Photodynamic therapy for Barrett's esophagus with high-grade dysplasia: a cost-effectiveness analysis

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 three strategies for the treatment of patients with Barrett's oesophagus (BE) and high-grade dysplasia (HGD). These were endoscopic surveillance with biopsy after thorough investigation (SURV), distal oesophagectomy (ESO) and photodynamic therapy (PDT).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 50-year-old men with BE with HGD. Patients were asymptomatic, treatment naive (except for chronic acid suppression), and fit for ESO.

Setting
The setting was a hospital. The economic study was carried out in Canada.

Dates to which data relate
The clinical data were derived from studies published between 1990 and 2004. Some data on resource use were derived from a study published in 1999. The price year was 2003.

Source of effectiveness data
The clinical data used in the decision model were:

- the probability of ablating HGD with PDT,
- the rate of progression to cancer after PDT,
- the rate of oesophageal stricture after PDT,
- the rate of progression to cancer from HGD,
- the mortality from ESO for HGD, and
- the mortality from ESO for cancer.
Modelling
A Markov model was constructed to simulate the treatment of a hypothetical 50-year-old man with BE with HGD using the three approaches under examination. Patients who underwent ESO did not receive any further SURV. Patients on the PDT strategy would receive SURV in the event that eradication of HGD was confirmed, or would undergo ESO in the case of persistent or recurrent HGD or in the case of progression to adenocarcinoma. Patients who underwent SURV initially were assumed to repeat the diagnostic test every 3 months, and ESO was performed in the case of progression to adenocarcinoma. The time horizon of the model was 5 years, with 3-month cycles. Fixed event rates derived from the literature were fitted to an exponential curve to determine 3-month cycle probabilities. A simplified version of the model was depicted.

Sources searched to identify primary studies
Most of the epidemiological data were derived from primary studies that were not described. Survival with BE and HGD and early oesophageal adenocarcinoma came from the National Cancer Institute Surveillance Epidemiology and End Results (SEER) database. Some mortality data followed the age-specific mortality of the Canadian male population (life tables).

Methods used to judge relevance and validity, and for extracting data
Clinical inputs with the three main strategies were obtained from a review of the literature review, but details were given only for PDT. Published reviews and proceedings from key conferences were also searched. No information on the primary studies was provided.

Measure of benefits used in the economic analysis
The summary benefit measures were life-years (LYs) in the cost-effectiveness analysis and quality-adjusted life-years (QALYs) in the cost-utility analysis. Utility weights used to calculate the QALYs were defined only for the post-ESO state. This value was derived from a published study, but no details of the instruments used or the patient population were provided. Both benefit measures were discounted at an annual rate of 3%.

Direct costs
The analysis of the costs was carried out from the perspective of a third-party payer. It included the costs associated with PDT sessions, endoscopy with biopsy, and ESO. Physician services and hospital admissions and procedures were considered. The unit costs and the resource quantities were not presented separately. Canadian sources were used to derive costs whenever possible, otherwise US sources were used. For example, the costs of physician services were obtained from the Ontario Ministry of Health and Long-Term Care Schedule of Benefits. Hospital costs came from the Ontario Case Costing Initiative programme. Some market prices were communicated directly from the manufacturers. The resource use data were based mainly on expert opinion and consensus. Discounting was relevant, given that 5-year costs were evaluated, and an annual rate of 3% was used. The price year was 2003.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The productivity costs were not considered.

Currency
Canadian dollars (CAD).

Sensitivity analysis
The issue of uncertainty was investigated in a probabilistic sensitivity analysis, in which economic and clinical inputs were assigned probabilistic distributions. Subsequently, cost-effectiveness acceptability curves were generated using 10,000 Monte Carlo simulations. Details of the type of probabilistic distributions and the coefficients of these distributions were reported.

**Estimated benefits used in the economic analysis**
The expected LYs were 12.53 with SURV, 18.14 with PDT and 18.90 with ESO. Thus, ESO was associated with the highest LYs.

The QALYs were 11.85 with SURV, 17.04 with PDT and 15.85 with ESO. Thus, PDT resulted in the highest QALYs.

**Cost results**
The total costs per patient were CAD 17,817 with SURV, CAD 22,381 with PDT and CAD 24,963 with ESO.

**Synthesis of costs and benefits**
Incremental cost-effectiveness and cost-utility ratios were calculated in order to combine the costs and benefits of the alternative strategies.

The incremental cost per LY gained was CAD 814 with PDT over SURV and CAD 3,379 with ESO over PDT.

In the cost-utility framework, ESO was dominated by PDT, which had an incremental cost per QALY gained over SURV of CAD 879.

The probabilistic sensitivity analysis showed that, in the cost-effectiveness framework, ESO had the highest probability of being cost-effective for thresholds above CAD 3,500 per LY, with this probability reaching 99% at a threshold of CAD 25,000 per LY. In the cost-utility analysis, PDT had the highest probability of being cost-effective (99% at a ceiling ratio of CAD 25,000 per QALY).

**Authors' conclusions**
Photodynamic therapy (PDT) was a cost-effective alternative to oesophagectomy (ESO) and continued surveillance (SURV) in patients with Barrett's oesophagus (BE) and high-grade dysplasia (HGD), especially when the analysis took the impact of treatment on quality of life into consideration.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparators appears to have been appropriate in that all possible strategies for patients with BE and HGD were considered. The three interventions were extensively described. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The clinical data were derived from the literature. Apart from the use of some specific databases, no clear information on the design and other characteristics of the primary studies was provided. It is therefore not possible to judge the validity of the data given the information reported in this paper, although it was stated that some transition probabilities were estimated from observational studies. The authors stated that a review of the literature was performed to identify relevant studies, but no details of the methods or conduct of the search were given, except for the case of PDT efficacy rates.

**Validity of estimate of measure of benefit**
Benefit measures (LYs and QALYs) were modelled using the Markov model. Appropriate discounting was performed in accordance with Canadian recommendations. The utility weights were derived from a published source, and some
details on the values used and the assumptions made were reported.

**Validity of estimate of costs**
The analysis of the costs was consistent with the stated perspective. The cost categories included were appropriate. A breakdown of the cost items was not given and only macro-categories of costs were reported. This might limit the possibility of replicating the analysis in other settings. The sources of the costs were reported for most items and generally Canadian sources were used. Statistical analyses of the costs were not performed but probabilistic distributions were assigned to all economic inputs. The sensitivity analysis addressed the issue of variability in the cost estimates. The price year was reported, thus simplifying reflation exercises in other time periods.

**Other issues**
The authors stated that their findings were in line with those from other published studies, but did not report the findings of such publications in detail. Some limitations of the analysis were discussed. For example, the use of some assumptions (all members of the cohort were free of cancer at baseline; patients who underwent ESO were deemed cured with no further need for SURV) that might not be realistic or reflect patient management in some settings. The authors presented their results in full and provided cost-effectiveness planes and cost-effectiveness acceptability curves. The key finding of the analysis was that ESO would be the preferred strategy when only mortality was considered, but PDT would be the preferred option when morbidity was also included. Thus, particular attention should be given to the methods used to estimate the utility weights associated with postoperative ESO.

**Implications of the study**
The study results support the use of PDT for the treatment of patients with BE and HGD. However, the authors pointed out that treatment should be individualised, taking into account patient preferences, co-morbidities and local expertise.

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**Bibliographic details**

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**Other publications of related interest**
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