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 treatment of high-grade dysplasia (HGD) in Barrett's oesophagus was studied. The treatment strategies considered were:

- prophylactic oesophagectomy;
- photodynamic therapy (PDT) followed by endoscopic surveillance;
- PDT with oesophagectomy, where patients diagnosed with residual HGD were referred for prophylactic oesophagectomy; and
- endoscopic surveillance every 3 months, with surgery or chemoradiation when cancer is detected.

Further details about each strategy were provided in the paper.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised 55-year-old white men with HGD in Barrett's oesophagus (i.e. at high risk of developing Barrett's oesophagus and oesophageal adenocarcinoma), who were candidates for all four alternative strategies considered at analysis.

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

Dates to which data relate
The effectiveness and resource use data were modelled using data from papers published between 1976 and 2003. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.

Modelling
A Markov model was used to estimate the clinical and quality of life implications and the associated costs of the four
treatment options studied. A lifetime horizon was considered and the cycle length was 3 months. The health states considered were normal (i.e. no Barrett's oesophagus), metaplasia (i.e. with Barrett's oesophagus without HGD), HGD (i.e. with Barrett's oesophagus and HGD), cancer (with adenocarcinoma of the oesophagus), having surgery and dead.

**Outcomes assessed in the review**
The model input parameters identified were:

the prevalence of cancer, and high- and low-grade dysplasia;

the annual rate of progression from early to late cancer, HGD to cancer, metaplasia to cancer and normal to metaplasia, metaplasia, HGD and cancer after PDT;

the annual rate of regression from HGD to metaplasia, metaplasia to normal and metaplasia to normal after PDT;

the efficacy of PDT;

procedure-related morbidity; and

the mortality from procedures and treated and untreated late cancer.

Some other parameters were also reported, such as the morbidity rates associated with the procedures and the false-positive and false-negative rates associated with the health states.

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

**Sources searched to identify primary studies**
The authors searched MEDLINE, abstracts from major gastroenterologic scientific meetings and the references of the reviewed studies.

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

**Methods used to judge relevance and validity, and for extracting data**
The authors reported that they considered a follow-up period of longer than one year, or the sample size of the study, in order to estimate appropriately some of the effectiveness parameters.

**Number of primary studies included**
At least 84 primary studies were used to identify the model input parameters.

**Methods of combining primary studies**
Some of the data from the primary studies were combined using a random-effects model, and 95% confidence intervals were reported. However, as the authors reported, some of the parameters used in the reference case were obtained directly from individual papers.

**Investigation of differences between primary studies**
Not reported.
Results of the review
The key model input parameters identified were as follows.

The prevalence of cancer was 4% (range: 2 to 15).

The prevalence of HGD was 1.6% (range: 0.036 to 7).

The prevalence of low-grade dysplasia was 7.9% (range: 0.54 to 37).

The annual rates of progression were:

from early to late cancer, 14% (range: 5 to 24);
from HGD to cancer, 7.4% (range: 2 to 27);
from metaplasia to HGD, 0.7% (range 0.56 to 2.4);
from metaplasia to cancer, 0.5% (range: 0.08 to 3.2);
from normal to metaplasia, 0.5% (range: 0.2 to 1);
from normal to metaplasia after PDT, 0.8% (range 0 to 1.3);
from normal to HGD after PDT, 0% (range: 0 to 1.3); and
from normal to cancer after PDT, 0.4% (range: 0 to 2).

The efficacy of PDT for HGD was 77% overall and 36% for reverting to normal.

The efficacy of PDT for early cancer was 77% overall and 40% for reverting to normal.

Mortality from surgery was 4% (range: 2 to 20).

Mortality from endoscopy was 0.0045% (range: 0 to 0.03).

Mortality from perforation was 25% (range: 14 to 50).

Mortality from untreated late cancer per annum was 40% (range: 29 to 80).

Mortality from treated late cancer per annum was 32% (range: 24 to 80).

Methods used to derive estimates of effectiveness
The authors made at least one assumption to estimate some of the effectiveness parameters.

Estimates of effectiveness and key assumptions
The authors assumed that all patients with HGD or early cancer were cured after oesophagectomy.

Measure of benefits used in the economic analysis
The measures of health benefit used were life expectancy and the quality-adjusted life-years (QALYs). These were derived through modelling. For the estimation of QALYs, valuations of health states were taken from published studies that used patient preferences (de Boer et al. 2002 and Provenzale et al. 1999, see 'Other Publications of Related Interest' below for bibliographic details) or were assumed by the authors. In addition, intermediate outcomes were reported. Specifically, the number of deaths (after 1 year, 5 years and for the lifetime horizon) per 100 patients diagnosed with HGD due to cancer, surgery and endoscopy. The future benefits were discounted at a rate of 3% per
annum.

