Faecal occult blood screening for colorectal cancer: is it cost-effective?

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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 use of the faecal occult blood (FOB) test for colorectal cancer (CRC) screening in an unselected population of men and women aged 50 to 74 years; those in the pilot study were aged 45 to 74 years.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised unselected men and women aged 50 to 74 years; the pilot study involved patients aged 45 to 74 years.

Setting
The setting was primary care, community and hospital. The economic analysis was carried out in Nottingham, UK.

Dates to which data relate
The effectiveness and resource use data were based mainly on a single screening trial whose participants were recruited between February 1981 and January 1991. All participants were followed-up until June 1995. Some other effectiveness outcomes were obtained from studies published between 1993 and 1996. The price year was 1995 to 1996.

Source of effectiveness data
The evidence for the final outcomes was based on a single study and on a literature review.

Link between effectiveness and cost data
The costing was based on a series of audits of resource use for trial participants, which had been conducted for each stage of the screening and treatment processes.

Study sample
Power calculations were used to determine the sample size; the study was originally designed to have 80% power to detect a 23% reduction in mortality at the 5% significance level. The sample size was subsequently increased from 106,000 to 156,000 in 1989, in the light of lower than anticipated control-group mortality.

Of the 152,850 individuals recruited to the study, 76,466 were randomly assigned to the screening group and 76,384 to the no-screening group. After excluding those patients who could not be traced or who had emigrated, there were
75,253 participants in the screening group and 74,998 controls. There were 44,838 (59.6%) participants in the screening group who completed at least one screening: 28,720 (38.2%) of these individuals completed all the FOB tests offered, whilst 16,118 (21.4%) completed at least one screening but not all the tests offered. There were 30,415 (40.4%) participants who did not complete any test.

**Study design**
This was a randomised controlled trial carried out in general practices in a UK city. The median follow-up was 7.8 years (range: 4.5 - 14.5). The original loss to follow-up was 1,213 individuals in the screening group and 1,386 in the control group; furthermore, 40.4% of the screening-group participants did not complete any test. The participants were identified through the general practice at which they were registered. Family doctors at each participating practice examined the study list, and removed any person whom they judged should be excluded because of serious illness, including a diagnosis of CRC within the previous 5 years. Before randomisation, the individuals on the list were sorted by household; households were then stratified by size, gender and average age of eligible members. The identified controls, who were not told about the study, received no intervention and continued to use health care facilities as usual.

Screening was stopped in February 1995, by which time screening-group participants had been offered FOB tests between three and six times. The information on the development of CRC was obtained from local hospitals, the regional cancer registry, and the family doctors' reports. The Office of Population Censuses and Surveys routinely notified the study coordinator of the date and causes of death of any study participant. A single pathologist reviewed the histology of all cancers treated by polypectomy. Pathologists, unaware of the participant's study group, assessed CRC stage and classified adenomas. When the cause of death was uncertain, a second investigator reviewed the case-notes. In cases of disagreement, a third investigator examined the case-notes and made the final decision. Investigators were unaware of the screening status of study participants throughout the assessment of CRC mortality.

**Analysis of effectiveness**
The principle used in the analysis was intention to treat. The primary outcome measure was CRC mortality. The other outcomes reported were the CRC incidence per 1,000 person-years, the detection methods, and the rate of interval cancer, the number of cancer cases between two screening rounds for patients with negative test results. A Poisson log-linear model was used to calculate the confidence interval (CI), and to investigate the effect of age and gender. The Kaplan-Meier product limit method was used to calculate survival from the date of CRC diagnosis, censoring at the date of death or at 30 June 1995.

**Effectiveness results**
The CRC incidence was 1.49 per 1000 person-years in the screening group. Of the 893 cancers (20% stage A) diagnosed in screening-group participants, 238 (26.4%) were detected by FOB screening, 249 (27.9%) presented after a negative FOB test or investigation, and 400 (44.8%) presented in non-responders.

