Cost of treatment for onychomycosis: data from a 9-month observational study

Stier D M, Henke C, Schein J, Doyle J, Schonfeld W H, Broering J

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 pharmacotherapy compared with local treatment for patients suffering from toenail onychomycosis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was patients suffering from toenail onychomycosis or toenail and fingernail onychomycosis. Patients were excluded because of initial treatment with both oral medication and debridement, absence of any treatment over the study period, or because of the presence of only fingernail disease.

Setting
The study was carried out at the University of San Francisco (US) in collaboration with the Eureka Research and Lewin Group (San Francisco, California).

Dates to which data relate
Both effectiveness and cost data were obtained from a 9-month observational study initiated in 1996. The price year was 1997.

Source of effectiveness data
The evidence for the final outcome was obtained from a single study.

Link between effectiveness and cost data
Costs and effectiveness data were taken (prospectively) from the same sample of patients.

Study sample
The study sample in the Onychomycosis Collaborative Observational Evidence (OnyCOE) databases consisted of 148 individuals. Eligibility was based on: the treating physician's clinical diagnosis of onychomycosis; and the initiation of a new diagnostic or treatment event at the enrolment visit. Twenty patients were excluded because of lack of either baseline physician data or both the 4- and 9-month patient report evaluation. The final study sample consisted of 124 patients who were primarily middle-class and Caucasian with a slight preponderance of males (60%). Most patients reported a good general health status. No sample size power calculations were reported.
Study design
This was a prospective cohort study.

Analysis of effectiveness
The analysis of effectiveness was based on treatment completers only. Data on the effectiveness of the treatments were obtained from physicians and patients’ reports at baseline, and at 4 and 9 months thereafter. At baseline, physicians assessed the number of affected toenails and, at each subsequent visit, they evaluated the overall change in patient’s fungal nail compared with baseline, using a 5-point scale. The criteria used to assess change were left to the discretion of each physician. Patients received a mailed questionnaire on health-related quality of life (HR-QOL), satisfaction with treatment and change in the appearance of their nails. The HR-QOL included 7 items measuring frequency of onychomycosis-related toenail symptoms and another 7 items measuring the bothersomeness (nuisance) of these symptoms. The responses to these questions were combined to form the Toenail Symptom Index (TSI) incorporating both symptoms and bother into one variable. The change in TSI was used as the primary measure of treatment effectiveness.

Effectiveness results
Clinical improvement was significantly greater for patients treated initially with oral medication than for patients initially treated with local therapy, both according to the physician-reported global assessment scale (86 versus 35%, p=0.002) and the patient-reported TSI (94 versus 49%, p=0.003).

Clinical conclusions
Patients treated initially with oral medication compared with those who received local therapy had superior clinical outcomes compared with local therapy.

Measure of benefits used in the economic analysis
Benefits were essentially those identified and described in the effectiveness results. These were measured on the basis of both physicians and patients' evaluations. The HR-QOL used included 7 items measuring frequency of onychomycosis-related toenail symptoms and another 7 items measuring bothersomeness of these symptoms. The responses to these questions were combined to form the Toenail Symptom Index (TSI) incorporating both symptoms and bother into one variable. The change in TSI was used as the primary measure of treatment benefit as perceived by the patients.

Direct costs
The purpose of the research was to estimate total costs of treatment for patients with toenail onychomycosis, to estimate costs for specific types of services and to examine how the costs differed depending on the initial treatment strategy (oral medication or not). Data concerning resource use were taken from provider notes and patient questionnaires. At the 4- and 9-month evaluations, patients reported all provider encounters, medications, laboratory tests and outpatient surgeries. Neither patients nor providers were asked about hospitalisations, since inpatient care was not considered relevant to the management of this clinical condition. The provider notes were used as the primary source for data concerning medication treatment while patient reports were the primary source for other resource use. Resource use and total costs were reported separately. Unit costs for each type of service were obtained from available fee schedules, but they were not reported. To price tests, procedures, and office visits, two sets of fees were used to reflect the variability of costs under different systems: Medicare fees and standard fees. The average wholesale price for each medication reported was determined from the Drug Topics 1997 Red Book. No discount rate was applied since the follow-up was only 9 months. The price year was 1997.

Statistical analysis of costs
A base model to estimate total costs was developed including some predictor variables: initial treatment type, gender, clinical trial participation, age, severity and a random effect for study site. Cost estimates based on multivariable results
are reported separately for each treatment group, using least squares means. Confidence intervals and tests for the differences between oral and local therapy were reported.

**Indirect Costs**
Indirect costs were not included in the analysis since the study was conducted from the perspective of the healthcare system.

