Cost-effectiveness of colorectal cancer screening: comparison of community-based flexible sigmoidoscopy with fecal occult blood testing and colonoscopy
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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 investigated different strategies for colorectal screening. The four screening regimes evaluated were flexible sigmoidoscopy every 10 years, colonoscopy every 10 years, and biennial and annual rehydrated Hemoccult faecal occult blood testing (FOBT). The four strategies were compared with no screening.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised average-risk individuals aged 55 to 64 years. The distribution of the population across the initial disease states was specified in the model. The population was assumed to be homogenous (other than the initial disease states) since the transition probabilities were independent of the initial states.

Setting
The setting was secondary care. The economic study was carried out in Australia.

Dates to which data relate
The effectiveness data were obtained from studies dating from 1987 to 2001. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Modelling
A Markov decision analytical model was used. This model simulated the progression of an individual through a defined series of states until death. The individual began the cycle in one of the following states: "normal", "adenoma < 10 mm", "adenoma > 10 mm", "cancer Dukes stage A", "cancer Dukes stage B", "cancer Dukes stage C" or "cancer Dukes stage D". The model assumed a distribution reflecting the prevalence of each state in the target population. An individual in the "normal" state could develop an adenoma of less than 10 mm, develop cancer or remain normal. An individual with an adenoma of less than 10 mm could remain in that state or progress to the adenoma greater than 10 mm state. Individuals in this latter state could progress to cancer or remain in that state. When an individual had cancer they could remain in the same state, advance to later stages, or die. The model consisted of five different arms representing the pathways of no screening and the four different screening regimes. A cohort of 10,000 patients was passed through each arm and were followed for 10 years.
Outcomes assessed in the review
The outcomes assessed in the review were:

the prevalence of each state;
the mortality rates from cancer;
the natural progression of cancer;
the probability of diagnosis without a screening programme;
the screening test characteristics (i.e. sensitivity, specificity, compliance);
the probability of an adenoma being removed by colonoscopy; and
the life expectancy of the target population.

Study designs and other criteria for inclusion in the review
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
Approximately 17 studies were included in the analysis.

Methods of combining primary studies
In the cases when the range of reported values was wide, the most commonly reported value was used and the impact was tested in sensitivity analyses.

Investigation of differences between primary studies
Not reported.

Results of the review
The probabilities of entering the model in the feasible states were:

0.79 for normal;
0.18 for an individual having an adenoma less than 10 mm in diameter and 0.027 for having an adenoma of greater than 10 mm; and
for an individual who had developed colorectal cancer, 0.00269 that the cancer was at Dukes stage A, 0.00126 at Dukes stage B, 0.00108 at Dukes stage C, and 0.00036 at Dukes stage D.

The mortality rates for cancer in Dukes stage A, B, C or D were 0.17 (A), 0.26 (B), 0.54 (C) and 1.00 (D), respectively.

The transitional probabilities were:

for of an adenoma less than 10 mm arising from a normal individual, 0.0133;
for an adenoma less than 10 mm progressing to an adenoma of greater than 10 mm, 0.003;
for an adenoma greater than 10 mm progressing to Dukes stage A, 0.05; and
for colorectal cancer Duke stage A arising from a normal individual, 0.00007.

The sensitivity of FOBT was 0.6 for cancers, 0.1 for adenomas greater than 10 mm, and 0.92 for adenomas less than 10 mm. The specificity of FOBT was 0.92 and its compliance was 0.6.

The probability of flexible sigmoidoscopy being successful was 0.98, and its reach was 0.75. The sensitivity of flexible sigmoidoscopy was 0.95 for cancers, 0.95 for adenomas greater than 10 mm, and 0.85 for adenomas less than 10 mm. Its specificity was 0.98 and its compliance was 0.42.

The sensitivity of colonoscopy was 0.95 for cancer, 0.95 for adenomas greater than 10 mm, and 0.85 for adenomas less than 10 mm. The probability of perforation was 0.002, while the probability of death following perforation was 0.075.

The probability of an adenoma greater than 10 mm being removed by colonoscopy rather than surgery was 0.9.

The life expectancy of the target population was 14.65 years.

Methods used to derive estimates of effectiveness
The authors made a number of key assumptions in their Markov decision analytical model for colorectal cancer.

Estimates of effectiveness and key assumptions
The authors assumed that:

non-compliers with screening had the same probability of a colorectal abnormality as those not screened;
abnormalities detected by screening had the same disease course as those detected clinically;
the dwell time of cancer in Dukes stages A, B, C and D was one year, thus, a Dukes stage A cancer would progress to a Dukes stage B after 1 year;
survival at each Dukes type was the same regardless of whether it was detected by screening or by clinical symptoms;
if complications arose as a result of a colonoscopy, any adenoma or cancer would be detected as a consequence of the colonoscopy and the treatment of complications;
the annual probability that Dukes stage D would be detected was 1 regardless of whether screening was performed; and if an adenoma was detected by colonoscopy it would be removed, either during the colonoscopy or surgically.

