Defining a clinically significant adverse impact of diagnosing Barrett's esophagus

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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 study examined screening with surveillance of Barrett's oesophagus (BE). This consisted of oesophagogastroduodenoscopy (EGD) offered to all men with symptoms of gastroesophageal reflux disease (GERD) at the age of 50 years for the prevention of oesophageal adenocarcinoma.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 50-year-old white men with a history of GERD.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
Most of the effectiveness data and some resource use data were derived from studies published between 1976 and 2003. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and expert opinion.

Modelling
A published Markov model on the natural history of cancer development was used to assess the cost-effectiveness of screening with BE surveillance, compared with no screening, in a hypothetical cohort of 100,000 white men of 50 years of age. A simplified schematic of the model was reported. The health states considered were no BE, BE without dysplasia, BE with dysplasia, cancer, oesophagectomy and death. Patients could receive screening for BE (EGD) or no screening. Patients diagnosed with BE underwent repeat EGD biopsies every 3 years. Those without BE did not undergo repeat EGD. Patients diagnosed with low-grade dysplasia (LGD) underwent EGD every 6 months, while those diagnosed with high-grade dysplasia (HGD) underwent EGD every 3 months. Patients diagnosed with cancer underwent oesophagectomy, if resectable. Patients could die from cancer, surgery and other causes. Diagnostic error was incorporated in the analysis. The patients were followed until age 80 or death. The cycle length was one year.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the prevalence of disease,
disease progression and regression,
the cancer treatment probabilities,
the diagnostic inaccuracy rates, and
the health state utilities.

**Study designs and other criteria for inclusion in the review**
The authors did not state whether a systematic review of the literature was undertaken to identify the primary studies. It was only stated that data on screening efficacy in preventing mortality due to cancer were taken from retrospective studies.

**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**
Forty-seven studies were used as the primary sources of clinical data.

**Methods of combining primary studies**
A narrative approach appears to have been used to combine the primary estimates.

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

**Results of the review**
The prevalence of BE in GERD was 0.1, the prevalence of LGD in GERD was 0.01, the prevalence of HGD in GERD was 0.007, and the prevalence of cancer in BE was 0.067.

The annual progression probability was:

from no dysplasia to LGD, 0.05;
from no dysplasia to HGD, 0.01;
from no dysplasia to cancer, 0.005;
from LGD to HGD, 0.05;
from LGD to cancer, 0.025;
from HGD to cancer, 0.055; and
for cancer incidence in BE, 0.005.

The annual regression probabilities were 0.0175 from BE to normal, 0.63 from LGD to no dysplasia, 0.1 from HGD to no dysplasia, and 0.07 from HGD to LGD.

In terms of the cancer treatment probabilities:
the rate of resectability was 0.5 without surveillance and 0.95 with surveillance;
the surgical mortality was 0.05 without surveillance and 0.027 with surveillance;
the cancer cure rate was 0.2 without surveillance and 0.8 with surveillance; and
mortality from endoscopy was 0.000021.

Mortality from all other causes was age- and gender-dependent.

In terms of the diagnostic inaccuracy, the probabilities of diagnosis were:
0.145 for LGD in the case of BE with no dysplasia;
0.175 for BE with no dysplasia in the case of LGD;
0.083 for HGD in the case of LGD;
0.115 for LGD in the case of HGD;
0.11 for cancer in the case of HGD;
0.05 for LGD in the case of cancer; and
0.175 for HGD in the case of cancer.

The utility values were 1 (range: 0.90 to 1) for GERD and 0.97 (range: 0.83 to 1) for post-oesophagectomy.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions based on expert opinion or consensus.

**Estimates of effectiveness and key assumptions**
The authors assumed that:

the annual rate of developing BE was 0.005;
the mortality rate from unresectable cancer was 0.9;
the toll incurred by diagnosing BE was 0% in the base-case;
the utility associated with diagnosed cancer was 0.5; and
the utility associated with undiagnosed cancer was 0.8.
Some data on diagnostic inaccuracy were also based on authors' opinions.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). These were estimated by combining utility data and life expectancy derived from the literature. An annual discount rate of 3% was applied to future benefits. The proportion of cancer deaths prevented was also reported.

