Colorectal cancer screening: differential costs for younger versus older Americans

Ladabaum U, Phillips K A

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
Several strategies for colorectal cancer (CRC) screening were examined. These included annual faecal occult blood testing (FOBT), flexible sigmoidoscopy every 5 years (FS), FOBT-FS combined, and colonoscopy every 10 years (COLO). Two different starting ages for screening were compared, screening from 50 to 80 years or from 65 to 80 years.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of 50- and 65-year-old healthy individuals with an average risk for CRC.

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

Dates to which data relate
The effectiveness data and some resource use data were derived from studies published between 1964 and 2004. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A Markov model was used to estimate the costs and benefits associated with the two screening strategies and the no-screening option in a hypothetical cohort of 100,000 healthy individuals. The main health states were:

- normal;
- small (<10 mm) adenomatous polyp;
- large (>10 mm) adenomatous polyp;
- localised, regional, or distant CRC; and
dead.

Without screening, CRCs were diagnosed only when they led to symptoms. The patients were followed at yearly cycles until age 100 or death. With COLO, any polyps found were removed and any CRCs detected were biopsied. If FOBT or FS detected a small or large polyp or CRC, COLO followed, with polypectomy or biopsy as necessary. If COLO was normal after a positive screening test, screening resumed in 10 years using the primary screening strategy. After polyp detection, patients underwent surveillance COLO every 5 years. Patients developing CRC underwent COLO at diagnosis, 3 years later, and every 5 years thereafter.

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

- polyp prevalence,
- the percentages of small and large polyps,
- the annual transition rates among health states,
- the rates of symptomatic presentation and mortality,
- survival,
- the sensitivity and specificity of the screening strategies,
- the complication rates associated with specific tests,
- the utilisation rates of different screening techniques, and
- screening uptake.

**Study designs and other criteria for inclusion in the review**
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. In addition, details of study designs and patient groups were not reported. Life tables were used to derive all-cause mortality data.

**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**
Eleven primary studies provided the clinical data.

**Methods of combining primary studies**
Not reported.
Investigation of differences between primary studies
Not reported.

Results of the review
The polyp prevalence at age 50 was 15%.

The rate of small polyp was 95%, while the rate of large polyps was 5%.

The annual transition rates were as follows:

- to small polyp from normal, 1.1 to 1.9% (age-specific);
- to large polyp from small polyp, 1.5%;
- to cancer without polypoid precursor, 0.006 to 0.086% (age-specific); and
- to cancer from large polyp, 5%.

The annual rates of symptomatic presentation of localised cancer and regional cancer were, respectively, 22% per year over 2 years and 40% per year over 2 years.

The annual mortality rate was 1.74% per year in the first 5 years from treated localised cancer and 8.6% per year in first 5 years from treated regional cancer.

The mean survival from distant cancer was 1.9 years.

The mortality rate from cancer treatment was 2%.

The sensitivity of FOBT for cancer was 40%.

The sensitivity of FOBT for large polyp was 10%.

The sensitivity of FOBT for small polyp was 8%.

The specificity of FOBT was 92%.

The proportion of polyps or cancer within reach of FS was 50%.

The sensitivity of FS for cancer within reach of a sigmoidoscope was 90%.

The sensitivity of FS for large polyp within reach of a sigmoidoscope was 80%.

The sensitivity of FS for small polyp within reach of a sigmoidoscope was 70%.

The specificity of FS for lesions within reach of a sigmoidoscope was 95%.

The sensitivity of COLO for cancer was 95%.

The sensitivity of COLO for large polyp was 90%.

The sensitivity of COLO for small polyp was 85%.

The major complication rate with COLO was 0.1%.

The major complication rate with FS was 0.01%.
The mortality rate with COLO was 0.01%.

The mortality rate with FS was 0.001%.

The utilisation rate was 25% for FOBT, 20% for FS, 20% for FOBT-FS, and 35% for COLO.

The national CRC screening uptake in the USA at the time of the study was 40%.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the expected number of life-years per person after age 50. This was obtained from the Markov model. The life-years were discounted at an annual rate of 3%. Other model outputs, which were not combined with the costs, were CRC incidence, the proportion of localised, regional and distant cancer, and the percentage of deaths attributable to CRC.

**Direct costs**
The analysis of the costs was carried out from the perspective of the third-party payer. It included the costs associated with screening tests, COLO with biopsy or lesion removal, endoscopy complications, and management of CRC by stage (localised, regional, or distant). The unit costs were presented separately from the quantities of resources used for some items only. Some resource use was estimated from published studies. The costs came from multiple sources. Specifically, procedural costs were obtained from Medicare fee schedules (including professional fees and procedure reimbursement) as well as from a health maintenance organisation. The costs of complications came from relevant diagnostic-related groups. The costs for care of stage-specific CRC were obtained from a report to the National Cancer Institute, reports from health maintenance organisations, and estimates for Medicare enrollees. Discounting was relevant and an annual discount rate of 3% was applied. The costs were expressed using 2003 prices. Published costs were updated to 2003 values using the medical services component of the Consumer Price Index.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included as they were not relevant to the perspective of the third-party payer.

