Endoscopic screening for gastric cancer

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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 biennial screening (surveillance endoscopy) for gastric cancer in asymptomatic populations with intermediate epidemiologic risk.

Type of intervention
Screening.

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

Study population
The study population comprised a hypothetical cohort of Chinese men aged 50 years and older. Other sub-groups of individuals at different epidemiological risk of disease, such as women aged 50 years or older, both genders aged older than 50 years and men with HP, were also considered.

Setting
The setting was primary care. The economic study was carried out in Singapore.

Dates to which data relate
The effectiveness data were derived from studies published between 1978 and 2005. No dates for resource use were explicitly reported. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies and authors' opinions.

Modelling
A Markov model was constructed to simulate patient management associated with screening versus non-screening in a hypothetical cohort of eligible individuals. The simulation followed patients undergoing screening every two years from 50 to 70 years of age, until all patients had died or up to the age of 99 years. At each cycle, the length of which was not reported, patients moved across three health states. These health states were healthy, gastric cancer by various stage, and dead. The structure of the model was not presented.

In the screening arm of the model:

suspicious lesions detected by screening were biopsied;

positive cases of gastric cancer were staged by endoscopic ultrasound and computed tomography imaging of the abdomen;
all Stage I to III tumours were treated by curative resection;

patients with Stage III tumours were given chemo-radiotherapy;

while for Stage IV cancers, supportive care with or without palliative therapy was the primary treatment.

In the unscreened arm of the model:

stomach cancers were diagnosed only when patients presented with symptoms; and

gastric cancers were treated with the same protocol as that reported above.

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

the incidence of gastric cancer (age-standardised rate, ASR),

the annual decrease in incidence,

stages of stomach cancer at diagnosis in the screened and unscreened population,

5-year survival rates by stage,

the accuracy of screening oesophago-gastroduodenoscopy (OGD), and

the utility values associated with different disease stages.

**Study designs and other criteria for inclusion in the review**
A systematic literature review was undertaken to identify the primary estimates needed to populate the decision model. The incidence rates were derived from the Singapore Cancer Registry for 1993 - 1997, life-expectancy was obtained from Singapore Health Statistics for 2003, while the distribution of gastric cancer by stage was derived from local studies. The utility scores were obtained from the Quality-of-Life Repository for gastric cancer. Information on the characteristics of the other studies was not provided. It was stated that no randomised clinical trial was available for the efficacy of screening endoscopy and that the best available data were used.

**Sources searched to identify primary studies**
PubMed was searched from 1980 to 2004 to identify relevant studies.

**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**
The clinical estimates were derived from 15 primary studies.

**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 incidence of gastric cancer (ASR) in the Chinese male population at 50 years was 25.9/100,000.

The annual decrease in incidence was 2.3% per year.

The distribution of stomach cancer at diagnosis was 7% in Stage I, 17% in Stage II, 33% in Stage III and 43% in Stage IV in the unscreened population. The distribution in the screened population was 85% in Stage I, 4% in Stage II, 8% in Stage III and 3% in Stage IV.

The 5-year survival rates were 90% in Stage I, 70% in Stage II, 40% in Stage III and 0% in Stage IV.

The sensitivity of screening OGD was 84% and the specificity was 100%.

The utility values were 0.65 for Stages I and II (surgery), 0.4 for Stage III (chemo-radiotherapy) and 0.5 for Stage IV (palliative care, average of chemo-radiotherapy, surgery and stent).

Methods used to derive estimates of effectiveness
The authors made some assumptions in order to derive the clinical estimates.

Estimates of effectiveness and key assumptions
The incidence of gastric cancer was assumed to be similar between the screened and unscreened populations.

The distribution of gastric cancer staging in the screened population became similar to the unscreened population after screening stopped.

Patients who survived 5 years after treatment for gastric cancer were presumed to have been cured.

Full compliance and adherence with regular screening and treatment were assumed.

Measure of benefits used in the economic analysis
The summary benefit measures used were cancer deaths, life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using a modelling approach. The utility weights used to calculate QALYs were derived from the literature. The number of endoscopies performed was also reported but was not combined with the costs. An annual rate of 3% was used to discount future benefits to present values.

Direct costs
The authors stated that a societal perspective was chosen, but only the direct costs were included. The cost categories in the analysis were screening endoscopy, gastric cancer treatment (by stage), national screening programme (including quality management, education, and training), and joining the screening programme (transport, morbidity from endoscopy complications, follow-up, and counselling). The unit costs were not presented separately from the quantities of resources used. The costs were derived from actual hospital finance records in Singapore and a screening programme (for colorectal cancer) in the United Kingdom. Sources of resource consumption were not reported. When various treatment options were available, the most conservative option was selected. Discounting was relevant given that the long-term costs were estimated, and an annual discount rate of 3% was used. All costs were inflated to 2003 values.

Statistical analysis of costs
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
One- and two-way sensitivity analyses were carried out to assess the robustness of the cost-utility ratios to variations in the model inputs. The model inputs investigated were the ASR, cost of screening, distribution of disease stage at diagnosis, survival rate, cost of treatment, starting age of screening, frequency of screening, screening accuracy, utility scores and discount rate. Clinical data were varied over ranges derived from the literature. The ranges of costs were determined using a lower bound from a developing country (India) and an upper bound from a developed country (USA). Worst- and best-case scenarios for other variables were also calculated. Finally, a sub-group analysis was performed. This considered groups of individuals at different risk for gastric cancer (women only, all population, men with HP).