The incidence of cancer in the control group was 1.44 per 1,000 person-years; there were 856 cases (11% stage A).

The rate of interval cancer was 28%.

There were 360 deaths from CRC in the screening group, compared with 420 in the control group; this represented a 15% reduction in cumulative CRC mortality in the screening group (odds ratio 0.85, 95% CI: 0.74 - 0.98, p=0.026).

**Clinical conclusions**
The study findings, along with evidence from other trials, suggest that consideration should be given to a national programme of FOB screening in order to reduce CRC mortality in the general population.

**Modelling**
A semi-Markov model with four possibilities for disease progression was used to compute costs and effects associated
with each screening strategy. The primary clinical data for the model were derived from the accumulated results of the Nottingham trial, supplemented, where necessary, by literature values. The costs and effects were calculated separately for males and females for 5 scenarios (simulations).

Scenario 1: this was based on the reported results of the Nottingham trial.

Scenario 2: this assumed an age and gender distribution for the general UK population based on the 1991 Census.

Scenario 3: this followed scenario 2, with the exceptions that lifetime was adopted as the timeframe of the model, and age/gender-specific compliance rates in rounds beyond the Nottingham trial period were assumed to continue to decline at the same rate as within the trial period.

Scenario 4: this assumed that compliance fell to a plateau at round 4 (after 6 years) and was constant thereafter.

Scenario 5: this used the higher compliance rate of a Danish trial for the first round, and thereafter assumed compliance fell by 10% for each subsequent round.

Outcomes assessed in the review
The outcomes obtained from other studies were compliance rate, rate of interval cancer, and the quality-adjusted (QA) estimates.

Study designs and other criteria for inclusion in the review
A Danish randomised controlled trial was used as one of the sources of the clinical data incorporated in the model. The study designs of other data sources were not reported.

Sources searched to identify primary studies
Not reported.

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
A total of 6 published studies provided the values used in the study model.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The compliance rate in the Danish trial was 70% in the first round. The rate of interval cancer in the Danish trial was 31%. The QA estimates were not reported, albeit to say that they were within the range identified in the evaluation of
breast cancer screening for women aged above 50 years.

**Measure of benefits used in the economic analysis**

The measure of benefits adopted was the quality-adjusted life-years (QALYs) gained in comparison with the no-screening strategy for a cohort of 100,000 participants.

**Direct costs**

The costs were discounted. The resource use quantities were not reported separately from the costs, whereas the cost structure was reported separately. The cost analysis covered the costs of CRC detection and treatment. The cost analysis was conducted from the perspective of the National Health Service. The primary cost data were derived from a series of audits of resource usage for trial participants, which had been conducted for each stage of the screening and treatment process: invitation and FOB testing, diagnosis and investigation, treatment and follow-up. The price year was 1995 to 1996. The cost analysis made no allowance for certain cost factors which were likely to be present in a fully operational system, such as the requirement for substantial additional capital investment in endoscopy facilities nationwide, staff training, and call-recall system.

**Statistical analysis of costs**

No statistical analysis of costs was carried out.

**Indirect Costs**

Indirect costs were not included.

**Currency**

UK pounds sterling (£).

**Sensitivity analysis**

A set of one-way sensitivity analyses was performed on:

- FOB cost;
- colonoscopy cost;
- the cost difference between treating early-stage cancer, as opposed to late-stage cancer;
- the screening interval, annually instead of biennially;
- survival following early-stage detection;
- the discount rate for survival gains; and
- the FOB test sensitivity and specificity, within scenario 3.

**Estimated benefits used in the economic analysis**

The number of QALYs gained for male participants was 257, 257, 576, 623 and 911 in scenarios 1 to 5, respectively. For the female participants, the corresponding values were 322 (scenario 1), 332 (scenario 2), 941 (scenario 3), 1,030 (scenario 4) and 1,219 (scenario 5).

