Health benefits and cost effectiveness of endoscopic and nonendoscopic cytosponge screening for 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.

CRD summary
The aim of the study was to assess the cost-effectiveness of two screening strategies (cytosponge and conventional endoscopy with biopsy) for detection of Barrett's oesophagus in 50-year-old men with a history of gastroesophageal reflux disease symptoms to reduce mortality from oesophageal adenocarcinoma. The authors concluded that screening using cytosponge was cost-effective and could prevent oesophageal adenocarcinoma deaths. The study was mostly well conducted and reported. The authors’ conclusions appear to be appropriate.

Type of economic evaluation
Cost-utility analysis

Study objective
The study objective was to assess the cost-effectiveness of two screening strategies (cytosponge and conventional endoscopy with biopsy) for detection of Barrett's oesophagus in 50-year-old men with a history of gastroesophageal reflux disease symptoms as a means of reducing mortality from oesophageal adenocarcinoma.

Interventions
Two screening interventions were assessed: cytosponge followed by endoscopy as a confirmatory test for cytosponge-positive cases; and conventional endoscopy with biopsy. These were compared to a no screening strategy. A third screening strategy (ultrathin nasal endoscopy) was explored in a supplementary analysis. Patients found to have high-grade dysplasia or intramucosal cancer after screening received treatment with endotherapy. Alternative treatment of management by oesophagectomy was considered in a supplementary analysis. Patients with treatable symptomatic cancer were treated with oesophagectomy. Patients found to have non-dysplastic Barrett’s underwent surveillance every three years; those with low-grade dysplasia underwent surveillance every six years.

Location/setting
UK/in-patient

Methods
Analytical approach:
A mixed decision tree and semi-Markov microsimulation model was used to model progression through the different stages of Barrett's oesophageal disease. Outcomes and costs over 50 years were estimated for a hypothetical cohort of 50-year-old men in the UK with histories of gastroesophageal reflux disease symptoms. The authors stated that the perspective was from the UK NHS.

Effectiveness data:
The key effectiveness inputs were sensitivity and specificity of the tests. Cytosponge was stated to have a sensitivity of 73.3% and a specificity of 93.8% for Barrett's oesophageal segments of 1cm or longer. These values were derived from a single paper in the literature. Endoscopic screening with biopsy was assumed to be a perfect test (100% sensitivity and specificity). Uptake of screening was assumed to be 45% for cytosponge and 23% for endoscopy. This assumption was stated to be based on recent evidence from the literature (two papers). The authors assumed an 80% uptake of confirmatory endoscopy for positive-cytosponge cases. This value was derived from two papers from the colorectal cancer literature.
Monetary benefit and utility valuations:
The utility associated with each of the Markov health states was stated to have been based on those used by the 2010 NICE Guideline Development Group of Barrett’s oesophagus.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs). Benefits were discounted at an annual rate of 3.5%.

Cost data:
Costs included the cost of screening, treatment, in-patient stay and outpatient follow-up care. Costs associated with cytosponge screening were based on the direct knowledge of one of the authors. All other costs were reported to relate to published NHS reference costs. Costs associated with each of the Markov health states were stated to have been based on those used by the 2010 NICE Guideline Development Group of Barrett’s oesophagus. Costs were reported in 2007-2008 prices and were discounted at an annual rate of 3.5%. Costs were converted to US dollars ($) using an exchange rate adjusted for power purchasing parity of £1=$1.52.

Analysis of uncertainty:
Deterministic sensitivity analysis was conducted to assess the impact of key parameters on the cost-effectiveness results. The results were reported as tornado diagrams and in supplementary tables. Probabilistic sensitivity analysis was performed to assess the effect of combined cost, utility and transition rate parameter uncertainty on the results. The results were reported using appropriate diagrams.