**Currency**
All costs were reported in 1997 US dollars ($).

**Sensitivity analysis**
No sensitivity analyses were performed, but confidence intervals were reported both for effectiveness and for costs.

**Estimated benefits used in the economic analysis**
See effectiveness results above.

**Cost results**
The mean cost per patient was reported separately for those who initially received treatment with oral medication or local therapy.

For those initially treated with oral medication, mean total costs in the follow-up interval from baseline through month 4 ($685 (SD $149) for Medicare and $748 (SD $166) for standard fees) far exceeded those during the interval from month 5 through 9 ($71 (SD $112) and $102 (SD $190)).

For those initially treated with local therapy, mean total costs in the follow-up interval from baseline through month 4 ($212 (SD $135) for Medicare and $307 (SD $209) for standard fees) were almost equal to those during the interval from month 5 through 9 ($209 (SD $241) and $271 (SD $283)).

Among patients initially treated with oral medication, the cost of medications comprised the largest single cost component, while among those initially treated locally, the largest costs were due to protocol visits.

The total cost of treatment was significantly higher for patients initially treated with oral medication than for patients initially treated with local therapy, whether calculated by Medicare fees ($299 higher) or by standard fees ($219 higher).

No discount rate was applied (9-month follow-up).

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratio was most favourable for oral treatment when calculated using the physician's global assessment and standard fees ($304 per patient improved) and least favourable when calculated using the patient reported TSI and Medicare fees ($695 per additional patient improved). In the case of physician's global assessment and Medicare fees the ratio was equal to $515 per patient improved while in the case of patient's assessment and standard fees it was equal to $491 per patient improved.

**Authors' conclusions**
The study showed that, over a 9-month timeframe, the treatment of a person with onychomycosis is more costly using the newer oral antifungal agents than using local treatment. However, oral antifungal medication is significantly more effective in producing clinical improvement. The incremental cost-effectiveness ratio is more or less favourable for the
oral treatment depending on the way of assessment of effectiveness (physician or patient) and the set of fees considered.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of comparators was clear. The clinical management of onychomycosis can include local therapy, oral treatment or a combination of the two.

**Validity of estimate of measure of effectiveness**
Effectiveness estimates were derived from an observational study, which does not ensure a level of internal validity equivalent to a clinical trial. No data on the possible difference in health status between patients initially treated with oral therapy and patients initially treated locally were reported. Assessments were based on the discretion of the examining physicians. It would appear that compliance for the interventions is problematic as the drop out rate was fairly substantial. These factors may have hindered the validity of the results.

**Validity of estimate of measure of benefit**
A measure of benefit was obtained from physicians' global assessment and patients' reports. The criteria used by the physicians to assess change in the patient's fungal nail involvement were not reported. Difficulties in the interpretation of incremental cost-effectiveness ratios may arise given the unclear measure of benefit.

**Validity of estimate of costs**
The estimation of total costs of treatment for patients with onychomycosis was one of the main goals of the study. Confidence intervals were reported for each category of costs and the use of both Medicare fees and standard fees might be interpreted as being, in effect, a sensitivity analysis. However, the study presented some limitations (as suggested by the authors): costs for hospitalisations and costs associated with adverse reactions to treatment were not included. Moreover, given the perspective of the study (healthcare system), direct non-medical costs and indirect costs were not considered. The inclusion of these categories of costs might have changed, in part, the results of the analysis.

**Other issues**
It is interesting to note that the costs associated with patients initially treated with oral medication are much higher in the first 4-months of follow-up compared with the subsequent 5 months, while the costs associated with patients initially treated locally are almost equally distributed. Assuming linearity in monthly costs after month 4 (reasonable, in particular, for local therapy) the authors noticed that cost equivalence between oral medication and local therapy would be reached at about month 21 from baseline using Medicare fees, and at month 17 using standard fees. Therefore, extrapolations suggest that treatment with oral medication could result in decreased cost of treatment over a 24-month time frame.

**Implications of the study**
The use of oral antifungal agents is likely to be cost-effective, in particular for a long-term time frame.

**Source of funding**
Funding from Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA.

**Bibliographic details**

**PubMedID**
Other publications of related interest

Indexing Status
Subject indexing assigned by NLM

MeSH
Adult; Aged; Antifungal Agents /therapeutic use; Cost-Benefit Analysis; Female; Health Care Costs; Humans; Male; Middle Aged; Onychomycosis /drug therapy; Prospective Studies

AccessionNumber
22001008107

Date bibliographic record published
30/09/2001

Date abstract record published
30/09/2001