Potential effect of cyclooxygenase-2-specific inhibitors on the prevention of colorectal cancer: a cost-effectiveness analysis
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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.

Health technology
The use of cyclooxygenase-2-specific (COX-2) inhibitors in the prevention of colorectal cancer (CRC).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was hypothetical. It comprised persons aged 50 years with average CRC risk, or those with at least one first-degree relative who had the disease.

Setting
Although not specifically stated, it appears that the study has been undertaken in a secondary care setting. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were obtained from articles published between 1980 and 2000. No dates for resource use were reported. The price year appears to have been 1998.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies. In addition, some parameters were estimated on the basis of opinions.

Modelling
A decision analytic model was constructed to evaluate the clinical and economic outcomes associated with the three scenarios in the three groups of patients. The model was a Markov model. Further details of the model were reported elsewhere (see Other Publications of Related Interest).

Outcomes assessed in the review
The outcomes assessed in the review included:

the incidence of CRC with or without adenoma;
symptomatic presentation of localised or regional cancer;
mortality from treated localised or regional cancer;
mean survival from distant cancer;
the mortality rate from cancer treatment;
the sensitivity of the faecal occult blood test for cancer or polyp;
the specificity of the faecal occult blood test;
polyps or cancers within the reach of a sigmoidoscope;
the sensitivity of sigmoidoscopy for polyp or cancer within the reach of a sigmoidoscope;
the specificity of sigmoidoscopy;
the sensitivity of colonoscopy for polyp or cancer;
the major complication rate with colonoscopy or sigmoidoscopy;
the mortality rate with colonoscopy or sigmoidoscopy;
the reduction in CRC incidence with COX-2 inhibitors;
the rate of excess major complications from COX-2 inhibitors; and
mortality given major COX-2 inhibitor complication.

**Study designs and other criteria for inclusion in the review**
Not reported. The search of the literature focused on articles published in English.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
Fifteen primary studies were included in the review.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
The authors did not specifically investigate differences between the primary studies. However, where there was uncertainty over the value of a parameter, the authors tested a range of values for the parameter in a sensitivity analysis. For example, the reduction in the CRC risk due to COX-2 inhibitors.

**Results of the review**
The incidence of CRC was reduced by 30% with COX-2 inhibitors.

The sensitivity of colonoscopy was 90% for polyp and 95% for cancer.

The sensitivity of sigmoidoscopy for a polyp or cancer within the reach of the sigmoidoscope was 90%.

The specificity of sigmoidoscopy was 95%.

The rate of major complications was 0.1% with colonoscopy and 0.01% with sigmoidoscopy.

**Methods used to derive estimates of effectiveness**
The authors made assumptions to derive estimates of effectiveness.

**Estimates of effectiveness and key assumptions**
The authors assumed that COX-2 inhibitors were not associated with excess major complications. Therefore, the rate of excess major complications from COX-2 inhibitors was 0% per year.

**Measure of benefits used in the economic analysis**
The outcome measure used in the economic analysis was the number of life-years saved (LYS). An annual discount rate of 3% was applied to the number of life-years saved.

**Direct costs**
The costs were discounted at an annual rate of 3%. The unit costs were reported, but the quantities were not reported separately. The direct costs included in the analysis related to the following resource categories:

- faecal occult blood testing,
- flexible sigmoidoscopy (with or without biopsy),
- colonoscopy (with or without biopsy),
- endoscopy complications,
- CRC care by stage (localised, regional, distant),
- COX-2 inhibitors, and major COX-2 inhibitor complication.

The costs were estimated from actual data, mainly obtained from other studies and Medicare. The procedural costs were derived from Medicare fee schedules. These included professional fees and median procedure reimbursement to facilities by Medicare. The costs of complications were obtained from relevant Diagnostic-Related Groups. The costs for colon cancer care were stage-specific and were extracted from reports to the National Cancer Institute. They were treated as the total cost by stage in the year of diagnosis. The cost of COX-2 inhibitors was based on the retail cost to the pharmacy at the University of California, San Francisco. The price year appears to have been 1998.

**Statistical analysis of costs**
No statistical tests of the costs were undertaken.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were carried out on all parameters to investigate variability in the data. Both one- and two-way analyses were performed. The ranges were selected on the basis of assumptions and the literature.

**Estimated benefits used in the economic analysis**
In persons at average risk of CRC, the number of life-years per person was 18.703 with no intervention, 18.729 with a COX-2 inhibitor, 18.768 with colonoscopy every 10 years, 18.773 with sigmoidoscopy and faecal occult blood testing, 18.776 with colonoscopy every 10 years plus a COX-2 inhibitor, and 18.778 with sigmoidoscopy, faecal occult blood testing and a COX-2 inhibitor.

In persons with one first-degree relative with CRC, the number of life-years per person was 18.561 with no intervention, 18.632 with a COX-2 inhibitor, 18.731 with colonoscopy every 10 years, 18.760 with colonoscopy every 5 years, 18.753 with colonoscopy every 10 years plus a COX-2 inhibitor, and 18.770 with colonoscopy every 5 years plus a COX-2 inhibitor.

