Statin therapy in rheumatoid arthritis: a cost-effectiveness and value-of-information analysis
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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.

CRD summary
The objective was to evaluate the long-term cost-effectiveness of statin therapy for patients with rheumatoid arthritis. The authors concluded that statin therapy could be highly cost-effective. The quality of the study and the reporting were good and the results appear to be reliable.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to evaluate the long-term cost-effectiveness of statin therapy for patients with rheumatoid arthritis.

Interventions
Statin therapy (atorvastatin 40mg) alongside disease-modifying antirheumatic drugs (DMARDs) was compared with DMARDs alone over a 10-year period.

Location/setting
USA/secondary care.

Methods
Analytical approach:
A state-transition Markov model was used to examine the impact of the therapies on cardiovascular disease and rheumatoid arthritis over time. The model was developed in two parts. The coronary heart disease (CHD) model predicted events over time based on lipid profiles, while the rheumatoid arthritis model predicted the outcomes of changes in disease activity for quality of life. The base-case scenario considered female patients with a similar profile to those in a recent clinical trial. A 10-year horizon was adopted and the authors stated that the perspective was that of the US health care payer.

Effectiveness data:
The clinical data were based on a single-centre randomised controlled trial, called the Trial of Atorvastatin in Rheumatoid Arthritis (TARA, McCarey, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). The trial compared atorvastatin 40mg with placebo over a six months. Framingham risk equations were used to predict the long-term events based on the TARA data. It was assumed that the results for atorvastatin were representative of all statins. Other published sources were used to inform the assumptions and distributions. The key clinical parameters were the number of CHD events, and the response to statin therapy, which was measured by the rheumatoid arthritis Disease Activity Score (DAS28).

Monetary benefit and utility valuations:
The utility estimates for CHD events were from a published systematic review. The estimates for the rheumatoid arthritis utilities were derived, using the DAS28 and the Health Assessment Questionnaire (HAQ), from a cohort of Swedish rheumatoid arthritis patients.

Measure of benefit:
The measure of benefit was the number of quality-adjusted life-years (QALYs) gained and these were discounted at an
annual rate of 5%.

Cost data:
The analysis considered the direct medical costs of the acquisition of the statins and the treatment of rheumatoid arthritis (other drugs, out-patient visits, health professionals, diagnostic tests, and hospitalisation). These costs were from Medicare reimbursement rates and a published US costing exercise, as well as the direct rheumatoid arthritis treatment costs estimated using baseline HAQ scores. The cost of statin therapy was based on its wholesale acquisition price. The costs were adjusted using the medical care component of the US Consumer Price Index to reflect the 2005 price year US dollars ($). An annual discount rate of 5% was applied.

Analysis of uncertainty:
One-way and probabilistic sensitivity analyses were performed to assess the uncertainty in the parameter estimates. A full uncertainty analysis was also performed to determine the value, from future studies, of perfect information for the relevant variables.

Results
Over 10 years, the incremental cost of statin therapy ($62,046) over no statin therapy ($57,356) was $4,690. The mean gain in QALYs with statin therapy (3.38) over no statin therapy (2.94) was 0.44.

The incremental cost-effectiveness ratio of statin therapy, over no therapy, was $10,650 per QALY gained (95% CI 1,525 to 156,565).

The probabilistic sensitivity analysis showed that at a willingness-to-pay of $50,000 per QALY the probability that statin therapy was cost-effective was 90%. The value of information analysis identified the change in the DAS28 and C-reactive protein (CRP) scores over the first six months (and to a lesser extent between six and 12 months) with therapy, followed by the health utilities associated with the HAQ and DAS28 scores, as the key uncertain parameters.

Authors’ conclusions
The authors concluded that statin therapy could be highly cost-effective for the treatment of rheumatoid arthritis patients due to its dual effects in reducing the risk of CHD and in treating rheumatism.

CRD commentary
Interventions:
The intervention was adequately described and the comparator was appropriate, as it represented the usual practice in the study setting.

Effectiveness/benefits:
The clinical data were derived from a single-centre RCT. Some of the details, such as the sample size and baseline characteristics, were reported, which will allow some assessment of its validity. It was implied that this was the only available RCT for atorvastatin in rheumatoid arthritis, but this was not explicitly stated, making it difficult to be sure. The authors suggested that other statins had been studied, but they assumed that atorvastatin represented statins as a class. They did not explain why all statin trials were not synthesised for the model. This makes it unclear if the best available evidence was used. The follow-up period of 10 years should have been long enough to capture the full effects of the treatment. The authors acknowledged the limitations of using the Framingham risk equations to estimate the long-term data. The utility estimates were provided and referenced, but it was not clear how the utilities were combined from the two outcomes, DAS28 and HAQ. A separate paper might clarify this issue (Kobelt, et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details). QALYs were an appropriate measure of benefit given the impact of treatment on quality of life and survival.

Costs:
The authors reported the perspective and all the relevant costs for this perspective appear to have been included. The derivation of, and sources of, the cost items were described, but no details of resource use were reported, which may limit the transferability to other settings. The price year was reported and the results can be revalued for future years. The costs were inflated using the medical care component of the US Consumer Price Index, which was appropriate as
health care price inflation tends to be greater than overall inflation.

Analysis and results:
The analytical approach appears to have been satisfactory and was well reported. The model structure was given in a diagram. An appropriate incremental analysis was performed to determine the cost-effectiveness of the treatment strategy. The sensitivity of the results to variations in the key parameters was addressed by one-way and probabilistic sensitivity analyses, as well as a value of information analysis. Some of the distributions assigned in the probabilistic analysis might not reflect best practice (the use of triangular distributions), but this is unlikely to have had a big impact on the conclusions. The reporting was good and the base-case estimates of costs and effectiveness were presented. The authors discussed the key limitations of their study, but did not mention gender differences, despite their base case being female patients only.

Concluding remarks:
The quality of the study was good and, the methods and results well reported. The findings appear to be generally reliable and, the authors’ conclusions are appropriate and consistent with the evidence presented.

Funding
No funding received.

Bibliographic details

PubMedID
19178122

DOI
10.2165/00019053-200927010-00004

Original Paper URL

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Anticholesteremic Agents /economics /therapeutic use; Arthritis, Rheumatoid /drug therapy /economics; Coronary Disease /prevention & control; Cost-Benefit Analysis; Decision Support Techniques; Female; Humans; Hydroxymethylglutaryl-CoA Reductase Inhibitors /economics /therapeutic use; Male; Markov Chains; Quality of Life; Randomized Controlled Trials as Topic

AccessionNumber
22009100906
Date bibliographic record published
02/12/2009

Date abstract record published
13/10/2010