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 evaluated the clinical effectiveness, resource use and cost impacts of infliximab for the treatment of moderate to severe Crohn's disease. The authors concluded that infliximab's effectiveness at reducing Crohn's disease flares led to significant treatment cost reductions. Although the outcomes may reflect effectiveness in practice, potential for confounding and the lack of a comprehensive incremental cost analysis made it difficult to draw cost-effectiveness conclusions from this study.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
The study evaluated the clinical effectiveness, resource use and cost impacts of infliximab for treatment of moderate to severe Crohn's disease after standard treatments failed.

Interventions
Infliximab treatment was compared to no infliximab treatment. Infliximab was prescribed at a dose of 5mg/kg. The dose could be increased to 10mg/kg if clinical symptoms did not improve.

Location/setting
UK/outpatient

Methods
Analytical approach:
Cost and effectiveness outcomes were derived from a single retrospective study where resource use and outcomes were measured in the 12 months prior to commencing infliximab treatment and the 24 months afterwards. The study included 380 patients and used medical records from 18 hospitals. The stated perspective was NHS and personal and social services.

Effectiveness data:
Effectiveness data were derived from the retrospective study. Patients included in the trial must have begun infliximab infusions on or after 1 January 2003, could not have received any previous biologic treatment for Crohn's disease before beginning infliximab treatment, must have received care only from the participating care centre for the entire two-year period and must have had no missing data. The primary measures of effectiveness were C-reactive protein levels and the number of recurrent Crohn's disease flares. Crohn's disease flares were defined as a recurrence of the symptoms present at initial consultation. Surgical procedure rates, hospitalisation rates, outpatient consultations, concomitant medication use and severe adverse event rates were measured. All effectiveness data were reported as annualised means.

Monetary benefit and utility valuations:
Not relevant.

Measure of benefit:
There was no single summary measure of benefit. The measures of benefit were the effectiveness outcomes stated...
above.

Cost data:
Resource use data were derived from the retrospective study. Cost categories included surgical procedures, hospitalisations, outpatient consultations and concomitant drug costs (including corticosteroids and immunomodulators). Costs were calculated using Personal and Social Service Research Unit (PSSRU) costs for outpatient consultations. Costs for hospitalisations and procedures were obtained from the NHS Healthcare Research Group. Medication costs were derived from the British National Formulary. Costs were stated in British pounds sterling. All costs were reported as annualised means.

Analysis of uncertainty:
Statistically significant differences between the two interventions were assessed using analysis of variance (ANOVA) tests and $\chi^2$ tests. Fixed-effect and random-effects models were used when pooling data from the 18 hospitals to account for between-hospital variability.

**Results**
Levels of C-reactive protein fell from $30.3 \pm 37.2\text{mg/L}$ in the pre-infliximab period to $15.0 \pm 20.7\text{mg/L}$ ($p<0.0001$) during the zero to 12-month post-infliximab period and held steady at $15.6 \pm 19.9\text{mg/L}$ at 24 months. The mean number of Crohn's disease flares decreased from $2.9 \pm 2.4$ in the pre-infliximab period to $1.6 \pm 1.8$ in the zero to 24-month post-infliximab period ($p<0.0001$).

Costs for in-patient surgical procedures decreased from £752.46 pre-infliximab to £539.23 post-infliximab but this difference was not statistically significant. Elective and non-elective hospitalisation frequency and hospitalisation costs decreased in the post-infliximab period. Annualised elective hospitalisations decreased from 0.18 to 0.11 ($p=0.0035$). Non-elective hospitalisations decreased from 0.46 to 0.29 ($p<0.0001$). Hospitalisation reductions were accompanied by decreases in mean cost per hospitalisation. Elective hospitalisations decreased in mean cost from £1,908.85 to £1,194.01 ($p<0.0001$) and mean annualised cost of non-elective hospitalisations decreased from £1,107.65 to £630.71 ($p<0.0001$). The mean number of total health care consultations increased ($p<0.0001$) but was associated with a decrease in outpatient consultations costs from £913.48 to £832.23 ($p<0.0001$) and a decrease in diagnostic test costs from £411.00 to £190.04 ($p<0.0001$).

The mean annualised costs of infliximab during the study period were £7,128.02. Prednisolone was used by more than 60% of patients in the pre-infliximab period and decreased to 45% during infliximab. Azathioprine was used in 56% of patients and mesalazine was used in 50% of patients in the pre-infliximab period.

**Authors' conclusions**
The authors concluded that infliximab's effectiveness at reducing Crohn's disease flares led to significant treatment cost reductions.

**CRD commentary**
Interventions:
The study evaluated the outcomes of infliximab. There appeared to be an implicit comparison of infliximab against no infliximab rather than infliximab compared to another relevant treatment for a specific population. The authors indicated that adalimumab was also found to be effective in the treatment of Crohn's disease but were unable to evaluate their comparative effectiveness given the study design.

Effectiveness/benefits:
The retrospective no-protocol design of the study means that the outcomes may better reflect effectiveness in practice than efficacy in a trial but the non-randomised before-and-after design also means that there is the possibility of confounding of the results. The study had a follow-up of two years but Crohn's disease is a chronic lifelong disease and the study did not capture long-term effects of treatment. The authors indicated that mixed- and random-effects models were used to pool data from different study centres. It would have been useful to know the between-hospital variance.

As the authors acknowledged patient quality of life was not among the study outcomes, which inhibits cost-effectiveness evaluation in the UK study setting.
Costs:
The cost estimates were based on the retrospective design and the outcomes may better reflect effectiveness in practice than efficacy in a trial but the non-randomised before-and-after design also means that there is the possibility of confounding of the results. The authors may not have intended to undertake a full cost-effectiveness analysis but enough information was reported for readers to consider drawing cost-effectiveness conclusions. Costs of the concomitant medications for the two periods were not reported. These would need to be accounted for in a full cost-effectiveness analysis and the net incremental costs of the treatments and outcomes calculated. It appeared as though the cost of concomitant treatments decreased with the provision of infliximab.

Costs were derived from appropriate UK sources and were clearly reported. Costs were reported at aggregate categorical levels without a price year which makes it difficult to transfer the data to other settings. Eighteen UK hospitals was a good sized sample and increased the likelihood that the study included representative costs of treatment for moderate to severe Crohn's disease in the UK.

Analysis and results:
The authors presented results comprehensively with consistent reporting of variances and p-values. The authors thoroughly compared their results to those of other studies, including a study that indicated adalimumab was an effective treatment for moderate to severe Crohn's disease.

The authors considered the limitations of their study appropriately: they indicated that the retrospective design could lead to inconsistent treatment protocols and data recording across centres; that patient consultations were not at standardised times, which necessitated the use of annualised means; and that patients initiating treatment with infliximab may have improved or worsened without infliximab, which the study design could not capture due to the before-and-after study design.

The authors may not have intended to undertake a full cost-effectiveness analysis. For a full cost-effectiveness analysis, net incremental costs of treatments and outcomes needed to be calculated and the value of the incremental benefit needed to be considered.

Concluding remarks:
Although the outcomes may reflect effectiveness in practice, potential for confounding and the lack of a comprehensive incremental cost analysis made it difficult to draw cost-effectiveness conclusions from this study.

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MeSH
Adolescent; Adult; Aged; Aged, 80 and over; Antibodies, Monoclonal /economics /therapeutic use; Child; Child, Preschool; Cost-Benefit Analysis; Crohn Disease /drug therapy /economics; Delivery of Health Care /economics; Female; Gastrointestinal Agents /economics /therapeutic use; Great Britain; Health Care Costs; Health Resources