Cost-effectiveness of aspirin, celecoxib, and calcium chemoprevention for colorectal cancer

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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 assessed the cost-effectiveness of aspirin, celecoxib, or calcium for the prevention of colorectal cancer, with a screening programme, for the general population or those who had undergone colorectal polypectomy. Calcium chemoprevention was likely to be cost-effective after polypectomy, but the evidence was weak. Aspirin could be cost-effective for the general population aged 50 to 60 years. The methods were robust and transparent and indicated the uncertainty in the results. The authors’ conclusions are valid.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of aspirin, celecoxib, or calcium for the prevention of colorectal cancer, with a programme of screening using the faecal occult blood test (FOBT), for the general population and for people who had undergone colorectal polypectomy.

Interventions
For the general population, aspirin 300mg daily was compared with no chemoprevention.

For those who had undergone colorectal polypectomy (intermediate-risk population), aspirin 300mg daily, celecoxib 400mg daily, or calcium 1,200mg daily, were compared with no chemoprevention.

Different starting ages and duration of chemoprevention were considered. The screening programme was the UK Colorectal Cancer Screening Programme.

Location/setting
UK/primary care.

Methods
Analytical approach:
The analysis was based on a published state-transition model that was modified to include the chemoprevention strategies. The authors stated that it took the perspective of the UK NHS. A lifetime horizon was considered.

Effectiveness data:
The efficacy of chemoprevention was from a meta-analysis of relevant published clinical trials that were identified by a systematic review. Other data were mainly from clinical trials. Some on the efficacy of earlier detection and removal of adenomas and the subsequent treatment of colorectal cancer were from official surveillance data and the NHS Cancer Screening Programme. Other official UK databases were used, such as that of the Northern and Yorkshire Cancer Registry and Information Service. Where data were not found in the literature, expert opinion was used.

Monetary benefit and utility valuations:
A systematic review of the literature was undertaken to identify health-related quality of life (HRQoL) data. One study that collected public preferences for health conditions was found and this was used to estimate the utilities for colorectal cancer. Age-specific health utilities for people without cancer were age-adjusted based on the Health Survey for England. National Institute for Health and Clinical Excellence (NICE) guidelines were used to assess the utilities for
chemoprevention adverse effects.

Measure of benefit:
Quality-adjusted life-years (QALYs) and life-years were the summary benefit measures and they were discounted at an annual rate of 3.5%.

Cost data:
The economic analysis included the costs of chemoprevention, physicians’ visits, colonoscopy with or without polypectomy, diagnostic tests, treatment of bowel perforation and bleeding, management of adenoma and colorectal cancer (by stage), and treatment of complications (dyspepsia, gastrointestinal bleeding or ulcer, stroke, and myocardial infarction). The unit costs were from official NHS sources, such as the British National Formulary, the Personal Social Services Research Unit, and NHS reference costs. All costs were in UK pounds sterling (£). The price year was 2008 and a 3.5% annual discount rate was applied.

Analysis of uncertainty:
A one-way sensitivity analysis was carried out assuming that celecoxib was associated with no harm. A two-way sensitivity analysis was performed, for aspirin and for calcium, assuming that harm was increased and effectiveness was decreased, over ranges of values. A probabilistic sensitivity analysis was conducted, using Monte Carlo simulation and conventional probability distributions for each type of input; gamma distributions for the costs, beta for the utilities and probabilities, and normal or log normal for the risks of harm on chemoprevention.

Results
General population: In those aged 50 to 60 years, the total discounted costs were £997 with no chemoprevention, and £1,367 with aspirin. The life-years were 16.87 with no chemoprevention, and 16.91 with aspirin. The QALYs were 13.74 with no chemoprevention and 13.76 with aspirin. The incremental cost and was £10,169 per life-year gained and £22,800 per QALY gained.

