Evaluating costs for onychomycosis treatments: a practitioner's perspective

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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 examined several treatments for patients with onychomycosis. Specifically, griseofulvin (GRI), itraconazole (ITRA), fluconazole (FLU), terbinafine (TERB) and 8% ciclopirox lacquer (CICLO). Some combination therapies were also considered. Different dosages and duration of treatment were also considered for each drug under analysis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients requiring treatment for onychomycosis.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
Both the effectiveness and resource use data were derived from studies published between 1993 and 2003. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A user-friendly computerised economic model, the Toenail Onychomycosis Economic Model was used to assess the total costs of onychomycosis treatment. This included not only the costs of medication (base-case analysis) but also other health insurance costs (alternative analysis). No other details of the model were given.

Outcomes assessed in the review
The outcomes estimated from the literature were the rates of complete cure.

Study designs and other criteria for inclusion in the review
A systematic review of the literature was undertaken to identify primary studies. Only double-blinded, randomised clinical trials enrolling at least 50 patients were included in the review. The studies had to report complete cure of a
target toenail as an outcome measure. Those studies that reported mycologic cure and clinical cure separately were excluded. Other exclusion criteria were assessment of fingernail onychomycosis and evaluation of medications not available in the USA. A total of 2 clinical trials for GRI, 9 clinical trials for ITRA, 1 clinical trial for FLU, 9 clinical trials for TERB and 2 clinical trials for CICLO were found. For each study, information on the study population, treatment regimen, length of follow-up and study design was provided. Most of these studies included head-to-head comparisons of the drug under analysis.

Sources searched to identify primary studies
MEDLINE was searched for publications in the English language using combinations of the terms "randomized", "onychomycosis", "therapy" and "trial". A manual search was also undertaken. The Physicians’ Desk Reference was also searched for relevant studies.

Criteria used to ensure the validity of primary studies
The use of clinical trials as the source of the evidence should have ensured a high validity of the primary estimates.

Methods used to judge relevance and validity, and for extracting data
Not reported.

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

Methods of combining primary studies
Some primary estimates were pooled by dividing the total number of patients with complete cure of a target toenail from all studies by the sum of the number treated. Pooling was performed only when the clinical trials used the same treatment regimens.

Investigation of differences between primary studies
Not reported.

Results of the review
In the 2 studies assessing GRI, the rate of complete cure was 5% (95% confidence interval, CI: 0.14 to 26) for GRI 500 mg once daily and 44% (95% CI: 31.8 to 58.5) for GRI 1 g once daily.

In the 6 studies assessing ITRA (2 studies were sub-sets of the other included trials), the rate of complete cure was:

- 23% (95% CI: 15.7 to 32.5) at 3 months and 26% (95% CI: 18.9 to 35.2) at 4 months;
- 28% (95% CI: 20 to 54) at 3 months and 24% (95% CI: 7 to 50) at 4 months;
- 14% (95% CI: 7.4 to 21.1);
- 23.2% (95% CI: 17.3 to 29.8);
- 51% (95% CI: 34.0 to 68.6); and
- 14% (95% CI: 7.8 to 21.5).

When data from some trials were pooled, the complete cure rate for ITRA was 27.6% (95% CI: 21.8 to 34.0).
In the single study assessing FLU, the rate of complete cure was 13% (95% CI: 6.1 to 23.0) at 4 months, 20% (95% CI: 11.6 to 29.7) at 6 months, and 26% (95% CI: 16.9 to 37.7) at 9 months.

In the 9 studies assessing TERB, the rates of complete cure ranged from 32.2% (95% CI: 22.8 to 42.9) to 78% (95% CI: 52 to 94). When data from some trials were pooled, the complete cure rate for TERB was 40% (95% CI: 34.9 to 45.6) or 52% (95% CI: 42.7 to 60.3).

In the 2 studies assessing CICLO, the rate of complete cure was 7% (95% CI: 4.1 to 11.1) with pooled data and 4.4% when the recurrence rate at 60 weeks (37.5%) was considered.

Measure of benefits used in the economic analysis
The summary benefit measure was the completed cure rate. This was derived directly from the literature.

Direct costs
The primary economic analysis included only medication costs, while the modelling analysis included other health insurance costs such as medications, physician visits, laboratory tests, procedures and the treatment of adverse events. Thus, the perspective of the analysis appears to have been that of the payer, although the author stated that a societal perspective was used in the modelling analysis. The unit costs and the quantities of resources used were presented separately for some items. The resource use data were derived from treatment patterns observed in the clinical trials and from expert opinion. The medication costs were derived from three alternative pricing sources, specifically, the Minneapolis Veteran Affairs (VA) for VA prices, the Red Book listing for average wholesale prices, and a large commercial pharmacy for commercial prices (for an individual without insurance). All costs in the decision model were estimated using VA prices. Discounting was not relevant as the costs were incurred during less than 2 years. The price year was 2001.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not considered in the economic analysis.