In persons with two first-degree relatives with CRC, the number of life-years per person was 18.477 with no intervention, 18.573 with a COX-2 inhibitor, 18.708 with colonoscopy every 10 years, 18.749 with colonoscopy every 5 years, 18.739 with colonoscopy every 10 years plus a COX-2 inhibitor, and 18.764 with colonoscopy every 5 years plus a COX-2 inhibitor.

The model tracked persons from the age of 50 years to the age of 80 years.

**Cost results**
In persons at an average risk of CRC, the cost per person was $830 under no intervention, $6,950 with a COX-2 inhibitor, $2,150 with colonoscopy every 10 years, $2,010 with sigmoidoscopy and faecal occult blood testing, $8,410 with colonoscopy every 10 years plus a COX-2 inhibitor, and $8,260 with sigmoidoscopy, faecal occult blood testing and a COX-2 inhibitor.

In persons with one first-degree relative with CRC, the cost per person was $2,160 with no intervention, $7,830 with a COX-2 inhibitor, $2,820 with colonoscopy every 10 years, $3,380 with colonoscopy every 5 years, $8,860 with colonoscopy every 10 years plus a COX-2 inhibitor, and $9,530 with colonoscopy every 5 years plus a COX-2 inhibitor.

In persons with two first-degree relatives with CRC, the cost per person was $2,940 with no intervention, $8,360 with a COX-2 inhibitor, $3,210 with colonoscopy every 10 years, $3,650 with colonoscopy every 5 years, $9,120 with colonoscopy every 10 years plus a COX-2 inhibitor, and $9,700 with colonoscopy every 5 years plus a COX-2 inhibitor.

**Synthesis of costs and benefits**
The costs per LYS were calculated and compared across all scenarios, with no intervention and with screening alone.

Compared with no intervention in persons at average risk of CRC, the cost per LYS saved was $233,300 with a COX-2 inhibitor, $20,200 with colonoscopy every 10 years, and $16,800 with sigmoidoscopy and faecal blood testing.

Compared with screening alone, the cost per LYS was $823,800 with colonoscopy every 10 years plus a COX-2
inhibitor, and $1,112,900 with sigmoidoscopy, faecal occult blood testing and a COX-2 inhibitor.

Compared with no intervention in persons with one first-degree relative with CRC, the cost per LYS was $80,300 with a COX-2 inhibitor, $3,900 with colonoscopy every 10 years, and $6,200 with colonoscopy every 5 years. Compared with screening alone, the cost per LYS saved was $280,500 with colonoscopy every 10 years plus a COX-2 inhibitor, and $591,300 with colonoscopy every 5 years plus a COX-2 inhibitor.

Compared with no intervention in persons with two first-degree relatives with CRC, the cost per LYS was $56,700 with a COX-2 inhibitor, $1,200 with colonoscopy every 10 years, and $2,600 with colonoscopy every 5 years. Compared with screening alone, the cost per LYS was $195,500 with colonoscopy every 10 years plus a COX-2 inhibitor, and $404,700 with colonoscopy every 5 years plus a COX-2 inhibitor.

The authors found that the major determinants of the incremental cost-effectiveness of a COX-2 inhibitor were its cost and chemoprevention efficacy. In the one-way sensitivity analyses, when the CRC cancer risk reduction was lower than its assigned value in the base-case (30%), the costs per LYS saved by COX-2 inhibitor use in unscreened persons increased significantly. However, in those with a family history of the disease, a reduction in the risk of CRC by at least 50% with COX-2 inhibitor use incurred costs of less than $50,000 per LYS. In the two-way sensitivity analyses, COX-2 inhibitor use needed to achieve considerably greater reductions in the risk of cancer at a significantly lower cost to be comparable with screening.

Authors’ conclusions
The use of a cyclooxygenase-2-specific (COX-2) inhibitor in the prevention of colorectal cancer (CRC) was likely to result in substantially higher costs per life-year saved (LYS) compared with the costs incurred under the current screening strategy. Further, while the use of a COX-2 inhibitor in conjunction with screening improved health outcomes, it did so at prohibitive costs. Finally, on the basis of the outcomes of their model, the authors argued that the combination of a COX-2 inhibitor and screening was unlikely to increase the current recommended screening intervals.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used. Screening was current practice, and decreased both the incidence and mortality associated with CRC.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. The estimates of effectiveness obtained from the primary studies were not combined. While this may raise concerns about the selective use of data from these studies, the authors tested the robustness of their results to changes in the underlying parameters by undertaking sensitivity analysis. Similarly, the values of estimates assumed by the authors were investigated in a sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive the measure of health benefit, a Markov model, was appropriate.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted (that of a third-party payer) were included in the analysis. The unit costs were reported separately, but the resource quantities were not reported. A sensitivity analysis of the quantities was not conducted, which may limit the interpretation of the study findings. A sensitivity analysis of the prices was conducted.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies. They did, however, address the issue of generalisability. In particular, the authors discussed the possible use of COX-2 inhibitors for other types of cancer and other diseases. In addition, the analysis also examined three sub-groups of patients, which ensured that the results were generalisable. The authors do not appear to have presented their results selectively.

**Implications of the study**

The authors did not recommend any change to the current recommended screening strategy. However, they argued that their results support more frequent screening in persons with a family history of CRC than for persons at average risk.

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**Other publications of related interest**


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