Surveillance colonoscopy or chemoprevention with COX-2 inhibitors in average-risk post-polypectomy patients: a decision 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
Colonoscopic surveillance and chemoprevention with COX-2 inhibitors in average risk post-polypectomy patients.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was based on average-risk patients with adenomatous polyps, who had already undergone colonoscopy and polypectomy.

Setting
The setting was hospital. The study was carried out in Birmingham, USA.

Dates to which data relate
Transition probabilities were derived from some studies published between 1987 and 2000. Cost data were estimated from 1999 Medicare reimbursement rates alongside the institution considered, and were also supported by the literature (from 1996 to 2000). The price year was 1999.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A Markov model was used in order to obtain estimates of benefits and costs associated with the three strategies considered for patients aged 50 after complete colonoscopy and polypectomy. The time horizon was 10 years (10 cycles of 1 year). DATA 3.5 TreeAge software was used.

Outcomes assessed in the review
Several outcomes were estimated in the review, viz: probability of adenoma formation, rate of malignant transformation, probabilities of complications from colonoscopy and polypectomy, annual rate of ulcer disease from the celecoxib in the first year and thereafter, and cost of colorectal cancer.
Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
The relevant literature concerning the probability values used in the model was identified through MEDLINE.

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
Nine studies used to derive transition probabilities and cost data were included in the review.

Methods of combining primary studies
The narrative method was used to combine primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The results of the review were as follows:

The probability of adenoma formation was 0.106 (range used in the sensitivity analysis, 0.05 - 0.20) in the first 3 years and 0.05 (range: 0.02 - 0.15) after the third year;

the malignant transformation rate was 0.10 (range: 0.05 - 0.20);

the probability of complication from colonoscopy was 0.003 (range: 0.0005 - 0.004);

the probability of complication from colonoscopy and polypectomy was 0.02 (range: 0.005 - 0.05);

the annual rate of ulcer disease from celecoxib (year 1) was 0.02 (range: 0.01 - 0.15).

Measure of benefits used in the economic analysis
Two measures of benefit were used: high-grade lesion prevented, and years of life saved.

Direct costs
Direct costs included: cost of the drug at the average wholesale price; and cost of complications (colonoscopy and symptomatic ulcer disease) measured by the average DRG-related Medicare reimbursement rate at the institution considered. The cost boundary was that of the health services. Since the time horizon of the model was 10 years, costs were discounted at an annual rate of 3%. Costs and quantities were not reported separately. The price year was 1999.

Statistical analysis of costs
No statistical analysis was reported.

**Indirect Costs**
Indirect costs were not included, which was appropriate given the perspective.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and two-way sensitivity analyses were carried out to test for the following parameters with a high degree of uncertainty: probability of polyp formation, probability of colonoscopic complications, cost of colonoscopy, cost of complications from colonoscopy and from COX-2 inhibitors, costs determined by the development of colorectal cancer, number of years, patient compliance with colonoscopic surveillance, and sensitivity of colonoscopy for polyp detection.

**Estimated benefits used in the economic analysis**
With respect to the first benefit measure (high-grade lesions prevented), the same results were obtained in the discounted and undiscounted analyses. The incremental effectiveness of colonoscopic surveillance with respect to no surveillance was equal to 0.02, while the incremental effectiveness of the drug therapy with respect to colonoscopic surveillance was 0.07.

The second benefit measure (years of life saved) showed different results. In the undiscounted case, the incremental effectiveness of colonoscopic surveillance with respect to no surveillance was equal to 0.02976 while the incremental effectiveness of the drug therapy with respect to colonoscopic surveillance was 0.00705. By using a 3% discount rate, the incremental effectiveness of colonoscopic surveillance with respect to no surveillance was equal to 0.01995, while the incremental effectiveness of the drug therapy with respect to colonoscopic surveillance was 0.00579. These results were drawn from the base case analysis using a ten-year time horizon.

**Cost results**
The total costs of the three strategies with no discount rate were as follows: $1,016 for no surveillance, $1,813 for colonoscopic surveillance, and $13,187 for the drug.

The incremental cost of colonoscopic surveillance with respect to no surveillance was $797, while the incremental cost of the drug therapy with respect to colonoscopic surveillance was $11,374.

Using a 3% discount rate, the following total cost results were obtained: $1,014 for no surveillance, $1,572 for colonoscopic surveillance, and $11,503 for the drug.

The incremental cost of colonoscopic surveillance with respect to no surveillance was $558, while the incremental cost of the drug therapy with respect to colonoscopic surveillance was $9,931.

**Synthesis of costs and benefits**
In a ten-year period, after discounting, the incremental cost-effectiveness ratio of the drug compared to colonoscopic surveillance was $141,871 per high-grade lesion prevented and $1,715,199 per year of life saved. One-way sensitivity analyses showed that the results obtained were robust when varying within the range of all the parameters. In a two-way sensitivity analysis, celecoxib is a more cost-effective strategy only if associated with extremely low costs and very high level of efficacy.
Authors' conclusions
Therapy by COX-2 inhibitors in average-risk post-polypectomy patients is not cost-effective compared to colonoscopic surveillance, mainly because of the low incidence of high-risk lesions, the efficacy and low cost of colonoscopy, and the high cost of the COX-2 inhibitors.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness estimation cannot be fully assessed since not all the data used in the model were derived from a systematic review of the literature. More information on the search method should have been given. However, to compensate for this limitation, comprehensive sensitivity analyses were conducted on all the parameters to increase the robustness of the results.

Validity of estimate of measure of benefit
Health benefits were extrapolated from the same sources used to obtain effectiveness evidence.

Validity of estimate of costs
The authors limited the analysis to direct costs, which were the only relevant costs given the perspective adopted. The cost estimates are likely to be specific to the Medicare setting.

Other issues
The issue of generalisability to other settings was not addressed. Moreover, as the authors stated, some transitional probability values were not available in the literature and were therefore based on their own assumptions.

Finally, the results are not sensitive to a wide range of possible values of the efficacy of COX-2 inhibitors. Even at an efficacy level of 100% the drug strategy is far less desirable than colonoscopy and the incremental cost-effectiveness ratio for years of life saved remains extremely high. This might suggest that life years saved is not the most appropriate measure of benefit for post-polypectomy patients in a ten-year time horizon.

Implications of the study
Since little is known about the efficacy of the COX-2 inhibitors, the authors suggest further research. Some clinical trails are currently ongoing and they will clarify the effects of chemoprevention drugs. The main implication is that, at this time, the use of COX-2 inhibitors is not cost-effective from the third-party payer point of view.

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