Aggressive versus symptomatic therapy in established rheumatoid arthritis

The British Rheumatoid Outcome Study Group (BROSG) randomised controlled trial to compare the effectiveness and cost-effectiveness of aggressive versus symptomatic therapy in established rheumatoid arthritis

D Symmons,[1*] K Tricker,[1] C Roberts,[2] L Davies,[3] P Dawes[4] and DL Scott[5]

[1] RC Epidemiology Unit, University of Manchester, UK
[2] Biostatistics Group, University of Manchester, UK
[3] Health Economics Research Unit, University of Manchester, UK
[4] Staffordshire Rheumatology Centre, Stoke-on-Trent, UK
[5] Academic Rheumatology Unit, King's College Hospital, London, UK

* Corresponding author

Executive summary

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Executive summary

Objectives

To examine the effectiveness and cost-effectiveness of symptomatic versus aggressive treatment in patients with established, stable rheumatoid arthritis (RA).

Design

A randomised observer-blinded controlled trial and economic evaluation with an initial assessment at randomisation and follow-ups at 12, 24 and 36 months.

Setting

Five rheumatology centres in England. The 'symptomatic care' patients were managed predominantly in primary care with regular visits by a rheumatology specialist nurse. The 'aggressive care' patients were managed predominantly in the hospital setting.

Patients

Patients with RA for more than 5 years' duration were screened in rheumatology clinics. They were asked to participate if they had been on stable therapy for at least 6 months and had no evidence of systemic rheumatoid disease or other serious co-morbidity.

Interventions

The symptomatic care patients were seen at home every 4 months by a rheumatology specialist nurse and annually by the rheumatologist. The aim of treatment was symptom control. The aggressive care patients were seen at least every 4 months in hospital. Their treatment was altered (following predefined algorithms) with the aim of suppressing both clinical and laboratory evidence of joint inflammation.

Outcome measures

The main outcome measure was the Health Assessment Questionnaire (HAQ). Others included the patient and physician global assessment, pain, tender and swollen joint counts, the erythrocyte sedimentation rate and the OSRA (Overall Status in Rheumatoid Arthritis) score. X-rays of the hands and feet were performed at the beginning and end of the study. The EQ-5D was used in the health economic evaluation. Comprehensive costs were also estimated and were combined with measures of outcome to examine between-group differences.

Results

A total of 466 patients were recruited; 399 patients completed the 3 years of follow-up. There was a significant deterioration in physical function (HAQ) in both arms. There was no significant difference between the groups for any of the clinical outcome measures except the physician global assessment [adjusted mean difference 3.76 (95% CI 0.03 to 7.52)] and the OSRA disease activity component [adjusted mean difference 0.41 (95% CI 0.01 to 0.71)], both in favour of the aggressive arm. During the trial, second-line drug treatment was changed in 77.1% of the aggressive arm and 59.0% of the symptomatic arm. There were instances when the rheumatologist should have changed treatment but did not do so, usually because of mild disease activity. The symptomatic arm was associated with higher costs and higher quality-adjusted life-years (QALYs). There was a net cost of £1517 per QALY gained for the symptomatic arm. Overall, the primary economic analysis and sensitivity analyses of the cost and QALY data indicate that symptomatic treatment is likely to be more cost-effective than aggressive treatment in 58–90% of cases.

Conclusions

This trial showed no benefit of aggressive treatment in patients with stable established RA. However, it was difficult to persuade the rheumatologist and/or the patient to change treatment if the evidence of disease activity was minimal. Patients in the symptomatic arm were able to initiate changes of therapy when their symptoms deteriorated, without frequent hospital assessment. Approximately one-third of current

clinic attenders with stable RA could be managed in a shared care setting with annual review by a rheumatologist and regular contact with a rheumatology nurse.

Recommendations for further research

The following areas are suggested for further research.

- A trial to establish whether disease progression can be retarded in patients with mild, stable established RA using biological agents. There is evidence from the TEMPO Trial that the combination of methotrexate and etanercept can halt radiological progression in patients with active established RA. Would the same effect be seen in patients with relatively inactive disease?
- Refinement of the model of shared care that was found to be cost-effective in this trial. For example, is contact with a nurse every 4 months (based in either hospital or primary care) essential? Could the contact be replaced by a telephone call or a postal questionnaire?
- Development of a robust and fail-safe system of disease-modifying anti-rheumatic drug (DMARD) monitoring that is primary care based. If patients are going to be managed in shared care with annual review by a rheumatologist, then the DMARD monitoring should also be able to detect non-attendance for blood tests, should be able to prevent prescriptions from being issued if monitoring is not taking pace, should be able to detect abnormal results and bring them to the prescriber's attention and should protect the nurse or doctor from having to check large numbers of normal results. Such a system should be computerised and link into both GP and hospital systems. The rheumatologist should be available to provide advice in the case of abnormal results.
- Further studies to predict response to DMARDs.
- Further research to establish whether there is a minimum disease activity level below which disease progression does not occur.

Publication

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NHS R&D HTA Programme

The research findings from the NHS R&D Health Technology Assessment (HTA) Programme directly influence key decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC) who rely on HTA outputs to help raise standards of care. HTA findings also help to improve the quality of the service in the NHS indirectly in that they form a key component of the 'National Knowledge Service' that is being developed to improve the evidence of clinical practice throughout the NHS.

The HTA Programme was set up in 1993. Its role is to ensure that high-quality research information on the costs, effectiveness and broader impact of health technologies is produced in the most efficient way for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The HTA Programme commissions research only on topics where it has identified key gaps in the evidence needed by the NHS. Suggestions for topics are actively sought from people working in the NHS, the public, service-users groups and professional bodies such as Royal Colleges and NHS Trusts.

Research suggestions are carefully considered by panels of independent experts (including service users) whose advice results in a ranked list of recommended research priorities. The HTA Programme then commissions the research team best suited to undertake the work, in the manner most appropriate to find the relevant answers. Some projects may take only months, others need several years to answer the research questions adequately. They may involve synthesising existing evidence or conducting a trial to produce new evidence where none currently exists.

Additionally, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme is able to commission bespoke reports, principally for NICE, but also for other policy customers, such as a National Clinical Director. TARs bring together evidence on key aspects of the use of specific technologies and usually have to be completed within a short time period.

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Reports are published in the HTA monograph series if (1) they have resulted from work commissioned for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

The research reported in this monograph was commissioned by the HTA Programme as project number 94/45/02. The contractual start date was in May 1997. The draft report began editorial review in August 2003 and was accepted for publication in February 2005. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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