Pharmacoeconomic analysis of oral therapies for onychomycosis: a US model
Marchetti A, Piech C T, McGhan W F, Neugut A I, Smith B T

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
Oral pharmacologic therapies for the treatment of onychomycosis. The technologies investigated were as follows: (a) itraconazole, (b) terbinafine, (c) griseofulvin and (d) ketoconazole.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Hypothetical patients suffering from onychomycosis, manifested in either the fingernail or toenail.

Setting
Primary care. The economic study was conducted in Secaucus, New Jersey, USA.

Dates to which data relate
Effectiveness and resource data were obtained from information published between 1967 and 1995. The price year was not specifically stated.

Source of effectiveness data
Review/synthesis of previously completed studies.

Modelling
A decision analysis model was used in estimating benefits/costs.

Outcomes assessed in the review
The outcome was the mycologic cure rate from onychomycosis.

Study designs and other criteria for inclusion in the review
Studies included in the analysis complied with a two step inclusion protocol. Firstly studies had to investigate either onychomycosis or tinea unguium by dermatophytes, the comparators of which were oral GTI, ITR, KET and/or TER and explicitly included efficacy outcomes. Studies using another oral therapy fluconazole had to be excluded as data were limited to case reports and safety and preliminary efficacy evaluations. The second stage of the inclusion protocol specified that the results would be grouped by infection area (fingernail or toenail), success defined by mycologic cure
rate and having dosages and treatment lengths within those specified by current practice. Randomized controlled trials and other studies of unspecified design, were included in the review.

Sources searched to identify primary studies
The starting point of the review was the use of a previous review of oral therapies for onychomycosis that had been conducted in Europe and Canada in 1994. The inclusion protocol was used to update this review process to exclude studies which were not relevant to current clinical practice. Further studies were also identified, although the means of their identification was 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
14 primary studies were included in the meta-analyses. Of these 12 were used in the meta analysis of toenail studies and 9 in the meta analysis of fingernail studies. Study types in the analyses included six randomised control trials and eight studies of indeterminate type.

Methods of combining primary studies
Meta-analysis was used in the combination of results from primary studies. The method was similar to that used in the original study using the random effects method.

Investigation of differences between primary studies
The authors investigated differences between studies in the meta analyses and found no significant correlation between the studies' efficacy and evaluation period, mean age or sex ratio. The authors did further report, however, that this analysis was limited due to reporting inconsistencies.

Results of the review
The mycologic cure rate of toenail infections using the different oral therapies reported by the meta analysis were as follows:

GRI 41% (95% CI: 4% - 78%),
ITR 79% (95% CI: 57% - 102%),
KET 16% (95% CI: 9% - 23%)
and TER 87% (95% CI: 80% - 93%).

Similarly for fingernail infections the cure rates were as follows:

GRI 68% (95% CI: 53% - 85%),
ITR 93% (95% CI: 86% - 100%),
KET 60% (95% CI: -3% - 122%)
and TER 93% (95% CI: 85% - 100%).

Measure of benefits used in the economic analysis
Mycological cures and disease free days.

Direct costs
No discounting was reported. Quantities of resource use were reported separately from costs. Regimen costs consisted of drug acquisition costs, medical care management costs and adverse drug reaction costs. The dosages, frequency and duration of drug treatment, medical care requirements and resources consumed in therapy and control of adverse events were determined by an expert panel consisting of practising dermatologists, and an epidemiologist and health economist. Published 1995 Medicare rates were used to identify physician fees. The 1995 Clinical Diagnostic Lab Fee Schedule was used to estimate laboratory fees and the 1996 Red Book was used to determine the costs of drugs. Costs included extra medication for patients who failed to respond to the initial treatment (this was assumed to be the next best alternative therapy). All costs were determined from the perspective of a third party payer in the United States and totals were calculated by means of a decision model. Price years were not stated. Costs refer to a two year time period for fingernail infections and three years for toenail infections.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analysis was conducted using the rank order stability analysis method. Length of treatment, mycologic cure rate, relapse rate and drug acquisition cost were examined in the sensitivity analysis.

Estimated benefits used in the economic analysis
For toenail onychomycosis, TER had an incremental mycological cure rate of 8% over and above the cure rate for ITR. In comparison with GRI the cure rate was 46% higher and relative to KET it showed an additional 71% success rate. Over the three year period the expected number of disease free days per patient for TER was 876. This represented an incremental benefit of 10 days over ITR, 340 days compared with GRI and 369 days compared with KET. Similarly, for fingernail onychomycosis the mycological cure rate for both TER and ITR represented an incremental benefit of 25% compared with GRI and 33% compared with KET. The expected number of disease free days over the two year period was 617 for TER. This represented an incremental benefit of 2 days compared with ITR, and 167 and 179 days compared with GRI and KET respectively.

Cost results
The expected costs per patient with toenail infections including relapse were $1,543 for GRI, $1,535 for ITR, $2,359 for KET and $977 for TER therapy. For fingernail infections these costs were $822 for GRI, $894 for ITR, $1,287 for KET and $550 for TER.

Synthesis of costs and benefits
An incremental cost effectiveness analysis was not conducted as TER was the dominant strategy. Sensitivity analysis demonstrated that the results of the model were stable although the ranking order of GRI and ITR were sensitive to changes in the parameters.

Toenail onychomycosis: the expected costs per mycologic cure were $2,385 for GRI, $1,535 for ITR, $10,025 for KET and $797 for TER; the expected costs per disease free day were $2.88 for GRI, $1.83 for ITR, $4.65 for KET and $1.12 for TER.
Fingernail onychomycosis: the expected costs per mycologic cure were $837 for GRI, $767 for ITR, $1,512 for KET and $454 for TER; the expected costs per disease free day were $1.83 for GRI, $1.45 for ITR, $2.94 for KET and $0.89 for TER. (All the above are undiscounted figures).

**Authors' conclusions**

The authors concluded that TER was a more cost-effective option than GRI, ITR or KET for the treatment of onychomycosis, and this was consistent with results reported in other studies. The authors did note however, that the costs of evaluating and managing side effects caused by drug interactions in patients using contraindicated medications was not examined in the model, although this would increase the dominance of TER in the model. The authors argued that further well designed randomised control trials need to be conducted to increase the consistency of reporting methods.

**CRD Commentary**

This is a well designed study although more detail could have been provided with regard to the following issues:

1. The methods used for identifying additional studies published after 1994 have not been stated. This could mean that additional studies were identified in a non systematic manner.

2. The authors further noted that inconsistencies in reporting and study design limited the comparison of results. In particular they noted a lack of consistency in evaluation periods and relapse assessment methods.

3. The price years used and discounting were not stated despite the fact that the model assumes that the costs of treatment cover either two or three years.

**Implications of the study**

There is a need for further well designed randomised control trials to evaluate the efficacy of oral therapies for onychomycosis.

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**Other publications of related interest**


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