The cost-effectiveness of fluconazole prophylaxis against primary systemic fungal infections in AIDS patients

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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
Fluconazole prophylaxis for primary systemic fungal infection in AIDS patients.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
A hypothetical cohort of AIDS patients. No further details were given.

Setting
Hospital. The economic study was carried out in Boston, Massachusetts USA.

Dates to which data relate
The main effectiveness data were taken from previously completed studies conducted between 1989-95. Resource and cost data were mainly derived from 1989-95. Resources were measured in 1994 values.

Source of effectiveness data
Estimates of the incidence data and CD4 decline were derived from reviews of previously completed studies.

Modelling
A Markov model was used to classify the natural history of AIDS into three sectors or classes of states: chronic, acute opportunistic infection (OI) and death.

Outcomes assessed in the review
Outcomes assessed in the review included the monthly probabilities of defined events and, in the case of fluconazole efficacy, the percentage reduction of a primary systemic fungal infection. Additionally the probability of a CD4 decline were described.

Study designs and other criteria for inclusion in the review
The inclusion/exclusion criteria were not stated.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated even though it would have been applicable.

Number of primary studies included
25 studies were included in the review.

Methods of combining primary studies
Narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
For patients with CD4 counts below 200/mm³ the baseline probabilities according to three CD4 levels (101-200, 52-200, 0-50) were as follows:

Primary fungal infection (0.0026, 0.0039, 0.0060);
survive fungal infection (0.8, 0.8, 0.8);
other opportunistic infection (0.037, 0.0434, 0.93);
survive other opportunistic infection (0.7, 0.7, 0.7);
fungal relapses (0.0043, 0.0043, 0.0043);
fluconazole efficacy (0.7, 0.7, 0.7);
chronic AIDS death (0.0, 0.0070, 0.068);
non-AIDS death (0.00071, 0.00071, 0.00071);
CD4 decline from 101-200 to 51-100/mm³ (0.047, NA, NA);
CD4 decline from 51-100 to 0-50/mm³ (NA, 0.0917, NA).

These values were used as the baseline inputs to the Markov model. For sensitivity analysis each parameter was tested over a plausible range.

Measure of benefits used in the economic analysis
The measure of benefits in the economic analysis was life expectancy in survival months. The authors used quality-of-life estimates (not incorporated into the baseline model inputs) from the literature in order to conduct a sensitivity analysis. Benefits were reported for four policy alternatives (based on the timing of intervention): no prophylaxis, <50
CD4 cells/mm³, <100 CD4 cells/mm³, <200 CD4 cells/mm³ for non-endemic and endemic categories.

**Direct costs**
Standard care, acute fungal infection, acute other opportunistic infection, fluconazole and chronic suppressive therapy costs were included in the analysis. Quantities were analysed separately from costs. The quantity/cost boundary adopted was that of the hospital. All costs were converted to 1994 dollars by means of the Medical Care Component of the Consumer Price Index.

**Currency**
US dollars ($).

**Sensitivity analysis**
In order to take account of the variability in the data, one-way and a two ways sensitivity analyses were carried out on all the main incidence and costs variables.

**Estimated benefits used in the economic analysis**
The discounted life expectancy was (non-endemic and endemic):

- 28.20 months and 27.92 months for no prophylaxis;
- 28.23 months and 27.97 months for <50 CD4 cells/mm³;
- 28.27 months and 28.05 months for <100 CD4 cells/mm³;
- 28.42 months and 28.32 months for <200 CD4 cells/mm³.

**Cost results**
The total cost for non-endemic and endemic categories were:

- $36,100 and $37,800 for no prophylaxis;
- $36,900 and $38,300 for <50 CD4 cells/mm³;
- $37,900 and $38,900 for <100 CD4 cells/mm³;
- $40,500 and $41,000 for <200 CD4 cells/mm³.

These totals were based on standard care costs of $355. Acute fungal infection and acute other opportunistic infection costs were estimated to be $19,856 and $17,147 respectively. The fluconazole and chronic suppressive therapy costs were estimated to be $206 and $355 respectively.

**Synthesis of costs and benefits**
Discounted incremental cost-effectiveness expressed in $ per life year saved were $240,000 in the non-endemic <200 CD4 cells/mm³ category and $96,000 in the <200 CD4 cells/mm³ endemic group. Providing a <200 policy to the average AIDS patient in a non-endemic area has an incremental cost of $4,400 relative to no prophylaxis.

**Authors' conclusions**
Fluconazole prophylaxis is unlikely to be cost-effective unless its costs are lowered or it is focused on patients in regions with endemic fungal infections.
CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear. Fluconazole prophylaxis has been considered to be an efficacious therapy. Factors other than efficacy have also to be analysed. You, as a user of this database, should consider whether these are widely used health technologies in your own setting.

Validity of estimate of measure of benefit
The estimate of measure of benefit used in the economic analysis is likely to be internally valid. The data have not been used selectively.

Validity of estimate of costs
Adequate details of methods of quantity/cost estimation were given. Important cost items were not omitted.

Other issues
The authors' conclusions are likely to be justified, given the uncertainties in the data. The issue of generalisability to other settings was not addressed. Appropriate comparisons, however, were made with other studies. The results were not presented selectively.

Implications of the study
Further research is required to include the negative impact of resistance.

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