Medical decision analysis of chemoprevention against esophageal adenocarcinoma
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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 non-steroidal anti-inflammatory drugs (NSAIDs) to prevent oesophageal adenocarcinoma (AdCA) in patients with Barrett's oesophagus.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised patients aged 60 years with Barrett's oesophagus.

Setting
The setting was secondary care. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness evidence was gathered from 1988 to 2000, while the resource use data were from 1996 to 2002. The price year was stated as being the "current year" for the study.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies.

Modelling
A Markov model was used to extrapolate the data so that the lifetime costs and effects of each strategy could be calculated. The four health states in the model were Barrett's oesophagus, successful surgery (oesophagectomy), AdCA, and death. Patients with Barrett's oesophagus could move to any of the remaining health states. Patients with AdCA could move to either death or successful surgery (patients with unsuccessful surgery remained in the AdCA state). Following surgery, patients could only move to death. The risk of death with Barrett's oesophagus or following successful surgery was described by the annual age-specific death rate of the US population. The model employed a 1-year cycle length.

Outcomes assessed in the review
The outcomes assessed in the review included:
the age-specific mortality.
the incidence of AdCA in patients with Barrett's oesophagus,

the incidence of AdCA in patients with Barrett's oesophagus and high-grade dysplasia,

the prevalence of Barrett's oesophagus, and

the relative risk reductions associated with endoscopic surveillance and NSAIDs for AdCA.

**Study designs and other criteria for inclusion in the review**
Not stated.

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

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

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

**Number of primary studies included**
The numbers and types of studies included in the review were unclear. The model parameters were predominately based on authors' assumptions, which seem to have been based on the studies reviewed.

**Methods of combining primary studies**
Any synthesis of the study data was undertaken using authors' assumptions.

**Investigation of differences between primary studies**
Not investigated.

**Results of the review**
The authors did not formally combine the primary studies.

The effectiveness parameters for patients with Barrett's oesophagus were as follows:

the incidence of AdCA was 0.50% (range: 0.25 - 1.50);

the efficacy of surveillance alone in preventing AdCA was 50% (range: 0 - 50);

the efficacy of NSAIDs alone in preventing AdCA was 50% (range: 0 - 100); and

the combined efficacy of surveillance and NSAIDs in preventing AdCA was 75% (range: 50 - 100).

The effectiveness parameters for patients with Barrett's oesophagus and high-grade dysplasia were as follows:

the incidence of AdCA was 5.00% (range: 2.0 - 8);

the efficacy of surveillance alone in preventing AdCA was 25% (range: 0 - 50);
the efficacy of NSAIDs alone in preventing AdCA was 25% (range: 0 - 100);
the combined efficacy of surveillance and NSAIDs in preventing AdCA was 50% (range: 25 - 100).

The 5-year survival after oesophagectomy was assumed to be 20%. The health-related quality of life after oesophagectomy was assumed to be 100% (i.e. quality-adjusted life expectancy equivalent to life-years).

**Measure of benefits used in the economic analysis**
The measure of benefits used was the life-years gained. The authors stated that life-years after oesophagectomy were multiplied by an index of health-related quality of life. Given that only life-years after oesophagectomy were quality-adjusted (and not the other three health states in the model) and this quality-adjustment was 100%, the results of the model could be interpreted as life-years gained. The figure of 100% for post-surgery quality of life was based on an authors' assumption.

**Direct costs**
The resource use quantities were not reported, instead the average costs were reported. The study included the direct costs to a third-party payer. These were for endoscopic surveillance, medical care for AdCA, gastrointestinal disease associated with the use of NSAIDs, 325 mg/day aspirin, and oesophagectomy. The cost data were estimated on the basis of charge data and completed studies. The costs were discounted at an annual rate of 3%. The costs were adjusted to present values (study year) by assuming an interest rate of 3%, but further details of this adjustment were not given.

**Statistical analysis of costs**
The costs were treated deterministically, then varied in sensitivity analyses. The authors did not have access to patient-level data, thus statistical tests were not possible.

**Indirect Costs**
The indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
The sensitivity analysis focused on the cost of chemoprevention with NSAIDs, the incidence of AdCA in patients with Barrett's oesophagus, with or without high-grade dysplasia, and the efficacy of NSAIDs in preventing AdCA, with or without concomitant endoscopic surveillance. One-way sensitivity analyses were used to explore the generalisability and robustness of the model results. The ranges employed in the sensitivity analysis were based on authors' assumptions.

**Estimated benefits used in the economic analysis**
The life expectancy associated with each strategy was presented in graph. The strategies, in order of increasing life expectancy, are: no prevention, NSAIDs alone, surveillance alone, and surveillance and NSAIDs combined. The life-years were discounted at a rate of 3% per year. A model was used to extrapolate the data to a lifetime horizon.

