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 evaluated the cost-effectiveness of celecoxib plus a proton pump inhibitor (PPI), compared with diclofenac plus a PPI, for patients with osteoarthritis. The authors concluded that celecoxib was cost-effective, compared with diclofenac plus a PPI, in the UK. The methods used to update the National Institute for Health and Clinical Excellence (NICE) model were reasonable, but the time horizons may have differed and relevant comparators were excluded. Insufficient information was given to assess this economic evaluation.

Type of economic evaluation
Cost-utility analysis

Study objective
This study evaluated the cost-effectiveness of celecoxib plus a proton pump inhibitor (PPI), compared with diclofenac plus a PPI, for patients with osteoarthritis.

Interventions
The cyclooxygenase-2 inhibitor, celecoxib, 200mg per day, plus a PPI, was compared with the non-steroidal anti-inflammatory drug (NSAID), diclofenac, 100mg per day, plus a PPI.

Location/setting
UK/out-patient.

Methods
Analytical approach:
The authors updated a 2008 National Institute for Health and Clinical Excellence (NICE) published model (see Other Publications of Related Interest) of cyclooxygenase-2 inhibitors versus NSAIDs, for osteoarthritis. The time horizon was three months. The authors stated that the model's perspective was that of the UK NHS.

Effectiveness data:
It was assumed that celecoxib and diclofenac were equally effective at controlling the symptoms of osteoarthritis, but had different risks of gastrointestinal and cardiovascular adverse events; the relative risk of adverse events was the main outcome measure. The literature review from the 2008 NICE publication was updated, using the same search criteria. This identified one additional trial, the Celecoxib versus Omeprazole and Diclofenac in patients with Osteoarthritis and Rheumatoid arthritis (CONDOR) trial. The relative risks were adjusted for the higher doses used in the trials, compared with clinical practice, and for the addition of a PPI to celecoxib in the CONDOR trial. These data were synthesised with data from the Celecoxib Long-term Arthritis Safety Study (CLASS), in a fixed-effect meta-analysis. The adverse events were gastrointestinal symptoms, symptomatic ulcers, complicated gastrointestinal events, myocardial infarction, stroke, and heart failure. The relative risks were estimated for treatment both with and without a PPI.

Monetary benefit and utility valuations:
The utility values, for the different adverse events, were those used in the NICE model publication.

Measure of benefit:
Quality-adjusted life-years (QALYs) were the summary measure of benefit. Where necessary, a discount rate of 3.5% per year was applied to the benefits.

Cost data:
The costs included gastrointestinal adverse events, drugs, and the management of cardiovascular events. Those for gastrointestinal adverse events were updated using NHS reference costs for 2010 to 2011. The drug costs were updated using the British National Formulary. The costs for the management of cardiovascular events were from the Personal Social Services Research Unit (PSSRU). The price year was 2011 and the currency was UK £. Where necessary, an annual discount rate of 3.5% was used.

Analysis of uncertainty:
Sensitivity analyses were conducted for an average patient age of 65 years (55 years in the main analysis) and a time horizon of 24 months (three months in the main analysis). Analyses assuming equal cardiovascular risks, at ages 55 and 65 years, with model time horizons of three and 24 months were conducted. Analyses were conducted for CLASS and CONDOR results separately; different methods for calculating the event rates; the exclusion of dose adjustment; and comparing celecoxib without a PPI versus diclofenac plus a PPI. A probabilistic sensitivity analysis was conducted and the results were presented as a cost-effectiveness plane and a cost-effectiveness acceptability curve (CEAC). The distribution for the relative risk was its 95% confidence interval, while all other variables were assigned the distributions used in the NICE model publication.

Results
In the main analysis, celecoxib plus a PPI was cost-effective compared with diclofenac plus a PPI, with an incremental cost-effectiveness ratio (ICER) of £9,377 per QALY gained.

In all the scenario analyses the ICER was well below the £20,000 to £30,000 cost-effectiveness threshold generally assumed by NICE. For adverse event data from CONDOR alone, the ICER was £4,773 per QALY gained. For adverse event data from CLASS alone, the ICER was £9,538 per QALY gained. A time horizon of 24 months had little effect on the ICER, and increasing the age of the patients decreased the ICER.

The probabilistic sensitivity analysis showed that celecoxib plus a PPI was the cost-effective option 75% of the time, using a threshold of £20,000 per QALY.

Authors' conclusions
The authors concluded that celecoxib was cost-effective, compared with diclofenac plus a PPI, for patients with osteoarthritis, in the UK.

CRD commentary
Interventions:
While celecoxib and diclofenac were appropriate interventions, the original NICE model evaluated several other cyclooxygenase-2 inhibitors and NSAIDs. The aim was to update the NICE model, but the cost-effectiveness of celecoxib compared with these other drugs was not assessed. The specific PPI used was not reported.

Effectiveness/benefits:
As this study was an update of a published model, the justification for the assumption of equal effectiveness of cyclooxygenase-2 inhibitors and NSAIDs was not discussed. Similarly, the methods of the reviews that identified the CONDOR and CLASS trials were not reported, and the methods, sources, and values for the utility data were not given; this information was available in the NICE publication. The difference in QALYs was small and the choice of data could have had a substantial effect. The dose adjustment methods were well reported, but resulted in adverse event rates that were lower than in the general population, in some cases. The adverse events for the PPI were not evaluated. Osteoarthritis patients are unlikely to take cyclooxygenase-2 inhibitors and NSAIDs at the dosages or for the continuous periods that they did in the two six-month trials. They might use the drugs intermittently over much longer periods, and they are more likely to have cardiovascular and other comorbidities than the patients did in the trials. So, real-world efficacy and adverse event profiles may not have been reflected by the trials.

Costs:
Little information on the costs was given, as these details were reported in the NICE publication. The sources were appropriate for the UK NHS perspective. The costs were appropriately adjusted to the new price year.

Analysis and results:
The model type and cycle length were not reported; the authors stated that they were given in the original NICE publication, but there was some evidence that this model differed from the NICE model. The time horizon of the NICE model was lifetime, with three or 24 months of treatment, and a three-month cycle length, while this model had a time horizon of three months or 24 months. The NICE model and this model may not be making the same comparison, which could make a comparison of their results difficult. The authors acknowledged that the assumptions for the dose adjustment of the relative risk, and of equal stroke risk for cyclooxygenase-2 inhibitors and NSAIDs, were uncertain, but neither of these assumptions was varied in the sensitivity analysis.

Concluding remarks:
The methods used to update the NICE model appear to have been reasonable, except that the time horizons may have been different and relevant comparators were excluded. Insufficient information was given to assess the quality of the economic evaluation.

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