Currency
US dollars ($).

Sensitivity analysis
A deterministic sensitivity analysis was carried out to assess the impact of varying the amount of CICLO used on the treatment and medical management costs.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
Only VA (medication) costs will be reported here.

The total costs per patient were:

$298 (500 mg/day for 52 weeks) to $590 (1 g/day for 12 months) with GRI;
$340 (200 mg twice daily for 1 week per month for 3 months) to $680 (200 mg per day for 12 weeks) with ITRA;

$269 (4 months) to $606 (9 months) with FLU;

$236 (250 mg twice daily for 1 week per month for 3 months) to $1,728 (250 mg per day for up to 12 months) with
TERB; and

$117 with CICLO.

**Synthesis of costs and benefits**
The average cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative strategies.

The average VA cost per complete cure ranged from $1,101 to $5,960 with GRI, from $1,215 to $4,857 with ITRA,
from $2,073 to $2,332 with FLU, from $690 to $2,444 with TERB, and from $1,381 to $2,659 with CICLO.

The modelled (total) cost per complete cure ranged from $2,161 to $15,937 with GRI, from $2,269 to $8,265 with
ITRA, from $1,290 to $3,308 with TERB, and from $17,029 to $32,896 with CICLO.

When combination therapies were evaluated, the use of pulse ITRA for two cycles followed by pulse TERB for one or
two cycles led to a favourable cost-effectiveness ratio ($636 per complete cure). Other combination therapies were not
cost-effective.

When recurrence rates were explicitly considered, the long-term cost-effectiveness ratios were lower for TERB than for
ITRA.

The sensitivity analysis showed that approximately two thirds of the total cost per cure with CICLO were related to
medical management. Thus, a reduction in follow-up visits and number of debridements reduced the cost-effectiveness
ratios.

**Authors' conclusions**
Treatment strategies for onychomycosis that involved terbinafine (TERB) were highly cost-effective. Specifically, the
most cost-effective treatment was a combination of pulse itraconazole (ITRA) and pulse TERB, as well as pulse TERB.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was appropriate since all the treatments available in the author's setting
were considered. The dosages and length of treatment were reported clearly. However, each treatment was compared
with different alternative strategies in the primary studies, thus the results of the analysis referred to multiple
comparisons. Moreover, different dosages were often compared, which could compromise the clarity of the
comparison. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The author undertook a systematic review of the literature to identify relevant studies. The methods and conduct of the
review were reported, especially in terms of the search approach and the inclusion and exclusion criteria of the primary
studies. Only clinical trials were included, thus, since these usually provide high-quality evidence, the primary estimates
used in the analysis should be robust. One inclusion criterion specified a sample of at least 50 patients for each study in
order to ensure the validity of the clinical data. However, since many trials involved different treatments, samples of
patients were very small in some studies. The author noted that publication bias might have affected the results of the
analysis. Many details of the design and other characteristics of the primary studies were provided, but the issue of
heterogeneity across the primary studies was not explicitly addressed. The author stated that, owing to the loss to follow-
up, caution would be required when assessing the impact of relapse rates. Further, the issue of uncertainty surrounding
some clinical estimates was not investigated in the sensitivity analysis.
Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It will not easily comparable with the benefits of other health care interventions. However, the author justified the choice of the summary benefit measure, which was comprehensive and included both mycologic and clinical cure.

Validity of estimate of costs
The primary analysis of the costs was restricted to the costs of medication. However, a secondary analysis included other costs relevant from the perspective of the health insurer. The author stated that a societal perspective was chosen but patient costs were not considered, although out-of-pocket costs might have been relevant for the patients. The unit costs and the quantities of resources used were presented separately for some items, which will facilitate replication of the analysis in other settings. Resource consumption was derived from the clinical trials and reflected actual treatment patterns. Statistical analyses of the costs were not performed, but alternative sources of prices were used to make the analysis relevant for different payers. The price year was implicitly reported, which will assist with reflation exercises in other time periods.

Other issues
The author did not directly compare the current findings with those from other studies, stating instead that the results of this study were consistent with several published meta-analyses of efficacy and cost-effectiveness analysis. The issue of the generalisability of the study results to other settings was not explicitly addressed and few sensitivity analyses were carried out. Therefore, the external validity of the analysis was limited. The costs and benefits were combined through average cost-effectiveness ratios, but the use of an incremental analysis would have been more interesting. The study referred to patients with onychomycosis and this was reflected in the author's conclusions.

Implications of the study
The study results supported the use of TERB (alone or in combination with ITRA) for the treatment of onychomycosis. The author suggested that more head-to-head clinical trials should be carried out to corroborate the current findings.

Source of funding
None stated.

Bibliographic details

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16415282

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


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