**Cost results**
The incremental lifetime cost of surveillance combined with NSAIDs, compared with no prevention, was $7,700 in patients with Barrett's oesophagus alone and $6,610 in patients with Barrett's oesophagus and high-grade dysplasia.

No further cost results were reported. The costs were discounted at an annual rate of 3%. The cost of gastrointestinal
side effects of chemoprevention with NSAIDs was included in the analysis.

**Synthesis of costs and benefits**
The costs and life-years were combined to produce incremental cost-effectiveness ratios (ICERs) in the form of the cost per life-year gained. To calculate ICERs, the strategies of surveillance alone and NSAIDs alone were compared with no prevention, while surveillance combined with NSAIDs was compared with surveillance alone. As such, this was not a true incremental analysis.

The ICERs were presented in a graph. In order of increasing cost per life-year gained, the results for patients with Barrett's oesophagus alone were NSAID alone ($12,700), surveillance alone, surveillance combined with NSAIDs ($18,500).

The results for patients with Barrett's oesophagus and high-grade dysplasia were: NSAIDs alone ($3,900), surveillance combined with NSAIDs, surveillance alone ($5,000).

The authors stated that only the ICER for NSAIDs alone in patients with Barrett's oesophagus and high-grade dysplasia remained below $50,000 in all sensitivity analyses. They also stated that the most sensitive parameter was the incidence of AdCA in Barrett's oesophagus.

**Authors' conclusions**
Under baseline conditions non-steroidal anti-inflammatory drugs (NSAIDs), with or without concomitant endoscopic surveillance, appear to have been cost-effective treatment strategies for preventing oesophageal carcinoma (AdCA) in patients with Barrett's oesophagus. Chemoprevention of AdCA appears to have been more cost-effective in high-risk sub-groups, such as patients with Barrett's oesophagus and high-grade dysplasia.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator was not explicitly justified, but it appears that there was no standard current preventative programme. Thus, no prevention might have represented current treatment. You should decide if this represents a valid comparator in your own setting.

**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 were based on authors' assumptions, in consideration of the studies reviewed. The authors might have been selective in their use of data. The level of reporting around the issues of the search methods, study inclusion criteria, data extraction, and so on, makes it very difficult to ascertain whether the parameters were selected systematically. The authors considered wide ranges for the efficacy parameters in one-way sensitivity analyses. However, some of the ranges considered appear inconsistent. For example, the range of efficacy for NSAIDs alone or surveillance alone in preventing AdCA in patients with Barrett's oesophagus both included zero, but the range of efficacy for surveillance combined with NSAIDs began at 50%.

**Validity of estimate of measure of benefit**
The authors stated that the life-years gained post-surgery were multiplied by an index of health-related quality of life. However, this index was estimated to be 100%, and life-years gained in other health states in the model were not quality-adjusted. As such, the measure of benefits is the life-years gained, and not the quality-adjusted life-years (QALYs) gained. The index of health-related quality of life with AdCA or high-grade dysplasia could well be less than 100%, therefore QALYs might have been a more appropriate outcome measure. However, the data required to make this quality-adjustment might not have been available, and so life-years are an appropriate, if less generalisable, alternative.
All the categories of cost relevant to the perspective adopted were included in the analysis. These costs were derived in part from reimbursement data for Medicare and Medicaid in the USA, which limits the generalisability of the model to other countries and patients with other forms of health insurance. Other costs were derived from published studies. The costs and the quantities were not reported separately, and price data were not required. Only the cost of chemoprevention with NSAIDs was explored in a sensitivity analysis. The range for this parameter included $0, which would seem unreasonable.

**Other issues**

The authors made some comparison of their results with other studies that used the cost per life-year saved as the measure of cost-effectiveness. The issue of generalisability to other settings was not addressed. The results were presented in graphs, which makes the precise amounts unclear. The authors’ conclusions reflected the scope of the analysis. The authors acknowledged that the model relied on many assumptions, and that more data on the model parameters are required if one is to be certain about the results.

**Implications of the study**

The authors recommended that clinical trials be conducted to estimate parameters required for the economic model.

**Source of funding**

None stated.

**Bibliographic details**


**PubMedID**

12806608

**Indexing Status**

Subject indexing assigned by NLM

**MeSH**

Adenocarcinoma /prevention & control; Anti-Inflammatory Agents, Non-Steroidal /therapeutic use; Anticarcinogenic Agents /therapeutic use; Barrett Esophagus /complications; Cost-Benefit Analysis; Esophageal Neoplasms /prevention & control; Esophagus /pathology; Humans; Markov Chains

**AccessionNumber**

2200300911

**Date bibliographic record published**

31/03/2005

**Date abstract record published**

31/03/2005