A comparison of the cost-effectiveness of fecal occult blood tests with different test characteristics in the context of annual screening in the Medicare population


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
Three types of faecal occult blood test (FOBT) were used for annual screening for colorectal cancer (CRC). Two were guaiac-based FOBTs (Hemoccult II and Hemoccult-SENSA), while the other was an immunochemical FOBT.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of one million individuals aged 65 to 79 years.

Setting
The setting appears to have been primary care. The economic study was carried out in the USA.

Dates to which data relate
Most of the evidence of effectiveness and resource use was derived from studies published between 1993 and 2002. The price year was 2002.

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

Modelling
A micro-simulation model was constructed to develop the natural history of CRC and the impact of screening on reducing cancer incidence and mortality in a cohort of one million individuals who reflected a typical US cohort. The screening programme was implemented for 30 years, although the patients were followed for their lifetime. The simulation model was used to derive the number of CRC cases and deaths, life-years and costs with and without screening options. The Erasmus University (Rotterdam, The Netherlands) had developed and validated the model, details of which had been published elsewhere.

Outcomes assessed in the review
The outcomes assessed were:

- the sensitivity for CRC and for large (≥1 cm) and small (<1 cm) adenomas, and the specificity;
the distribution birth of the cohort and life tables of death from other causes than CRC; adenoma incidence; the duration of preclinical cancer; the sensitivity of diagnostic and surveillance colonoscopy; prognosis after screening; follow-up intervals during surveillance; and screening attendance.

**Study designs and other criteria for inclusion in the review**
It was not stated whether the review was conducted systematically. Details of all the primary studies and sources used to derive the model inputs were provided. The sample size of each study was reported. Some US statistics were also used.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
The authors discussed the validity of the different types of sources used.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
Approximately 29 primary studies provided the evidence.

**Methods of combining primary studies**
It would appear that the authors chose the best estimates arbitrarily from among the primary studies.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The sensitivity for CRC was 40% with Hemoccult II, 70% with Hemoccult-SENSA, and 70% with immunochemical FOBT.

The sensitivity for large (≥1 cm) adenomas was 10% with Hemoccult II and 17% with both Hemoccult-SENSA and immunochemical FOBT.

The sensitivity for small (<1 cm) adenomas was 5% with Hemoccult II and 9% with both Hemoccult-SENSA and immunochemical FOBT.

The specificity was 98% with Hemoccult II, 92.5% with Hemoccult-SENSA, and 98% (or 95%, depending on the model assumption) with immunochemical FOBT.
The annual adenoma incidence was 0.9% in the 40- to 49-year age group, 1.9% in the 50- to 59-year age group, 3.3% in the 60- to 69-year age group, and 2.6% in the 60- to 69-year age group.

The mean duration of preclinical cancer was 3.6 years.

The sensitivity of diagnostic and surveillance colonoscopy was 80% for adenomas of no more than 5 mm, 85% for 6- to 9-mm adenomas, and 95% for adenomas of 10+ mm.

The sensitivity of diagnostic and surveillance colonoscopy for cancer was 95%.

Screening attendance was 100%.

The results of other estimated data were also reported.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the decision model. In general, conservative assumptions were made.

**Estimates of effectiveness and key assumptions**
It was assumed that:

- no person had received any type of colorectal screening procedure prior to age 65;
- all individuals were 100% compliant;
- individuals with adenoma continued to have surveillance colonoscopies until they were diagnosed with CRC, or died from other causes;
- the mean duration of non-progressive adenomas was lifelong, while the mean duration of progressive adenoma was 16.4 years; and
- the probability of developing cancer from a removed adenoma was 0%.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the number of life-years saved with the screening strategy over the option of no screening. The benefits were obtained using the decision model and were discounted at an annual rate of 3%.

