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 either a novel biological agent (BIO), methotrexate (MTX) or intramuscular gold (IMG) as a therapy for rheumatoid arthritis (RA).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with established rheumatoid arthritis (RA).

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

Dates to which data relate
Data for some effectiveness, resource use and costs were taken from papers published between 1987 and 1993. Prices were from 1992.

Source of effectiveness data
The evidence for final outcomes was based on a review of selected papers and the authors' opinion and that of some rheumatologists.

Modelling
A decision tree was used to estimate costs and benefits.

Outcomes assessed in the review
The toxicity profiles and the efficacy of IMG and MTX were derived from the published literature.

Study designs and other criteria for inclusion in the review
It is not clear which study designs were included in the review and no inclusion or exclusion criteria were stated. The duration of follow up for the study was six months but the duration of the studies included in the review is not clear.
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
This was not clear but is likely to be between 10 and 15.

Methods of combining primary studies
Not undertaken.

Investigation of differences between primary studies
No investigation of differences between primary studies was undertaken. However, sensitivity analysis was undertaken to explore variability in outcomes.

Results of the review
Results are summarised below.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also taken from expert opinion and consensus between four rheumatologists, as well as from the results of a questionnaire sent to 31 rheumatologists (28 or 90% responded).

Estimates of effectiveness and key assumptions
The clinical response rate to therapy (complete plus partial) was 85% for MTX, 70% for IMG and 85% for BIO. The proportion of 'complete' clinical responses was 30%, 15% and 30% for MTX, IMG and BIO respectively. The frequency of adverse effects was 20% for all options. The proportion of major adverse effects was 10% for MTX, 11% for IMG and 10% for BIO. It was assumed that there were no dropouts within the 6-month time frame used for the study and in addition, the responders were considered to respond throughout the 6-month period. If necessary, it was assumed that repetitive administration of the BIO could be undertaken during the 6-month period with no increased toxicity or diminished efficacy.

Measure of benefits used in the economic analysis
Response to therapy involved one of the following three outcomes: no response, partial response or complete response. These efficacy results were based on a survey of local rheumatologists and relevant published data.

Direct costs
Since the follow up was for six months only, discounting was not required. Quantities were not reported separately from costs. Costs measured included medication and monitoring and complications (toxicity). The boundary adopted was the health service. The costs estimates were based partly on actual data (average of drug charges at local pharmacies and monitoring costs from local laboratories), partly on standard prices and partly on opinion (for minor side effects). 1992 prices were used.
Statistical analysis of costs
None.

Indirect Costs
Discounting was not required as the follow up period was only six months. Quantities were not analysed separately from costs. Costs measured included lost wages and money paid to others for the 'performance of household chores'. The boundary adopted was the patient. Each response status (complete, partial or no response) was assigned a different proportion of an estimated average 6-month cost and this was based on a guess. The source of cost data was two previously published population-based cohort studies that took a human capital approach to costing. 1992 prices were used and were reflated at a 5% annual rate.

Currency
US dollars ($).

Sensitivity analysis
The parameters of the study in which uncertainty was explored included the costs of medication and monitoring and response rates (both complete and partial combined and complete rather than partial response). The area of uncertainty investigated was the variability in data. One way and two way sensitivity analyses were carried out as well as analysis of extremes.

Estimated benefits used in the economic analysis
The clinical response rate to therapy (complete plus partial) was 85% for MTX, 70% for IMG and 85% for BIO. The proportion of 'complete' clinical responses was 30%, 15% and 30% for MTX, IMG and BIO respectively. The frequency of adverse effects was 20% for all options. The proportion of major adverse effects was 10% for MTX, 11% for IMG and 10% for BIO. It was assumed that there were no dropouts within the 6-month time frame used for the study and in addition, the responders were considered to respond throughout the 6-month period. If necessary, it was assumed that repetitive administration of the BIO could be undertaken during the 6-month period with no increased toxicity or diminished efficacy.

Cost results
The cost of medication and monitoring was $1,769 for MTX, $2,399 for IMG and $5,750 for BIO. The indirect costs of RA were $6,065 per six months in patients with no clinical response, 3,032.50 for a partial response and 606.50 if a complete clinical response resulted.

Synthesis of costs and benefits
Costs and benefits were not synthesised, rather the results were presented as a cost consequence analysis and then the total cost considerations were explored. The total cost for MTX was $5,430, for IMG was $6,725 and for the BIO agent was $9,411. The sensitivity analysis showed that the important parameters were medication plus monitoring costs of BIO and the effectiveness rate embodied in the proportion of complete clinical responders to the BIO therapy. Two-way sensitivity analyses using these two parameters were performed for BIO against IMG and BIO against MTX. For the BIO agent to be preferred to IMG it would have to have medication and monitoring costs of under $4,000 and an effectiveness rate exceeding 70%.

Authors' conclusions
The study indicated that the cost of the medication may be a critical consideration in the development and use of novel biological therapies in patients with RA.
CRD COMMENTARY - Selection of comparators
The choice of comparator was justified.

Validity of estimate of measure of benefit
The clinical analysis was very limited, as the authors recognised. The analysis of internal validity of studies reviewed was not discussed nor was the search strategy for locating the studies reported. The time span of the study was limited to 6 months. The time delay in response was also pointed out as an important omission.

Validity of estimate of costs
On the cost side, the indirect costs were thought to underestimate the true value. However, this is questionable. Currently there is a debate about how to value indirect costs (if at all) and the human capital approach taken here often provides the highest indirect cost estimate.

Other issues
More rigorous research is required to test the strength of the evidence presented.

Source of funding
None stated.

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