Treatment strategies aiming at remission in early rheumatoid arthritis patients: starting with methotrexate monotherapy is cost-effective


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.

CRD summary
The objective was to assess the cost-effectiveness of treatment strategies aimed at achieving remission in patients with early stage rheumatoid arthritis. The authors concluded that treatment starting with methotrexate monotherapy was favoured over treatment starting with methotrexate and leflunomide or methotrexate and an anti-tumour necrosis factor drug. The methods were adequate and both they and the results were reported in full. Given the scope of the study, the authors' conclusions appear to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of three treatment strategies aimed at achieving remission in patients with early stage rheumatoid arthritis.

Interventions
The three strategies were methotrexate monotherapy with the addition of leflunomide and a switch to methotrexate plus an anti-tumour necrosis factor (TNF) drug when patients experienced an inadequate response to treatment; methotrexate plus leflunomide, followed by methotrexate plus an anti-TNF drug; and methotrexate plus an anti-TNF drug.

Location/setting
Netherlands/out-patient secondary care.

Methods
Analytical approach:
The authors used a validated Markov model to assess the cost-effectiveness of the three interventions (Welsing, et al. 2006, see 'Other Publications of Related Interest' below for bibliographic details). The time horizon was five years. The authors reported that the analysis was performed, using two perspectives, that of the health care system and that of society.

Effectiveness data:
The clinical and effectiveness data were from two Dutch cohorts: the Nijmegen rheumatoid arthritis inception cohort and the Dutch Rheumatoid Arthritis Monitoring (DREAM) registry. Patients were selected from these two cohorts if they received one of the three treatment strategies between 2003 and 2008. The baseline characteristics of patients in each of the three groups were matched, based on the initial sample sizes in the two cohorts, using the ratio of one methotrexate patient to one leflunomide patient to three anti-TNF patients. In total, 112 patients were included in the methotrexate group, 47 in the leflunomide group, and 332 in the anti-TNF group. Missing outcome data were estimated using linear extrapolation.

Monetary benefit and utility valuations:
The utility estimates were from a published study, which used the European Quality of life (EQ-5D) questionnaire and British tariffs.
Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) gained. Future benefits were discounted at an annual rate of 4%.

Cost data:
The health care costs included general practitioner visits, out-patient visits, surgery, hospitalisation, and medications. The societal costs also included absence from paid work, which was valued using the friction cost method, travel expenses, and out-of-pocket costs, such as alternative treatments and home help. All costs were from the study that supplied the utility estimates, except those for medications, which were from the Dutch National Tariff list. All costs were reported in Euros (EUR) and future costs were discounted at an annual rate of 4%.

Analysis of uncertainty:
A probabilistic sensitivity analysis was undertaken to assess the impact of parameter uncertainty on the model's results. Probabilistic distributions were assigned to each mean value in the model. A value from each distribution was then drawn for all parameters, in 1,000 Monte Carlo simulations. The results were presented in a cost-effectiveness acceptability curve.

Results
The average QALYs gained per patient were 3.086 (95% CI 3.079 to 3.092) in the methotrexate group, 3.089 (95% CI 3.083 to 3.096) in the leflunomide group, and 3.093 (95% CI 3.086 to 3.099) in anti-TNF group.

From the health care system perspective, the average cost per patient was EUR 16,620 (95% CI 16,607 to 16,633) in the methotrexate group, EUR 18,313 (95% CI 18,301 to 18,327) in the leflunomide group, and EUR 17,574 (95% CI 17,574 to 17,588) in the anti-TNF group.

From a societal perspective, the average cost per patient was EUR 17,580 (95% CI 17,558 to 17,601) in the methotrexate group, EUR 19,269 (95% CI 19,247 to 19,290) in the leflunomide group, and EUR 18,521 (95% CI 18,499 to 18,542) in the anti-TNF group.

The leflunomide strategy was dominated by the anti-TNF strategy, as the anti-TNF strategy was less costly and more effective. Compared with the methotrexate strategy, the anti-TNF strategy had an incremental cost-utility ratio of EUR 138,056 per QALY gained (95% CI 137,007 to 139,123) from a health care perspective, and EUR 136,207 per QALY gained (95% CI 135,022 to 137,363) from a societal perspective.

Authors’ conclusions
The authors concluded that treatment starting with methotrexate monotherapy was favoured over the other two options.

CRD commentary
Interventions:
The interventions were well described. Two anti-TNF drugs were considered (adalimumab and etanercept) on the grounds that these were those most commonly prescribed in the authors' setting. It was not clear whether the effectiveness of other biologics differed from these, and this should be considered when interpreting the results of this analysis.

Effectiveness/benefits:
The clinical and effectiveness evidence was from two cohort studies. Treatment allocation was not randomised and participants could have varied in their baseline characteristics, which could have biased the results. To minimise this issue, the authors matched patients in the three groups on several baseline characteristics, but significant differences remained in disease duration and previous treatments. These data equated to an indirect comparison and the limitations of this were discussed by the authors. These data also closely reassemble what occurs in clinical practice, and might as a result be more generalisable.

Costs:
It appears that no major costs relevant to the health care system and societal perspectives were omitted. The sources for the cost information were reported, as were the time horizon and discount rate, but the price year was not, which will
hamper future inflationary exercises.

Analysis and results:
A validated Markov model was used to synthesise the cost and outcome information. Appropriate details of this model, including a diagram, were provided. The overall model uncertainty was appropriately evaluated, using probabilistic sensitivity analysis. The main limitation of their study was reported by the authors to be that their evidence was not from randomised studies.

Concluding remarks:
The methods were adequate and both they and the results were reported in full. Given the scope of the study, the authors' conclusions appear to be valid.

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