**Direct costs**
An annual discount rate of 3% was applied to the costs since the lifetime time horizon was adopted in the model. The unit costs were presented, but there was limited information on resource use. The health services included in the economic evaluation were screening tests, diagnostic follow-up, surveillance, and treatment procedures such as colonoscopy and polypectomy. Colonoscopy was considered with or without biopsy. The cost/resource boundary of the third-party payer was adopted. The costs were derived from Medicare reimbursement rates. Resource use was derived using data obtained from the literature review and experts’ opinions. All the costs were updated to 2002 values.

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

**Indirect Costs**
The indirect costs were not included in the economic evaluation.
Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were carried out. These examined the impact of different scenarios associated with test costs, sensitivity and specificity values, frequency of surveillance and level of compliance, on the estimated cost-effectiveness ratios. Threshold analyses were also carried out. These assessed different prices for the guaiac FOBT and immunochemical FOBT that would deliver equivalent cost-effectiveness ratios. The authors determined ranges of values on the basis of alternative estimates observed in the literature. Also considered were a best case for immunochemical FOBT and immunochemical FOBT as the base-case.

Estimated benefits used in the economic analysis
In general, the screening options reduced CRC-related mortality in comparison with no screening. Depending on the model assumptions, the estimated discounted life-years saved in the whole cohort of one million individuals was 232,107 with Hemoccult-SENSA, and ranged from 136,817 to 202,108 with Hemoccult II, and from 219,831 to 245,381 with immunochemical FOBT.

Cost results
Depending on the model assumptions, the estimated discounted costs in the whole cohort of one million individuals ranged from $197,556,566 to $453,629,724 with Hemoccult II, from $775,643,892 to $1,352,544,256 with Hemoccult-SENSA, and from $83,110,600 to $1,398,580,548 with immunochemical FOBT.

Synthesis of costs and benefits
Average cost-effectiveness ratios (ACER) versus no screening, and incremental cost-effectiveness ratios (ICER) versus each of the other screening strategies, were calculated to combine the costs and benefits of the alternative screening options. Depending on the model assumptions, the estimated ACER in the whole cohort of one million individuals ranged from $1,071 to $2,245 for Hemoccult II, from $3,342 to $5,827 with Hemoccult-SENSA, and from $357 to $5,716 with immunochemical FOBT.

Some examples of the ICER will be reported here. Immunochemical FOBT with 98% specificity at a test cost of $4.50 dominated Hemoccult II, but at a unit cost of $28, the ICER increased to about $11,000 per additional life-year gained. At a specificity of 95%, the ICER was $6,000 at a cost of $4.50 and $21,000 at a cost of $28. Immunochemical FOBT with a specificity of 98% dominated Hemoccult-SENSA independently of the test cost, but with a specificity of 95% and test costs of $28 (immunochemical FOBT) and $4.50 (Hemoccult-SENSA), the two screening options were almost identical.

The threshold analysis showed that when more favourable assumptions about the specificity (98%) of immunochemical FOBT were made, then the threshold price for immunochemical FOBT was in the range of $10 to $14 but no higher. For lower specificity values, even the current price of $4.50 was not justified on comparative cost-effectiveness grounds. However, a threshold value of $18 was obtained for immunochemical FOBT if the sensitivity for CRC increased to 87% and was 1.75 times that for large adenomas (≥1 cm). Other results of the threshold analysis were reported in the paper. Under a best-case scenario for immunochemical FOBT, the threshold value for the screening test was $29 relative to Hemoccult II and $60 relative to Hemoccult-SENSA.

When immunochemical FOBT was considered the base-case, the threshold payment levels corresponded to $18 and $27 for immunochemical FOBT with 98% specificity and were about $10 and $17 for Hemoccult II. The threshold payment level for Hemoccult II would be less than the current payment ($4.50). However, with a specificity of 95%, the payment levels for both guaiac screening tests were lower than those estimated above. With more intensive surveillance, the life-years saved increased slightly but the costs increased substantially. Consequently, the relative cost-effectiveness advantage of more sensitive screening tests would diminish with more intensive surveillance practices.
Finally, assuming 60% compliance with Hemoccult II and 90% compliance with immunochemical IFIBT, the threshold price of immunochemical FOBT increased approximately from $11 to $15.