**Estimated benefits used in the economic analysis**
Compared with no screening, gastric cancer screening in a population of 198,823 Chinese men aged 50 years and older in Singapore resulted in 743 cancer deaths averted, 8,234 absolute LYs saved, and 6,856 QALYs gained.

**Cost results**
The incremental costs of screening over no screening in a population of 198,823 Chinese men aged 50 years and older in Singapore were $183,876,000.

**Synthesis of costs and benefits**
Incremental cost-effectiveness ratios and cost-utility ratios were calculated in order to combine the costs and benefits of screening over no screening.

The incremental cost per cancer death averted was $247,600.

The incremental cost per LY saved was $22,346.

The incremental cost per QALY gained was $26,836.

Using the threshold of $28,000 per QALY on the basis of the Singapore gross national income, as suggested by the World Health Organization, screening was a cost-effective strategy.

The most striking results of the sensitivity analysis were as follows:

- the incremental cost per QALY rose to $64,800 with a population ASR of 10/100,000 (low risk equivalent to American men) and fell to $6,400 with a population ASR of 70/100,000 (high risk equivalent to Japanese men);
- a reduction in the cost of endoscopy made screening cost-effective even in a low-risk population (ASR of 11.1/100,000);
- the most cost-effective screening starting age was 65 years;
- the 2-year frequency of screening was the most cost-effective strategy in comparison with annual screening or screening...
Variations in other model inputs had a modest impact on the results of the analysis. Screening the whole Singapore population or only the population of women aged from 50 to 70 years were well above the cost-effectiveness threshold ($45,982 and $63,298 per QALY, respectively), while screening only Chinese men with known positive HP serology was more cost-effective, with an incremental cost per QALY of $17,455. Finally, it was estimated that a strategy of HP screening eradication combined with selective 2-yearly endoscopy would yield an incremental cost per QALY of $21,800 compared with no screening.

Authors’ conclusions
Screening for gastric cancer by 2-yearly endoscopy in a population at intermediate risk of gastric cancer (i.e. Chinese men aged 50 years and older in Singapore) is potentially cost-effective.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was appropriate since no screening represented the actual pattern of care in the authors’ setting. Different frequencies and starting ages for screening were also considered. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The clinical data used to populate the decision model were derived from a review of the literature. The authors reported the database that was searched to identify the primary studies. However, few details of the design and other characteristics of the primary sources were given. Local data sources, such as national registries, were supplemented with international studies and authors' opinions. Epidemiological data were appropriately derived from local sources. The authors did not address the issue of heterogeneity among the primary estimates. The use of alternative clinical estimates was addressed in a comprehensive sensitivity analysis. The authors stated that clinical trials on gastric cancer screening were not found in the literature, but the best available data were used, although retrospective studies have inherent limitations in terms of confounding factors and selection bias.

Validity of estimate of measure of benefit
Several benefit measures were used in the economic analysis. Some of them (e.g. cancer deaths averted) are comparable only with similar diseases, while other measures (i.e. LYs and QALYs) are more generalisable. The source of the utility values was provided, but it was not explicitly stated whether the utility weights were derived from a sample of patients or from the general population. Further, the approach used to elicit quality of life estimates was not reported. The authors acknowledged that utility values could vary in different cultures and ethnicity. Discounting was performed in accordance with international recommendations.

Validity of estimate of costs
The perspective of the cost analysis was not clear. Although the authors stated that a societal perspective was chosen, the indirect costs were not considered, although direct costs incurred by the patients were included. A detailed breakdown of the cost items was not provided and the costs were only presented as macro-categories. In addition, information on resource use was unclear and the unit costs were not reported. Thus, the analysis would be difficult to replicate in other settings. The sources of the cost data were reported and most costs were derived from local hospitals. The costs from other countries were used only when local data were not available. No statistical analyses of the costs were performed, but some sensitivity analyses were carried out on key cost items. The price year was reported, which will assist reflation exercises in other time periods.

Other issues
The authors did not compare their findings with those from other studies. They stated that there was no evidence of a cost-effectiveness analysis for gastric cancer screening in an intermediate-risk population. In terms of the
generalisability of the study results to other settings, it was pointed out that the current findings could be transferable to countries with a similar epidemiological context, especially considering that the cost of endoscopy in Singapore is higher than in other Asian countries. The authors stated that deliberately conservative assumptions were made in order to bias the results of the analysis against the screening strategy. It was also noted that the costs and benefits associated with the diagnosis and treatment of other incidental findings were not considered. The results of the analysis were presented selectively by reporting only incremental results (differences in benefits and differences in costs); the presentation of absolute values (especially with respect to total costs) would have been interesting from the perspective of a budget impact analysis.

Implications of the study
The study results support the use of biennial screening in individuals at intermediate risk of gastric cancer. The authors noted that the cost-effectiveness of gastric cancer screening in other sub-populations should be further investigated in prospective clinical trials.

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