**Direct costs**
The cost analysis adopted the perspective of the third-party payer. It included the costs associated with endoscopy (with biopsy), oesophagectomy, endoscopic palliation, annual post-surgical care, the management of incurable cancer and clinic visits. Direct non health care costs (such as transportation to and from clinic visits) or life insurance premiums (which are higher for patients diagnosed with BE) were not included among the imputed costs, but were considered as affecting the patients' QOL. The unit costs were not presented separately from the quantities of resources used. The costs were derived from published studies based on data from the Center for Medicaid and Medicare Services. Resource use appears to have been derived from published studies. Discounting was appropriately carried out, given the long timeframe of the analysis, and an annual rate of 3% was applied. The price year was presumably 2001.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included. However, the authors stated that indirect costs affected patients' preferences that were expressed as utility weights.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate and multivariate sensitivity analyses were carried out. In these, utility assumptions were varied in order to define the threshold decrement in utility associated with diagnosing BE that would enable screening to remain cost-effective compared with no screening at two levels of willingness-to-pay (WTP), namely $50,000 and $100,000 per QALY.

**Estimated benefits used in the economic analysis**
The expected QALYs were 16.466 with no screening and 16.637 with screening.

The proportion of cancer deaths prevented with screening was 56%.

**Cost results**
The expected cost per patient would be $104 with no screening and $2,443 with screening.

**Synthesis of costs and benefits**
An incremental cost-utility ratio was calculated to combine the costs and benefits of screening over no screening.

The incremental cost per QALY gained under base-case conditions was $13,721.
The sensitivity analysis showed that decrements in the utility associated with diagnosing BE could be as high as 9% at a WTP of $50,000, and as high as 10.5% at a WTP of $100,000, and that screening would remain cost-effective. Similar conclusions were reached when changes in other utility values were considered. In the worst case for screening, the threshold was never lower than 5%, which still represents a relatively high value.

Authors' conclusions
Screening with surveillance of Barrett's oesophagus (BE) was cost-effective in comparison with no screening, regardless of any possible decrements in utility caused by diagnosing BE.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator (no screening) was appropriate as this represented the standard alternative to the intervention examined in the study. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from published studies. The authors did not explicitly state whether a systematic review of the literature was undertaken, so it is possible that the primary studies might have been identified selectively. In addition, there was limited information on the design and other characteristics of the primary studies. Thus, the validity of the primary sources could not be assessed. The authors stated that most studies were retrospective, and these usually have a low internal validity. No information on the approach used to extract and combine the primary estimates was provided, and the issue of heterogeneity across the primary studies was not addressed. The robustness of the study conclusions to variations in clinical estimates was investigated in the sensitivity analysis. The use of experts' opinions that were not supported by published data introduced further uncertainty in the clinical analysis.

Validity of estimate of measure of benefit
QALYs are an appropriate benefit measure because they capture the impact of the intervention on both quality of life and survival, which are relevant dimensions of health for patients with cancer. The analysis focused on QOL aspects and most data on QOL were based on authors' consensus. Some utility weights were estimated from studies that used the time trade-off approach. The use of QALYs permits comparisons to be made with the benefits of other health care interventions. Discounting was applied.

Validity of estimate of costs
The costs included were consistent with the perspective considered in the analysis. A detailed breakdown of the cost items was not given, and neither was information on the unit costs and quantities of resources used. This limits the possibility of replicating the analysis in other settings. The cost estimates were specific to the study setting and were not varied in the sensitivity analyses. The impact of using alternative sources of the costs was not investigated. Moreover, no statistical analyses were carried out. The price year was implicitly reported, which will facilitate reflation exercises in other time periods. Few details of resource consumption were provided. Discounting was relevant and was appropriately carried out.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were carried out but only with respect to utility decrements, which were the main point of interest of the analysis. The authors stated that the issue of the cost-effectiveness of screening versus no screening had already been addressed in a previous study. The analysis referred to the general population of white individuals of 50 years of age and this was reflected in the authors' conclusions. There was no discussion of whether the results could be transferred to other patient populations (i.e. women or non-white men).
Implications of the study
The study results support a strategy of screening with BE surveillance.

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Other publications of related interest


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