Results
Compared to the no screening strategy, cytosponge resulted in an additional cost of $240 (95% CI $196 to $320) per screening participant; endoscopy resulted in an additional cost of $299 (95% CI $261 to $367) per screening participant; cytosponge resulted in a mean gain of 0.015 (95% CI -0.001 to -0.029) QALYs; endoscopy resulted in a gain of 0.013 (95% CI 0.003 to 0.023) QALYs; cytosponge had an ICER of $15,700 per QALY gained; and endoscopy had an ICER of $22,200 per QALY gained. Screening followed by treatment for those with specific cancers reduced the number of cases of incident symptomatic oesophageal adenocarcinoma by 19% for cytosponge and 17% for endoscopy. Endoscopy was dominated by cytosponge (cytosponge produced more QALYs at a lower cost).

In a supplementary analysis in which oesophagectomy management was considered for patients with high-grade dysplasia or intramucosal cancer instead of endotherapy, the ICER for cytosponge compared to no screening rose to around $26,000 per QALY and for endotherapy rose to around $36,500 per QALY. In a supplementary analysis where the cost of ultrathin nasal endoscopy was set at 50% of the cost of conventional endoscopy, ultrathin nasal endoscopy screening with endotherapy management compared with no screening was associated with an ICER of $19,100 per QALY.

Deterministic sensitivity analysis and scenario analysis showed that the results were robust to variation in single parameter values. Cytosponge screening with endotherapy management remained the most cost-effective strategy in all analyses. For all interventions the estimate of prevalence of Barrett’s and age at screening had the greatest effects on the ICER results.

Changing the uptake of either screening option did not affect the ICER but affected the proportion of symptomatic cases of oesophageal adenocarcinoma that could be prevented among screening invitees. Probabilistic sensitivity analysis indicated that at a willingness-to-pay threshold of $45,000 per QALY (equivalent to the UK threshold) base case results showed that the probability that either cytosponge or endoscopy was cost-effective was 94% compared to no screening. The results indicated that for a health care provider willing to pay up to $16,500 per QALY no screening was the optimal choice; above $16,500 per QALY cytosponge screening with endotherapy management was the optimal choice.

Authors’ conclusions
The authors concluded that screening using cytosponge was cost-effective for the given population and could prevent oesophageal adenocarcinoma deaths.

CRD commentary
Interventions:
The intervention and treatment strategies considered appeared appropriate. The authors mentioned one alternative screening intervention (video capsule endoscopy) which they stated was not considered as it provided no tissue sampling and had poor diagnostic accuracy. The authors justified their choice of treatments as they stated that endotherapy was the increasingly accepted standard of care.

Effectiveness/benefits:
All of the effectiveness parameters were reported clearly along with their standard error or range and sources. The authors did not justify their choice of sources for deriving effectiveness estimates. The source and results for derivation of the utility valuations were reported; no further details were reported for utility valuations.

The assumption that endoscopy was a perfect test was a key issue in the analysis. The authors stated that sensitivity of endoscopy was unlikely to be 100% but as both screening strategies included endoscopy the effect of any bias would be minimised. Sensitivity and specificity of endoscopy was not a parameter in the deterministic sensitivity analysis so the effect of any bias was not measured. But endoscopy was dominated even with the assumption of 100% accuracy so any effect on the results would not alter the conclusion.

Costs:
Costs and sources were reported clearly and all costs appeared appropriate for the stated perspective and setting. Appropriate cost adjustment techniques were used. Discounting was applied.

Analysis and results:
The model was described clearly. There was a diagram for the Markov component. A limitation of the study was the reliance on authors' assumptions to derive many of the parameter values, which were not justified. Various techniques were used to assess the validity of the model and these appeared appropriate. In the deterministic sensitivity analyses the range of values over which base case values were altered were reported clearly; the authors did not report their justification for the chosen ranges. The authors clearly reported the methodology and distributions used in the probabilistic analysis and these seemed appropriate.

Concluding remarks:
The study was mostly well conducted and reported. The authors' conclusions appear to be appropriate.

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