A cost/efficacy analysis of oral antifungals indicated for the treatment of onychomycosis:

griseofulvin, itraconazole, and terbinafine

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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 use of oral antifungals in the treatment of onychomycosis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Hypothetical non-pregnant patients presenting with toenail onychomycosis, without renal or hepatic impairment.

Setting
Primary care. The economic study was carried out in New Jersey, USA.

Dates to which data relate
Effectiveness data were extracted from studies mainly published in the period 1967 to 1996. The resource and cost information came from drug handbooks published in 1996. The price year was 1996.

Source of effectiveness data
The effectiveness data were derived from a synthesis of previously published studies.

Outcomes assessed in the review
The review assessed the mycologic cure rate associated with each treatment regime, where cure is defined as negative mycological culture on Sabouraud-dextrose agar and negative microscopic examination in 20% potassium hydroxide.

Study designs and other criteria for inclusion in the review
The studies all included a comparative agent treatment arm and provided information about mycologic cure and involved toenail infection only. For studies of griseofulvin the treatment length was at least 24 weeks. For studies of itraconazole continuous therapy the treatment length was at least 12 weeks at a dose of 200 mg/day, and for pulse therapy the treatment length was at least 1 week per month for 4 months at a dose of 400 mg/day. For studies of terbinafine continuous therapy the treatment length was at least 12 weeks at a dose of 250 mg/day, and for pulse therapy the treatment length was at least 1 week per month for 4 months at a dose of 500 mg/day.
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.

Number of primary studies included
In total 11 studies were included: 3 comparing itraconazole and terbinafine continuous therapy, 1 comparing itraconazole and terbinafine pulse therapy, 1 of itraconazole pulse therapy and 6 studies of griseofulvin.

Methods of combining primary studies
The mycologic cure rate for each treatment regime was determined as the weighted average based on the number of patients in the study and the cure rate for each study.

Investigation of differences between primary studies
Not stated.

Results of the review
The mycologic cure rates for toenail onychomycosis were: 36.7% for griseofulvin; 54.7% and 73.3% for itraconazole continuous and pulse therapy respectively; and 77% and 80% respectively for terbinafine continuous and pulse therapy.

Measure of benefits used in the economic analysis
The measure of benefits was mycologic cure rate defined as the percentage of infections cured.

Direct costs
The only costs that were taken into account within the analysis were the direct costs of the drugs. Quantities and prices were reported separately. The quantities were derived from the individual studies whilst the prices used were average wholesale prices derived from a published source. For the griseofulvin therapy the studies used different treatment lengths and drug doses and a weighted average cost was calculated based on the number of patients in each study. Costs were not discounted.

Statistical analysis of costs
Not stated.

Indirect Costs
Not assessed.

Currency
US dollars ($).
Sensitivity analysis
A sensitivity analysis was not formally undertaken although the authors did address the likely impact on the results of relaxing various assumptions.

Estimated benefits used in the economic analysis
The mycologic cure rates for toenail onychomycosis were: 36.7% for griseofulvin; 54.7% for itraconazole continuous therapy; 73.3% for itraconazole pulse therapy; 77% for terbinafine continuous therapy and 80% for terbinafine pulse therapy. Side effects and drug interactions were not considered within the analysis.

Cost results
The costs were estimated as $998.98 for griseofulvin; $1,008.72 for itraconazole continuous therapy; $627.65 for itraconazole pulse therapy;$ 499.50 for terbinafine continuous therapy and $310.80 for terbinafine pulse therapy. The costs associated with side effects, drug interactions, blood monitoring and relapse were not included within the analysis.

Synthesis of costs and benefits
An average cost of cure per infection was calculated for each treatment regime. The average cost of cure using griseofulvin was $2,721.28, using itraconazole continuous therapy was $1,845.05, using itraconazole pulse therapy was $855.88, using terbinafine continuous therapy was $648.96 and using terbinafine pulse therapy was $388.50. An incremental analysis was not undertaken as terbinafine pulse therapy dominates the other treatment regimes, and terbinafine continuous therapy dominates the continuous treatment regimes.

Authors' conclusions
Terbinafine is the most cost-effective treatment of toenail onychomycosis within both continuous and pulse therapy regimes. As terbinafine is the most effective drug and the cheapest, inclusion of relapse treatment would only strengthen the case for terbinafine versus the other treatment regimes. Terbinafine also has the fewest drug interactions and the lowest grade warning for use during pregnancy. However, use of terbinafine is restricted in patients with renal or hepatic function impairment.

CRD COMMENTARY - Selection of comparators
The reason for the choice of comparator is clear. The continuous regimes for these three drugs were commonly used in the treatment of toenail onychomycosis, and the pulse therapy regime was under investigation. You, as a user of this database, should consider whether these health technologies apply to your setting.

Validity of estimate of measure of benefit
Insufficient information concerning the method used to search the literature is given for the internal validity of the analysis to be assessed. The values used in the analysis are weighted averages calculated using all of the identified studies, weighted by study size, hence there is no apparent selective use of data.

Validity of estimate of costs
Resource quantities were reported separately from prices. Prices were derived from published drug schedules in the USA, which, whilst internally valid, are not generalisable to the UK. The analysis focuses upon the costs of drugs and omits any other aspects of treatment and costs on others in society, for example, physician visits, side effects, drug interactions, blood monitoring where treatment is prolonged, tests for pregnancy where these are required prior to prescription and patient costs. Some of these issues are dealt with qualitatively in the discussion.

Other issues
The authors relied on published data from the literature which has inherent biases. The data are often from specialised
medical settings and are not externally valid. The issue of generalisability to other settings and countries has not been addressed. Appropriate comparisons with other studies were not made.

Implications of the study
Further information is required concerning the use of pulse therapy for the treatment of onychomycosis.

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