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analysis was the life-years saved (LYS).
Direct costs
The direct costs included were those of the health service. These were for medical visits, screening tests, pathology tests, adenoma removal, treatment of cancer at each stage, treatment of complications, and the programme administrative costs. The authors used the Medicare Benefits Schedule fee for the cost of the FOBT test, pathology examinations and medical attendance. The cost of the screening tests, colonoscopy, flexible sigmoidoscopy and cancer treatment were based on data from a published study. Discounting was relevant since all the costs were incurred during 10 years. Thus, the costs were appropriately discounted at a 5% rate, in line with government policy. The authors reported the total and incremental costs for the five groups undergoing different strategies. The costs related to 2001 and were inflated using the consumer price index.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs were not included in the analysis.

Currency
Australian dollars (Aus$).

Sensitivity analysis
The robustness of the cost-effectiveness analysis was tested by studying the variables to which the costs and outcomes were most likely to be sensitive. The analysis was performed using Tornado diagrams. These depict multiple one-way sensitivity analyses in a single graph where a horizontal bar is generated for each variable analysed and arranged in order. The ranges for the sensitivity analysis were selected such that the costs were varied by 20% or by the range of approximations present in the literature.

Estimated benefits used in the economic analysis
Compared with no screening, the number of incremental LYS were 154 with flexible sigmoidoscopy, 213 with colonoscopy, 42 with biennial FBOT, and 203 with annual FOBT. The benefits were discounted at a rate of 5%.

Cost results
The costs of the five different screening strategies were Aus$3,530 for no screening, Aus$6,120 for flexible sigmoidoscopy, Aus$7,640 for colonoscopy, Aus$8,880 for biennial FOBT, and Aus$13,050 for annual FOBT.

Synthesis of costs and benefits
The costs and benefits were combined using an incremental cost-effectiveness ratio (i.e. the additional cost to obtain an extra life-year). Compared with no screening, the incremental cost-effectiveness ratio of screening was Aus$16,801 for flexible sigmoidoscopy and Aus$19,285 for colonoscopy.

Biennial and annual FOBT screening were less cost-effective at Aus$41,183 per LYS (biennial) and Aus$46,900 per LYS (annual), respectively, compared with no screening.

The analysis was sensitive to the probability that an adenoma of greater than 10 mm would progress to cancer with the cost-effectiveness increasing as the probability of progression increased.

The cost of the screening programme was an important determinant of the cost-effectiveness of FOBT. Its cost-effectiveness increased substantially with decreasing programme costs, but was still less than flexible sigmoidoscopy and colonoscopy. When the costs were not discounted, both sigmoidoscopy and colonoscopy were more cost-effective.
while FOBT was less so.

Authors' conclusions
Flexible sigmoidoscopy and colonoscopy were cost-effective strategies for reducing the burden of colorectal cancer.

CRD COMMENTARY - Selection of comparators
The strategies selected reflected the research recently undertaken, or being undertaken, in Australia and the current policy. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. They also did not report the sources searched to identify relevant studies, nor the inclusion and exclusion criteria used. In the cases when the range of reported values was wide, the most commonly reported value was used and the impact was tested in sensitivity analyses. The authors do not appear to have considered the impact of differences between the primary studies when estimating the effectiveness. However, the authors partially addressed all these limitations by conducting sensitivity analyses to account for the uncertainty and variability in the effectiveness data. Further, the authors clearly reported the assumptions behind their Markov decision model.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. All the benefits were appropriately discounted at 5% in accordance with government policy.

Validity of estimate of costs
All the categories of cost relevant to the health service perspective adopted seem to have been included in the analysis. In addition, for each category, all the relevant costs were included in the analysis. The authors reported the unit costs of each cost category, which will enhance the generalisability of their conclusions. The costs were obtained from published sources and were investigated in a sensitivity analysis, using appropriate ranges. Since all the costs were incurred during 10 years, the authors appropriately discounted the costs in line with government requirements. The costs of the FOBT test, pathology examinations and medical attendance were derived from Medicare fees, hence charges were used to proxy prices. The authors appropriately reported the date to which the prices related, which will assist any future inflation exercises.

Other issues
The results from the authors' model were compared with those from other key studies that evaluated the cost-effectiveness of colorectal cancer screening in average-risk individuals, two in the Australian setting. Overall, the results from this study were consistent with five of these six studies. The issue of generalisability was partly addressed through the sensitivity analysis. The authors do not appear to have presented their results selectively, although more information on the studies included in the analysis would have been desirable. The authors' conclusions reflected the scope of the analyses.

The authors reported a number of further limitations to their study. First, the values for the sensitivity of FOBT may have underestimated the effectiveness of the test, as there was a wide range of estimates available. Second, the estimates of complications and mortality from colonoscopy were derived from the literature and could have been overestimated. They may have been higher than in current practice since the increased use of the test means that less-experienced operators perform the procedure.

Implications of the study
The authors recommended that flexible sigmoidoscopy and colonoscopy be seriously considered as suitable screening...
tests for colorectal cancer screening in Australia.

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**Other publications of related interest**


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