**Direct costs**
The direct costs of a third-party payer were identified in this study. The health care resource use and costs of inpatient care (medical, surgical and diagnostic services) and follow-up (i.e. outpatient care and further procedures) were taken from Medicare and Medicaid allowances, and from published studies. The unit costs were reported in the paper and some details of resource use were provided. The price year was 2001 and future costs were discounted at a rate of 3% per annum. The costs estimated were the average costs per patient.

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

**Indirect Costs**
No indirect costs were included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were performed to assess variability in the data. The ranges for these analyses were taken from the literature and from authors’ assumptions.

**Estimated benefits used in the economic analysis**
Life expectancy was:

- 14.419 years after oesophagectomy,
- 14.376 years after surveillance,
- 14.756 years after PDT followed by oesophagectomy for residual HGD, and
- 14.811 years after PDT followed by surveillance for residual HGD.

The following quality-adjusted life expectancies were identified in the base-case:

- 18.817 QALYs after oesophagectomy (although this value appears to be erroneous since the related life expectancy was lower, i.e. 14.419 years);
- 11.819 QALYs after surveillance;
- 12.243 QALYs after PDT followed by oesophagectomy for residual HGD; and
- 12.307 QALYs after PDT followed by surveillance for residual HGD.

**Cost results**
The following total costs per patient were identified in the base-case:

- oesophagectomy, $24,045;
surveillance, $28,850; 
PDT followed by oesophagectomy for residual HGD, $45,525; and 
PDT followed by surveillance for residual HGD, $47,300.

The total incremental cost per patient of surveillance compared with oesophagectomy was $4,805. PDT followed by oesophagectomy for residual HGD had a total incremental cost of $16,675 per patient in comparison with surveillance. Using surveillance for residual HGD following PDT rather than oesophagectomy resulted in an incremental cost of $1,775 per patient.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios (ICERs) were estimated as the incremental cost per additional QALY gained. Dominated strategies were excluded from the estimation of ICERs after a dominance analysis. PDT followed by surveillance for residual HGD presented an incremental cost of $47,410 per QALY when compared with oesophagectomy. Surveillance and PDT followed by oesophagectomy proved to be extendedly dominated by PDT followed by surveillance. The results of this synthesis of the costs and benefits were most sensitive to changes in health utilities (mainly for the normal, metaplasia and postoperative health states) and to changes in operative mortality.

**Authors' conclusions**
Photodynamic therapy (PDT) followed by endoscopic surveillance for residual high-grade dysplasia (HGD) is cost-effective in comparison with oesophagectomy in cases of HGD in Barrett's oesophagus.

**CRD COMMENTARY - Selection of comparators**
This study compared four treatments for HGD in Barrett's oesophagus. The oesophagectomy option was identified as being the standard recommendation in cases of Barrett's oesophagus with HGD. You should consider how these options compare with current practice in your own setting prior to applying the results of this study.

**Validity of estimate of measure of effectiveness**
The effectiveness parameters were taken from a review of published studies. The paper did not indicate that a systematic review of the literature had been undertaken, but details of the sources search and search terms were reported. Some criteria used to select the studies from which the parameters were to be derived were also reported. Some of the data from the primary studies were combined using a random-effects model, although other parameters were chosen from single sources. As the authors reported, no randomised controlled trials comparing PDT with surgery were available, and the data provided by available studies are controversial. Variability in the model input parameters was considered through sensitivity analyses of key variables. The authors did not consider the reasons for or implications of the differences in the published studies, or any possible impact of these on this study.

**Validity of estimate of measure of benefit**
The measures of health benefit were obtained through modelling. Health state valuations were either taken from patients preferences identified in published studies or estimated by the authors. No details of how the authors reached consensus on their estimates were provided. Future health benefits were discounted to reflect the preference for current benefit.

**Validity of estimate of costs**
The paper reported that a third-party perspective was adopted and, as such, all appropriate costs appear to have been included. A breakdown of the unit costs was reported in the paper but specific details of resource use were not provided. This would hinder reflation exercises to other settings. The future costs were appropriately discounted. Sensitivity analyses were conducted to assess variability in the source data. A clear price year was reported, which will
enable future inflation exercises.

Other issues
This study was designed to reflect the situation in the USA. The authors did not consider whether their results may be applied to other countries. They compared their results with other similar studies and identified differences between them, which were justified because of the different follow-up periods of the reviewed studies and the different assumptions formulated. The authors do not appear to have presented their results selectively and their conclusions reflected the analysis. In terms of the generalisability of the results, the authors acknowledged that their study population was white men aged 55 years and warned that it might not be possible to apply their results to younger, female or non-white populations.

Implications of the study
The authors suggested that long-term randomised clinical trials, comparing PDT followed by endoscopic surveillance for residual HGD with oesophagectomy for HGD in Barrett's oesophagus, should be carried out to confirm the safety and efficacy of PDT.

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Bibliographic details

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Other publications of related interest


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