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 study examined the cost-effectiveness of biological therapies for the treatment of Crohn’s disease, psoriasis, and methotrexate-refractory rheumatoid arthritis. A wide variation in cost-effectiveness of the therapies was observed, as well as a variation in their relative efficacy. Adalimumab was associated with lower cost-effectiveness estimates compared with the other biologics in two or more of the diseases examined. The study used a valid cost-effectiveness methodology for different treatment areas. The authors’ conclusions appear robust.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study examined the cost-effectiveness of biological therapies for the treatment of three diseases: moderate-to-severe Crohn’s disease, psoriasis, and rheumatoid arthritis. A cross-indication analysis for biologics used in two or three of these diseases was also conducted.

Interventions
The biological therapies evaluated were: adalimumab and infliximab for Crohn’s disease; adalimumab, etanercept, infliximab, ustekinumab (45mg or 90mg) for psoriasis; abatacept, adalimumab, certolizumab, etanercept, golimumab, infliximab, rituximab, and tocilizumab for methotrexate-refractory rheumatoid arthritis.

Location/setting
USA/primary and secondary care.

Methods
Analytical approach:
The analysis was based on a review of the literature. Costs were estimated over a time horizon of one year. The perspective adopted in the study was not explicitly stated, although it may have been that of the payer.

Effectiveness data:
A systematic review of the literature was undertaken using PubMed to identify clinical randomised controlled trials (RCTs) of biological therapies for the three specified diseases. Inclusion criteria were clearly reported. Comparisons were with placebo or another biological therapy. Given the lack of head-to-head trials among these biologics, mixed-treatment comparison meta-analyses were carried out for each disease to pool estimates from individual trials and to calculate 95% confidence intervals. Treatment response rates (that varied depending on the disease considered) were key clinical endpoints.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Proportions of patients who responded and remitted were used as the summary benefit measures.

Cost data:
The costs of drug acquisition and administration were included. Full compliance was assumed. Blended costs were calculated as a weighted average of the estimated costs. Prescription volume data were used as an indicator of the size of the biologic market. US wholesale acquisition costs were used. Costs were in US $. The price year appears to have been 2011. Administration costs per infusion were taken from Medicare Current Procedural Terminology payment information.

Analysis of uncertainty:
Monte Carlo simulations were used to calculate confidence intervals around point estimates for costs and benefits.

Results
Total costs were not reported.

For Crohn’s disease, the probability of response was 42.9% with adalimumab and 39.0% with infliximab. The probability of remission was 37.4% with adalimumab and 28.7% with infliximab. The cost per additional responding patient was $116,291 with adalimumab (40mg every other week) and $125,169 with infliximab (5mg/kg). When compared with each other, the incremental cost per responding patient with infliximab over adalimumab was $8,878. The incremental cost per remitting patient was $52,983.

For psoriasis, the rate of response was 68.5% with adalimumab, 51.1% with etanercept, 66.8% with ustekinumab (45mg), 72.0% with ustekinumab (90mg), and 79.0% with infliximab. The rate of remission were 39.6% with adalimumab, 22.3% with etanercept, 40.1% with ustekinumab (45mg), 44.3% with ustekinumab (90mg), and 51.7% with infliximab. The cost per additional responding patients was $9,756 with adalimumab, $21,770 with etanercept, $13,821 with ustekinumab (45mg), $25,327 with ustekinumab (90mg), and $12,828 with infliximab. The cost per additional remitting patient was $16,380 with adalimumab, $48,726 with etanercept, $22,322 with ustekinumab (45mg), $40,008 with ustekinumab (90mg), and $19,061 with infliximab.

For methotrexate-refractory rheumatoid arthritis, the rates of response and remission were highest with adalimumab and etanercept, and lowest with rituximab, infliximab, and abatacept. The lowest estimates of the cost per additional responding patients were $27,853 with adalimumab, $29,140 with etanercept, and $31,363 with tocilizumab. The lowest estimates of the cost per remitting patient were $47,533 with adalimumab and $48,320 with tocilizumab.

In the cross-indication analysis, the weighted average one-year cost per additional responding patient across the psoriasis and rheumatoid arthritis diseases was $56,219 for adalimumab $62,283 for etanercept and $82,683 for infliximab. Across all three diseases, adalimumab was associated with lower one-year costs per additional responding patient ($23,984) and remitting patient ($41,919) compared with infliximab.

Authors’ conclusions
The authors concluded that a wide variation in cost-effectiveness of biological therapies was observed as well as a variation in the relative efficacy of biologics depending on the disease. Overall, adalimumab was associated with lower cost-effectiveness estimates compared with other biologics in two or more of the diseases examined.

CRD commentary
Interventions:
The selection of the comparators was appropriate as all available biological therapies for each disease were considered. Drug dosages were clearly reported.

Effectiveness/benefits:
An appropriate approach was used to identify clinical estimates as a systematic review of clinical literature was undertaken. Key details of the RCTs identified in the review and the statistical methods used in the meta-analysis were reported. The mixed-treatment comparison meta-analysis synthesized summary-level clinical evidence from multiple studies and adjusted for between-trial differences in placebo response rates. A clear description of the methods used for this indirect comparison was provided. Overall, the clinical side of the study appears to have been conducted satisfactorily. The authors noted that proportions of responding and remitting patients were benefit measures that had clinical and economic significance to payers and physicians. However, the use of QALYs might have been more useful to assess the relative cost-effectiveness of the biologics compared using standard thresholds.
Costs:
Although not explicitly stated, the perspective of the analysis might have been that of the third-party payer, as only drug costs were considered over a one-year time horizon. Thus, costs associated with the severity of the diseases were not included in the analysis. A longer time horizon would have been useful to estimate all costs associated to different rates of remission with each treatment. Typical US sources were used for unit costs and standard drug dosages were assumed. The price year was reported, which allowed reflation exercises.

Analysis and results:
Ranges of outcomes were reported to deal with uncertainty using a Monte Carlo simulation. The results were extensively presented for efficacy and cost-effectiveness ratios, as well as for all diseases. The authors acknowledged that a limitation of the study was the short time-horizon as all the diseases considered were chronic diseases. The main strength of the analysis was the cross-indication comparison and the use a sophisticated model for the synthesis of the clinical estimates. Model results might be transferable to settings with similar drug costs.

Concluding remarks:
The study used a valid cost-effectiveness methodology for different treatment areas. The authors’ conclusions appear robust.

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