Authors’ conclusions
Faecal occult blood tests (FOBTs), either guaiac-based or immunochemical-based, were very cost-effective screening strategies for the detection of colorectal cancer (CRC) in individuals aged 65 to 79 years who had not been screened before. In general, the threshold test price at which the immunochemical FOBT would provide a cost-effectiveness ratio comparable with that of Hemoccult II (or Hemoccult-SENSA) was higher than the $4.50 value that corresponded to the test cost of Hemoccult.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparators. The two guaiac FOBTs were both commonly used in the USA, while the immunochemical FOBT was a proposed, alternative screening option. The authors also stated that another approach (the Hemoquant test) was available, but it was not examined in the study because it represented a more complex type of test. The choice of colonoscopy as the ‘gold’ standard was appropriate, although the authors stated that it approximated to, but did not reach, 100% sensitivity. Nevertheless, it represented the best available ‘gold’ standard. The option of no screening was also considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness came from evidence derived from several published sources. It was unclear whether the review of the literature was conducted systematically, but numerous relevant studies appear to have been identified. Details of the studies and patient samples were reported. The authors discussed the validity of several sources and the problems of deriving robust estimates. Some data were also based on assumptions. Alternative scenarios were considered in the sensitivity analysis, to account for differences in the base-case estimates, and also due to the paucity of reliable data on test characteristics. This enhanced the robustness of the analysis.

Validity of estimate of measure of benefit
The choice of the summary benefit measure appears to have been appropriate, as it reflected the impact of the screening strategies on survival and is widely used in evaluations assessing the cost-effectiveness of CRC screening. Discounting was applied, but the impact of variations in the discount rate was not investigated. The authors stated that quality of life issues were not considered, mainly due to the lack of data.

Validity of estimate of costs
The perspective adopted in the study was clear. As such, it appears that all the relevant categories of costs have been included in the analysis. The unit costs were clearly presented, but details of resource use were less clear. The price year was reported, which will facilitate reflation exercises in other settings. The cost data were based on reimbursement rates, which could not have been appropriate for determining the true costs of the screening options. However, they were useful from the point of view of examining the relative differences in the costs. The costs were treated deterministically in the base-case and the cost estimates were specific to the study setting. Alternative scenarios for test costs, when relevant, were considered.

Other issues
The authors stated that their cost-effectiveness ratios were more favourable than those estimated in published studies, probably due to the low payment cost of the screening test. The issue of the generalisability of the study results to other settings was not explicitly addressed, but the external validity of the analysis was enhanced by the use of alternative scenarios. The authors noted that performing sigmoidoscopy in combination with FOBT would make the cost-effectiveness of the screening strategies less favourable. The inclusion of the extra cost of upper gastrointestinal endoscopy would favour immunochemical FOBT because of the lower rate of false positives in comparison with both
guaiac FOBT options. If patient and physician costs were included, the absolute cost-effectiveness estimates would increase by substantial margins and this would affect the rationale for considering Hemoccult-SENSA as an alternative base-case.

**Implications of the study**
The study results suggested that the choice of the preferred screening option should depend on the specific characteristics of the scenario considered, as changes in the model inputs led to variations in the relative cost-effectiveness of the screening strategies.

**Source of funding**
None stated.

**Bibliographic details**

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by CRD

**MeSH**
Aged; Colonoscopy; Colorectal Neoplasms /diagnosis; Cost-Benefit Analysis; Mass Screening /methods /economics; Occult Blood; Sensitivity and Specificity

**AccessionNumber**
22005008069

**Date bibliographic record published**
31/03/2005

**Date abstract record published**
31/03/2005