At a willingness-to-pay threshold between £20,000 and £30,000 per QALY gained, the probability of aspirin chemoprevention being cost-effective ranged from 0.4 to 0.8, but the sensitivity analysis found substantial uncertainty. For all other ages (40 to 60 years, 40 to 50 years, or 50 to 70 years), the incremental cost per QALY gained was over £30,000. The two-way sensitivity analysis suggested that if the relative risk of colorectal cancer was greater than 0.6, then aspirin would need to cause less harm than was assumed for it to have a cost per QALY gained below £20,000.

Intermediate-risk population: In those aged 61 to 70 years, the expected costs were £2,865 with no chemoprevention, £3,121 with aspirin, £3,159 with calcium, and £5,604 with celecoxib. The life-years were 12.55 with no chemoprevention, 12.57 with aspirin, 12.58 with calcium, and 12.61 with celecoxib. The QALYs were 9.72 with no chemoprevention, 9.73 with aspirin, 9.75 with calcium, and 9.77 with celecoxib.

Aspirin was excluded as it was less effective and less cost-effective than calcium. Compared with no chemoprevention, the incremental cost was £8,046 per life-year gained or £8,383 per QALY gained with calcium, and it was £60,805 per life-year gained or £55,696 per QALY gained with celecoxib. In general, the ratios for calcium were between £10,000 and £30,000, depending on the age range, but there was substantial uncertainty in all the results.

At willingness-to-pay thresholds between £10,000 and £100,000 per QALY gained, the likelihood of being cost-effective was between 50% and 60% for calcium and between 20% and 30% for aspirin. At thresholds up to £30,000 per QALY gained, the probability of celecoxib of being cost-effective was close to zero. The uncertainty around the key clinical parameters was confirmed in other sensitivity analyses, but celecoxib was never cost-effective.

Authors’ conclusions
The authors concluded that calcium chemoprevention was likely to be cost-effective for those who had undergone polypectomy, but the evidence was weak. Chemoprevention was less cost-effective in the general population, but aspirin could be cost-effective for those aged 50 to 60 years.

Further research was recommended to estimate the long-term benefits and harms of calcium compared with aspirin.
chemoprevention, and to assess calcium chemoprevention in the general population.

**CRD commentary**

**Interventions:**
The selection of the comparators was appropriate. The authors stated that studies had shown the efficacy of chemoprevention with calcium supplements, or with the nonsteroidal anti-inflammatory drugs aspirin or celecoxib.

**Effectiveness/benefits:**
The clinical inputs were generally from valid sources, including clinical trials, meta-analyses of clinical trials, and systematic reviews. The best available evidence is likely to have been used. The authors acknowledged that there was much heterogeneity among the published studies in their patient population, treatment duration, follow-up, etc, and a lot of uncertainty was found in the long-term harms and benefits of chemoprevention. They tried to overcome these issues with an extensive sensitivity analysis. Both QALYs and life-years were valid measures of benefit and allow comparisons with other disease areas. The utility weights were from valid sources that reflected the UK population and an appropriate instrument was used to assess them.

**Costs:**
The cost categories, data sources, and price year were clearly presented and reflation exercises should be possible. The key unit costs were given and the data were from official NHS sources. The impact of variations in the economic inputs, except for the price of celecoxib, does not appear to have been considered, but probabilistic distributions were appropriately assigned to the costs in the Monte Carlo simulation.

**Analysis and results:**
The results were clearly presented and discussed. An incremental approach was appropriately used to combine the costs and benefits of the strategies. The uncertainty was satisfactorily investigated and discussed. A clear description of the model was provided and the positive and negative effects of chemoprevention on other diseases were modelled. The authors stated that the results of clinical trials might not perfectly mimic real-life clinical practice, and their results might not be transferable to other settings as there are differences in population lifestyle and preventive treatments. They noted that the published evidence on the harms of chemoprevention was limited.

**Concluding remarks:**
The methods were robust and transparent and they highlighted the uncertainty in the cost-effectiveness of chemoprevention for colorectal cancer. The authors’ conclusions are valid.

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