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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
Systemic isotretinoin at a daily dose of 1mg/kg (cumulative dose of 120 mg/kg) in the treatment of patients with a diagnosis of moderate to severe acne.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with a diagnosis of moderate to severe acne.

Setting
Hospital. The economic study was carried out in South Africa.

Dates to which data relate
Effectiveness data were extracted from studies published between 1981 and 1997. Resource use data were obtained from reports published in 1997 and 1998. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a review of the literature and authors' assumptions.

Modelling
A modified Markov process was used to estimate the costs and effects associated with each treatment strategy.

Outcomes assessed in the review
The following outcomes were assessed: relapse rate; treatment effectiveness levels corresponding to excellent, fair, and poor responses; success rate; and average treatment period.

Study designs and other criteria for inclusion in the review
The review included published trials since 1981 fulfilling the following inclusion criteria:

(1) studies stating a clear diagnosis of acne vulgaris with success rate or treatment period;
(2) randomised controlled trials;
(3) trials specifying dosages of isotretinoin used;
(4) studies reporting on the clinical effectiveness of isotretinoin;
(5) studies with a sample size of at least 50 patients in the isotretinoin group.

Sources searched to identify primary studies
Studies were identified using a MEDLINE search, Internet searches, and publications from commercial organisations such as Roche (SA), Pharmaceutical Benefit Management (SA), and Borgan Consulting Inc. (USA).

Criteria used to ensure the validity of primary studies
Blinding was not considered as a selection criterion since this was not deemed to be a comparative study. The condition imposed on minimum sample size required (\( n \geq 50 \)) was deemed adequate to fulfil the requirements of the application of the statistical methods. Only papers that reported on clinical effectiveness were included.

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

Number of primary studies included
Initially 37 studies, subsequently refined to 18, were included in the review.

Methods of combining primary studies
Meta-analysis (weighted average).

Investigation of differences between primary studies
The homogeneity of results in terms of outcome measures was tested and the heterogeneous subset was not used to estimate the combined (total) value for the study outcomes. Chi-square or analyses of variance (ANOVAs) were used to perform homogeneity test.

Results of the review
The use of isotretinoin was associated with a relapse rate of 21.45% versus 96.34% for the oral antibiotics-based regimens (based on a 5-year relapse rate of 83%).

The isotretinoin therapy had effective levels of 84.8% corresponding to an excellent response, 11.9% to a fair response, and 3.3% to a poor response.

The success rate was between 84.22% and 86.71%.

The isotretinoin therapy had an average treatment period of 17.9 weeks.

Methods used to derive estimates of effectiveness
The authors also made assumptions about effectiveness.

Estimates of effectiveness and key assumptions
All physician contacts were considered to refer to dermatologist consultations. All female patients using systemic
isotretinoin were assumed to be using an oral contraceptive with 100% compliance rate.

**Measure of benefits used in the economic analysis**
The benefit measure was success rate.

**Direct costs**
Costs were not discounted despite the 120-month time frame adopted for the cost analysis. Although discounting would appear to have been appropriate, the authors provided some justification for choosing not to use it in the cost analysis. Quantities and cost items were reported separately (part 2). Cost analysis covered the costs of drugs, laboratory tests, pathology and pregnancy tests, and dermatologist consultations. The perspective adopted in the cost analysis was that of the health care funder. Charges were employed as a proxy for true costs. The source of cost data was different reports and price books. The date of the price data was 1998. The cost of topical therapy was not considered in the baseline analysis, but was included in the sensitivity analysis.

**Indirect Costs**
Not considered.

**Currency**
South African rand (R).

**Sensitivity analysis**
A series of one-way sensitivity analyses was conducted on isotretinoin relapse rate and oral antibiotic costs, including the cost of topical therapy. Threshold analysis was performed by finding the break-even between various strategies in terms of the period of continued treatment required for two alternative to achieve their respective clinical endpoints.

**Estimated benefits used in the economic analysis**
The success rate for the isotretinoin therapy was between 84.22% and 86.71%.

**Cost results**
The total costs for the four strategies after 5 years were as follows:

- isotretinoin, R8,941;
- oral antibiotics, R10,428;
- antibiotics/anti-androgen therapy, R14,327;
- stepped therapy, R9,983.

Costs were also reported after 2 years and after 10 years.

**Synthesis of costs and benefits**
Cost per successfully treated patient was calculated as the measure of cost-effectiveness. The ratio ranged from R8,941 for the isotretinoin therapy to R10,529 for the stepped therapy. The sensitivity analysis established the robustness of the results to changes in the parameters.
Authors' conclusions
From the model it is clear that, where systemic isotretinoin is clinically indicated, the sooner such therapy is initiated the more cost-effective the outcome will be. If isotretinoin is prescribed on diagnosis of moderate to severe acne, then the cost of treatment is significantly reduced in the long term when compared with standard oral antibiotic therapy.

CRD COMMENTARY - Selection of comparators
Oral antibiotic therapy, as standard therapy, was regarded as the comparator. You, as a database user, should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
The effectiveness results are likely to be internally valid given the comprehensive review performed and the quality assessment of the primary studies included in the review. However, insufficient details were provided on the method of estimation of the annual relapse rate of the oral antibiotic-based regimens.

Validity of estimate of costs
Quantities were reported separately from the costs and adequate details of methods of cost estimation were given. Cost results may, however, not be generalisable to other settings or countries.

Other issues
The overall validity of the study results suffered from lack of a standard and common clinical outcome for both systemic isotretinoin therapy (eradication as its objective) and antibiotic therapy (control as its objective), as the authors acknowledged. The issue of generalisability to other settings was not fully addressed.

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Other publications of related interest


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Subject indexing assigned by NLM

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