Cost effectiveness of the determination of autoantibodies against cyclic citrullinated peptide in the early diagnosis of rheumatoid arthritis

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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 examine the cost-effectiveness of the early diagnosis of rheumatoid arthritis, based on the presence of antibodies against cyclic citrullinated peptide (aCCP), in patients diagnosed with undifferentiated arthritis. The addition of aCCP to the American College of Rheumatology diagnostic criteria was very cost-effective, especially when indirect costs were included. The study was based on robust methodology, but the reporting of the data sources was limited. Further studies are needed to confirm the authors’ conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to examine the cost-effectiveness of early diagnosis of rheumatoid arthritis based on the presence of antibodies against cyclic citrullinated peptide (aCCP) in patients diagnosed with undifferentiated arthritis.

Interventions
The intervention was testing for aCCP in addition to American College of Rheumatology (ACR) criteria to diagnose rheumatoid arthritis. The comparator was diagnosis using ACR criteria only.

Location/setting
Germany/secondary care.

Methods
Analytical approach:
This economic evaluation was based on a published Markov model with a 10-year time horizon, and health states defined by the Health Assessment Questionnaire (HAQ). The authors did not explicitly report the perspective.

Effectiveness data:
The clinical evidence came from a selection of known, relevant, published sources. Disease progression and the patient population were based on a Swedish study (the Lund Study), which included 183 patients with rheumatoid arthritis, and mortality was taken from German life tables. The accuracy of testing for aCCP to determine rheumatoid arthritis was taken from a published cohort study. The key clinical input was the impact of late treatment on the disease progression, which was based on two published studies of rheumatoid arthritis populations.

Monetary benefit and utility valuations:
The utility values were derived from a published source that used the HAQ-dependent European Quality of life (EQ-5D) questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary benefit measure and were discounted at 5% per annum.

Cost data:
The economic analysis included the costs of: aCCP test, in-patient and out-patient treatment, rehabilitation, disease-modifying antirheumatic drugs (DMARDs) and non-DMARDs (including monitoring and side effects), and out-of-
pocket expenses. The average drug costs were calculated by weighting the costs of various agents with their prescription frequency. The economic data were taken from published reports, the details of which were not given. All costs were in Euros (EUR) and a 5% annual discount rate was applied. The price year was not reported.

Analysis of uncertainty:
A deterministic one-way sensitivity analysis was undertaken using published ranges of values for all the model inputs. The most influential inputs were then varied in a Monte Carlo simulation with 10,000 iterations. In a separate analysis, the costs associated with productivity losses were included on the basis of gender-specific, German, gross salaries and employers' contributions to social security.

Results
The mean cost per patient was EUR 15,010 with aCCP and EUR 14,995 without aCCP. The QALYs were 7.1237 with aCCP and 7.1073 without. The incremental cost per QALY gained with aCCP over no aCCP was EUR 930. The inclusion of indirect costs made the aCCP strategy dominant, which means it was both more effective and less expensive.

The deterministic analysis showed that these base-case findings were relatively stable, except for variations in the impact of late diagnosis and treatment on HAQ progression. Variation in this input led to a lower limit of dominant and to a higher limit of EUR 153,092 per QALY, but the effect of this variable was reduced when the indirect costs were included.

The probabilistic analysis indicated that the 95% confidence interval of the incremental cost-effectiveness per QALY ranged from dominant to EUR 5,429, while the aCCP strategy remained dominant in all simulations when the indirect costs were included.

Authors' conclusions
The authors concluded that testing for aCCP was a very cost-effective addition to the ACR criteria for the early diagnosis of rheumatoid arthritis, especially when including the indirect costs.

CRD commentary
Interventions:
The selection of the comparators was appropriate as the additional use of aCCP was compared with the current ACR approach, which was widely considered to be the reference methodology.

Effectiveness/benefits:
The clinical analysis was not extensively reported. The approach used to identify the primary sources of data was not stated and these studies may have been already known to the authors. A systematic search would have been more appropriate. Very little information on the methodological characteristics and other features of the other sources of data was provided, which limits the possibility of judging the validity of the clinical inputs. No details on the derivation of the utility values were provided, except for the use of the EQ-5D instrument, which is a validated tool for rheumatoid arthritis patients. QALYs are an appropriate benefit measure, which allow cross-disease comparisons and capture the impact of the interventions on patients' health.

Costs:
The authors did not explicitly state the perspective taken, but a broad viewpoint appears to have been considered, given the wide range of cost categories included. The inclusion of the indirect costs of diminished productivity was assessed in the sensitivity analysis, which showed the importance of this cost category. Little information on the sources of the economic data was provided, which limits the transparency of the economic analysis. The costs were presented as macro-categories and the price year was not reported, which limits the possibility of making reflation exercises in other time periods.

Analysis and results:
The costs and benefits were appropriately reported and were synthesised in an incremental analysis. Two methods were used to investigate the uncertainty and this appears to have been appropriate. The study findings were clearly reported.
and discussed. The issue of the generalisability of the results to other settings was not discussed, but the sensitivity analysis investigated alternative assumptions. The authors acknowledged some limitations of their study mainly arising from the sources for the clinical data, which did not have the same study populations. It was stated that this was the first study that analysed the cost-effectiveness of the early diagnosis of rheumatoid arthritis based on aCCP.

Concluding remarks:
On the whole, the study appears to have been based on robust methodology, but the reporting of the data sources was limited. Further studies are needed to confirm the authors’ conclusions.

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