did not report any search methods or inclusion criteria, and provided no justification for their selection of the estimates. It was not possible to judge the validity of the data given the information reported in this paper (see Wingard et al. 2004, Herbrecht et al. 2002 and Wenzel et al. 2005 for further details). It was unclear whether any other studies of invasive aspergillosis were available and whether they might have been useful for the analysis.

Validity of estimate of measure of benefit
Survival was used as the summary benefit measure. It was obtained directly from the effectiveness analysis. Survival was considered the most important outcome.

Validity of estimate of costs
The analysis of the costs was performed from a hospital perspective. It appears that all the relevant categories of costs have been included in the analysis. The authors identified that only crude cost estimates based on local average patient costs per day were available, therefore it is possible that there might have been some underestimation of the costs in the base analysis. However, this uncertainty was adequately addressed in the sensitivity analysis. The resource quantities and unit costs were based on four published sources (Wingard et al. 2004, Wenzel et al. 2005, Bates et al. 2001 and Kaiser et al. 1998). One of these sources (Kaiser et al. 1998) involved a case series of 35 patients with invasive aspergillosis. It was unclear whether adjustments for inflation were made as the price year was not explicitly stated. However, the price year appears to have been 2004. The cost data relating to renal failure were converted to 2004 CHF using purchasing power parities. Most of the cost data were adequately reported.

Other issues
The authors compared their findings with those from one other US-based study that adopted the perspective of a health care system, and found that they were in agreement. The generalisability of the results was not addressed. The authors did not present their findings selectively. The authors reported that there were some "intrinsic limitations" that are common to all model-based cost-effectiveness analyses, but did not elaborate on this topic. They acknowledged that the average hospital costs might have been crude (see 'Validity of estimate of costs' field).

**Implications of the study**
Although the authors did not suggest areas for further work, a randomised controlled trial would be valuable to validate their findings. Further research could also include an investigation of the costs from multiple hospital locations and further assessment of specific patient groups (e.g. patients with febrile neutropenia or other immunosuppressed conditions, or patients of different ages).

**Source of funding**
None stated.

**Bibliographic details**
Garbino J, Schnetzler G, Roberts C. Invasive aspergillosis: is treatment with 'inexpensive' amphotericin B cost-saving if 'expensive' voriconazole is only used on demand. Swiss Medical Weekly 2006; 136(39-40): 624-630

**PubMedID**
17086508

**DOI**
2006/39/smw-11259

**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**
Acute Kidney Injury /economics /etiology; Amphotericin B /adverse effects /economics /therapeutic use; Antifungal Agents /economics /therapeutic use; Aspergillosis /drug therapy /economics; Cost-Benefit Analysis; Decision Trees; Humans; Models, Economic; Pyrimidines /economics /therapeutic use; Triazoles /economics /therapeutic use; Voriconazole

AccessionNumber
22006002368

Date bibliographic record published
30/09/2007

Date abstract record published
30/09/2007