Gastric cancer screening of a high-risk population in Japan using serum pepsinogen and barium digital radiography


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 two screening tests for the detection of gastric cancer. The two tests, serum pepsinogen (PG) and barium digital radiography (DR), could be used individually or in combination. The criteria for the screening tests were accurately reported. For example, the PG-test positive criteria was a PG I level of less than 50 microg/L and a ratio of PG I to PG II of less than 3.0.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised the general population of middle-aged male individuals undergoing gastric cancer screening.

Setting
The setting was the community (workplace). The economic study was carried out in Japan.

Dates to which data relate
The effectiveness and resource use data were gathered between April 1995 and March 2002. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that included in the effectiveness analysis.

Study sample
Power calculations were not carried out. A sample of 17,647 males was identified in a workplace. The mean age of the sample was 50.4 (+/- 5.4) years (range: 40 - 60). The number of those screened for the first time in 1995 was 3,068, of which 2,160 were screened repeatedly with the two screening tests during the following years. It was not stated whether some individuals refused to participate or were excluded for any reason from the study sample.
Study design
This was a diagnostic study that was carried out in a workplace in Wakayama City in Japan. Each participant underwent both screening PG and DR tests. If either or both of the tests were positive, the participants were further examined by upper gastrointestinal endoscopy. The patients were followed for the entire duration of the 7-year study. No patient was lost to the follow-up assessment. The sequence of tests and the use of blinding were not reported.

Analysis of effectiveness
All patients included in the initial study sample were considered in the effectiveness study. The primary outcome measures were:

the percentage of participants requiring further tests,
the percentage of participants who underwent endoscopy,
the number of cancers detected,
the detection rates,
the positive predictive values, and
the standardised mortality ratios (SMRs).

The SMRs were calculated on the basis of gender, age, and year-specific gastric cancer mortality in Wakayama city as the standard population. The clinicopathological profiles of the detected cancers were also reported.

Effectiveness results
The percentage of participants requiring further tests was 40.5% with combined screening, 19.5% with PG, and 22.5% with DR.

The percentage of participants with a positive test who underwent endoscopy was 81.2% with combined screening, 78.8% with PG, and 84.1% with DR.

The number of cancers detected was 49 with combined screening, 31 with PG, and 34 with DR.

The detection rate was 0.28% with combined screening, 0.18% with PG, and 0.19% with DR.

The positive predictive value was 0.85% with combined screening, 1.14% with PG, and 1.02% with DR.

From 1991 to 1994, when the screening was carried out by conventional barium X-ray using photofluorography, 6 employees died from gastric cancer.

After the introduction of the new screening, there were 7 gastric cancer deaths over the period 1995 - 1998. The difference in the number of deaths was not significantly different in comparison with conventional screening.

The SMR of gastric cancer in the workplace, compared with a male population of the same age living in the same area, during the period 1995 - 1998 was 2.74 (95% confidence interval, CI: 1.20 - 5.92).

However, in the subsequent 3 years (1999 - 2001) of new screening, there was a reduction in cancer deaths, with only one employee dying from gastric cancer. Thus, the SMR for this period decreased to 0.87 (95% CI: 0.22 - 2.76).

The clinicopathological profiles of the detected cancers showed that the majority of cancers were in the early stage (88%). The cancers detected by the PG test alone were considerably smaller in size, as expected given the nature of the test.

All cancers were successfully treated either surgically or endoscopically.
Clinical conclusions
The effectiveness analysis showed that PG and DR were almost equally effective screening strategies for gastric cancer. Higher detection rates were observed with the combined screening approach. A significant reduction in mortality was also noted.

Measure of benefits used in the economic analysis
The summary benefit measure was the number of cases detected. It was derived directly from the effectiveness study.

Direct costs
The perspective adopted in the study was not stated. Only the costs of the tests (PG, DR and endoscopy) were included in the analysis. The unit costs were presented separately from the quantities of resources used. Resource use was estimated using data obtained from the sample of patients included in the effectiveness study. The source of the costs was unclear. The price year was not reported. Discounting was not relevant because of the short timeframe of the analysis and, appropriately, was not carried out.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were not included.

Currency
Japanese yen (JPY).

Sensitivity analysis
Sensitivity analyses were not carried out.

Estimated benefits used in the economic analysis
The number of cases detected was 49 with combined screening, 31 with PG, and 34 with DR.

Cost results
The total costs were JPY 198,955,000 with combined screening, JPY 70,537,000 with PG, and JPY 131,668,000 with DR.

Synthesis of costs and benefits
An average cost-effectiveness ratio (i.e. the cost per detected cancer case) was calculated to combine the costs and benefits.

The average cost-effectiveness ratio was JPY 4,060,306 with combined screening, JPY 2,275,387 with PG, and JPY 3,872,588 with DR.

Based on mass screening for gastric cancer nationwide, as performed in 2002 with standard barium X-ray photofluorography, the cost per cancer detected was calculated to be JPY 4,408,543, which was higher than all other strategies.
Authors' conclusions
The combined screening strategy represents an optimal gastric cancer screening strategy in Japan. In particular, the authors stated "the PG (serum pepsinogen) test is especially good at screening asymptomatic subjects, whereas symptomatic subjects or PG test-negative subjects should be screened by barium X-ray examination with DR (digital radiography)".

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators. The new screening tests were compared with each other, either individually or in combination. They were only compared with standard photofluorography in terms of mortality. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a single sample of individuals who underwent the two screening tests. Therefore, there was no need for a control group. An external comparison was made with the death rate in the general population of the city in which the study was carried out. The lack of a control group reduces the potential impact of selection bias and confounding factors. However, the sequence of the two tests was not described and it was unclear whether study investigators were aware of the results of the first test. The evidence came from a large city, which means that the study sample should be quite representative of the patient population. No justification for the size of the sample was provided but, given the large number of patients included in the analysis, the impact of chance on the study results should have been minimal. The follow-up appears to have been long enough for an accurate assessment of the development of gastric cancer.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. It will not therefore be comparable with the benefits of other health care interventions. However, cases of cancer detected are a commonly used benefit measure for interventions involving cancer screening.

Validity of estimate of costs
There was limited information on the analysis of the costs since the economic evaluation of the screening strategies appears to have been a secondary objective of the study. The unit costs of the screening tests were reported and resource use was derived from the sample of individuals included in the clinical study. This enhances the possibility of replicating the study in other settings. However, the perspective of the study was not stated and the costs associated with the subsequent treatment of detected and undetected cases were not considered. The cost estimates were specific to the study setting and the impact of alternative cost estimates was not investigated. Similarly, no statistical analysis of the costs was carried out. The source of the costs and the price year were not reported, which will hinder reflation exercises in other time periods.

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 not carried out and all estimates were specific to the Japanese context. Therefore, caution is required when extrapolating the current findings to other countries. The study referred to middle-aged men undergoing screening for gastric cancer and this was reflected in the authors' conclusions.

Implications of the study
The authors recommended that the two screening tests should be performed together to detect the highest number of gastric cancer cases in an efficient manner. The authors suggested that the next improvement in the current screening system would depend on target setting.
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