Cost-effectiveness of biologics in polyarticular-course juvenile idiopathic arthritis patients unresponsive to disease-modifying antirheumatic drugs

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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
This study examined the cost-effectiveness of four biologic treatments, etanercept, infliximab, adalimumab, and abatacept, for patients with polyarticular-course juvenile idiopathic arthritis and with a prior inadequate response or intolerance to disease-modifying antirheumatic drugs. The authors concluded that the biologic treatments were more effective than methotrexate for at least a year, but the cost to society was high. The cost-effectiveness methods were valid and key areas of uncertainty were considered. The authors’ conclusions appear to be robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of four biologic treatments, etanercept, infliximab, adalimumab, and abatacept, for patients with polyarticular-course juvenile idiopathic arthritis (JIA) and with a prior inadequate response or intolerance to disease-modifying antirheumatic drugs.

Interventions
The interventions were etanercept, infliximab, adalimumab, and abatacept, and the comparator was methotrexate.

Location/setting
Canada/secondary care and hospital.

Methods
Analytical approach:
The analysis was based on a decision-tree model, with a one-year horizon. The authors stated that a societal perspective was adopted.

Effectiveness data:
A literature review was undertaken to identify the sources of data in common databases, such as PubMed, EMBASE, and the Cochrane Library, and in the grey literature. The inclusion and exclusion criteria were reported. The search identified randomised controlled trials (RCTs), observational studies, and systematic reviews. The key clinical input was the American College of Rheumatology (ACR) Pediatric 30 (Pedi 30) scale improvement. Data from multiple sources were pooled in a meta-analysis, using the inverse variance method.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
The proportion of patients achieving an ACR Pedi 30 response was the benefit measure.

Cost data:
The economic analysis included the costs of the biologic treatments and methotrexate, concomitant drugs, drug administration materials, nursing time (administration and monitoring), dispensing fees, physician assessment, laboratory tests (tuberculosis screening and blood tests), and the treatment of serious infections. Productivity losses
were included only for those drugs that were administered in a hospital-based clinic or infusion centre (infliximab and abatacept). The unit costs were from public sources, including the Quebec and Ontario provincial drug plan formularies (drugs) and the Ontario Ministry of Health and Long-Term Care fee schedules (laboratory tests and physician fees). Other costs were from published reports. Productivity losses were estimated using the average wages from Statistics Canada for the parent or caregiver's time spent in the hospital. The costs of the treatment of serious infections were from the Canadian Institute for Health Information. All costs were in Canadian dollars (CAD) and the price year was 2008.

Analysis of uncertainty:
A probabilistic sensitivity analysis was carried out, using a Monte Carlo simulation, to generate confidence intervals (CIs) around the model outcomes and cost-effectiveness acceptability curves. The sensitivity analysis focused on the effectiveness estimates.

**Results**
In a hypothetical 40kg child, compared with methotrexate, the incremental costs were CAD 11,090 with etanercept, CAD 13,107 with adalimumab, CAD 7,873 with abatacept, and CAD 12,167 with infliximab. The incremental percentage of patients achieving an ACR Pedi 30 response was 47.6% with etanercept, 29.4% with adalimumab, 49.4% with abatacept, and 43.2% with infliximab. The incremental cost-effectiveness ratios, over methotrexate, were CAD 26,061 with etanercept, CAD 46,711 with adalimumab, CAD 16,204 with abatacept, and CAD 31,209 with infliximab.

Assuming maximum efficacy for the biologics over methotrexate, the incremental cost-effectiveness ratios decreased by 33% to 37%. In the opposite scenario, minimum efficacy, biologics were less effective and more expensive than methotrexate in a very small percentage of simulations, except for adalimumab (58% of simulations).

The willingness-to-pay values at which each biologic and methotrexate had an equal probability of being cost-effective (incremental cost per one additional ACR Pedi 30 responder) were CAD 23,000 with etanercept, CAD 45,000 with adalimumab, CAD 17,000 with abatacept, and CAD 27,500 with infliximab.

**Authors' conclusions**
The authors concluded that the biologics were more effective than methotrexate for at least a year, but the cost to society was high. They noted that long-term data from disease registries and observational studies might be used for more comprehensive economic evaluations.

**CRD commentary**

**Interventions:**
A justification for the selection of the comparators was provided. The four interventions were the most commonly used biologic treatments for JIA, and methotrexate was the usual treatment. The authors pointed out that a comparison among biologics could not be made because of a lack of published head-to-head data and differences between the populations in the individual studies.

**Effectiveness/benefits:**
A valid approach was used to identify the relevant sources of evidence. The literature was searched for various study designs. In general, RCTs and systematic reviews have high internal validity. The authors addressed issues around the calculation of treatment efficacy, considering the variability among studies. A meta-analysis was used to synthesise the available evidence. The authors found that the ACR Pedi 30 was the most commonly and consistently used outcome measure in the RCTs and thus selected it as their key model outcome. Quality-adjusted life-years (QALYs) would have been more appropriate, but the authors pointed out that the measurement of utilities in children is difficult.

**Costs:**
A broad perspective was considered and all the relevant cost categories appear to have been included. A list of cost items was reported, but the unit costs and resource quantities were not; only the total costs were presented. The data sources were reported and were typical of the Canadian setting. The price year and currency conversions were reported, making reflation exercises possible. The costs were varied in the sensitivity analysis.
Note: since this abstract was written, the author has pointed out that full details unit costs and resource quantities can be found in the technical appendix to the paper which can be found at the following url.

http://www.sickkids.ca/Research/TASK/Reports/index.html

The full technical report is also available for download here:

http://www.sickkids.ca/pdfs/Research/TASK/biologics/33871-biologics-append_JIA.pdf

Analysis and results:
An incremental approach was used to synthesise the costs and benefits of each biologic compared with methotrexate. The incremental findings were reported for both the base case and the alternative efficacy scenarios. A probabilistic sensitivity analysis was carried out to investigate the uncertainty in the model inputs. The width of the confidence intervals shows the amount of uncertainty for some cost-effectiveness ratios, but the findings generally followed a consistent trend. The authors justified the short horizon of the model, which was selected on the basis of the available evidence. The authors compared their results with those of other published studies that generally had similar findings. The results might be transferred to other settings with similar cost structures.

Concluding remarks:
The cost-effectiveness methods were valid and key areas of uncertainty were considered. The authors’ conclusions appear to be robust.

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