The discount rate for the survival gain was 6% (3% in the sensitivity analysis).
Cost results
The additional costs incurred for male participants due to the FOB screening, compared with the no-screening strategy for a cohort of 100,000 participants, were: 1,463,338 in scenario 1, 1,458,290 in scenario 2, 1,178,638 in scenario 3, 1,324,476 in scenario 4, and 2,031,605 in scenario 5.

The corresponding values for the female participants were 1,594,678 in scenario 1, 1,592,051 in scenario 2, 1,289,855 in scenario 3, 1,468,888 in scenario 4, and 2,055,855 in scenario 5.

The discount rate was 6%.

Synthesis of costs and benefits
The incremental cost-effectiveness ratios, i.e. the cost per QALY gained, for male participants were: 5.85 in scenario 1, 5.665 in scenario 2, 2.047 in scenario 3, 2.127 in scenario 4, and 2.231 in scenario 5.

The corresponding values for the female participants were 4.951 in scenario 1, 4.791 in scenario 2, 1.371 in scenario 3, 1.426 in scenario 4, and 1.686 in scenario 5.

Authors' conclusions
The estimates of cost per QALY gained from CRC screening show the procedure to be of similar cost-effectiveness to breast cancer screening in the short term. Over the longer term, however, the estimates for CRC screening appear superior.

CRD COMMENTARY - Selection of comparators
The strategy of no screening was regarded as the comparator. This allowed the active value of the FOB screening to be evaluated. You, as a user of this database, should determine whether these health technologies are widely used in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results is likely to be high as the effectiveness data were based on population-based randomised clinical trials and power calculations were performed. The study sample was representative of the general population, and groups were shown to be comparable in terms of age and gender at entry into the study.

Validity of estimate of measure of benefit
The estimation of benefits was modelled and the instrument used to derive the measure of health benefit, the semi-Markov model, appeared appropriate. However, more information would have been helpful, such as the procedures and methods used to estimate quality of life.

Validity of estimate of costs
There were several positive features that contributed to the validity of the cost analysis: the price year and perspective adopted in the cost analysis were specified; and the robustness of the cost results was investigated through sensitivity analysis. However, some limitations were also evident. The resource use profile was not reported separately from the costs, the details of the methods of cost estimation were inadequate, and the direct cost analysis did not appear comprehensive, as some cost items were omitted from the analysis. The effects of alternative procedures on indirect costs were not addressed.

Other issues
The authors' conclusions appear justified given the sensitivity analyses performed, although they warned that considerable caution must be exercised in the interpretation of the sensitivity results for simulations departing radically
from the Nottingham protocol. The issue of generalisability to non-UK settings was not addressed. However, it was unclear whether the ranges in the sensitivity analysis were chosen to address this issue. The study considered a population-based screening programme and adequately represented the intervention for the United Kingdom. Some comparisons were made with other studies. It was mentioned that the Nottingham trial only considered one of a number of feasible screening models for potential practical application. One further limitation of this study's protocol was that it made no formal attempt to re-invite non-compliers with FOB screening.

**Implications of the study**
Cheaper early-stage treatment evidently offers scope for cost economies, although whether this is likely to be practicable within an operational programme remains unclear. It was mentioned that the model's assumptions might well be inappropriate given the little primary information on the likely impact on long-term compliance of more frequent screening, the different entry ages, and the public's perception of test efficacy.

**Source of funding**
Funded by Nuffield Provincial Hospitals Trust, Medical Research Council and PPP Medical Trust.

**Bibliographic details**

**PubMedID**
9541081

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Aged; Colorectal Neoplasms /prevention & control; Computer Simulation; Cost-Benefit Analysis; England; Female; Humans; Male; Mass Screening /economics; Middle Aged; Models, Econometric; Occult Blood; Quality-Adjusted Life Years; Survival Rate

**AccessionNumber**
21998008078

**Date bibliographic record published**
28/02/2002

**Date abstract record published**
28/02/2002