**Currency**
US dollars ($).

**Sensitivity analysis**
Some sensitivity analyses were carried out to address the issue of the robustness of the base-case cost-effectiveness ratios to variations in some model inputs. Screening uptake was varied from 0 to 100%, and the actual figure (40%) was compared with a value of 75%, which represents the uptake for cervical and breast cancer screening. A threshold analysis was also performed to assess the impact of including future costs related to other diseases in patients who did not experience CRC morbidity and mortality.

**Estimated benefits used in the economic analysis**
In a hypothetical cohort of 100,000 persons, the estimated life-years per person were 18.686 with no screening, 18.709 with screening starting at age 65 years, and 18.744 with screening starting at age 50 years.

With no screening, CRC incidence was 5,918/100,000, the proportion of localised cancer was 40%, the proportion of regional cancer was 37%, the proportion of distant cancer was 23%, and 2.4% of deaths were attributable to CRC.
With screening starting at age 65, CRC incidence was 3,530, the proportion of localised cancer was 51%, the proportion of regional cancer was 33%, the proportion of distant cancer was 16%, and 1.2% of deaths were attributable to CRC.

With screening starting at age 50, CRC incidence was 2,180, the proportion of localised cancer was 58%, the proportion of regional cancer was 30%, the proportion of distant cancer was 12%, and 0.6% of deaths were attributable to CRC.

Cost results
In a hypothetical cohort of 100,000 persons, the estimated lifetime costs per person were $1,813 with no screening, $2,018 with screening starting at age 65 years, and $2,736 with screening starting at age 50 years.

Without screening, annual US costs (billions per year) related to CRC care, testing and complications were $2.1 for persons aged 50 to 64 years and $6.2 for persons aged 65 years and older. The costs were almost exclusively for CRC care.

With screening uptake at 40% (actual rate), annual US costs (billions per year) were $3.6 for persons aged 50 to 64 years and $5.9 for persons aged 65 years and older.

With screening uptake at 75%, annual US costs (billions per year) would be $5.0 for persons aged 50 to 64 years and $5.6 for persons aged 65 years and older. The greatest share of the costs was that for screening.

The sensitivity analysis showed that, as screening uptake increased, the rate of increase in costs for persons aged 50 to 64 years was greater than the rate of decrease in costs for those aged 65 years or older. Consequently, the total national costs for all ages combined increased as screening uptake increased.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs; i.e. the incremental cost per life-year saved) were calculated to combine the costs and benefits of the alternative strategies.

In comparison with no screening, the ICER was $9,008 with screening starting at age 65 years and $15,809 with screening starting at age 50 years.

In comparison with screening starting at age 65 years, the ICER was $20,529 with screening starting at age 50 years.

The threshold analysis showed that if a programme was needed to increase screening adherence to 75%, the higher programme costs would not raise the ICER above a threshold of $50,000 per life-year gained. Thus, the screening option (starting at age 50) would still remain cost-effective.

A preliminary analysis of the potential inclusion of future costs of care suggested that screening at age 50 remained cost-effective even if future health costs not related to CRC were as high as $34,000 annually per person.

Authors' conclusions
The widespread screening of persons aged 50 to 80 years increased the total national costs related to colorectal cancer (CRC) care and testing, but this included both increases in costs for adults aged 50 to 64 years and decreases in costs for those aged 65 years and older. Overall, CRC screening and polypectomy for people aged 50 to 65 was a cost-effective strategy.

CRD COMMENTARY - Selection of comparators
The rationale for the selection of the comparators was clear as the authors considered two CRC screening strategies (screening at age 50 or 65) that were consistent with the objective of the study. Each strategy was also compared with no screening. Different uptake rates were considered in the sensitivity analysis. You should decide whether they are
valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from selectively identified studies. A systematic review of the literature, to identify primary studies, does not appear to have been performed. There was limited information on the design and other characteristics of the primary studies. Thus, the validity of the primary sources could not be assessed. The methods used to extract and combine the primary estimates were not described, and the issue of heterogeneity across the primary studies was not addressed. With the exception of the uptake rate, the robustness of the study conclusions to variations in the clinical estimates was not investigated in the sensitivity analyses.

Validity of estimate of measure of benefit
The summary benefit measure (i.e. life-years) was appropriate since it captured the most relevant dimension of health for patients with CRC. The authors stated that the impact of the intervention on quality of life was not investigated, owing to the limited evidence on utility values for the relevant health states. Discounting was applied, as recommended by US guidelines.

Validity of estimate of costs
The analysis of the costs was consistent with the perspective adopted in the study. Some costs were presented as macro-categories and resource quantities were not provided for all items. This limits the possibility of replicating the analysis in other settings. However, the costs of cancer care were usually presented as aggregated data. The sources of the costs were presented for all groups of items. The authors noted that the cost results might not reflect actual expenditures from the perspective of individual payers because of differences in reimbursement policies. The price year was reported, which will facilitate reflation exercises in other settings. Discounting was relevant and was applied, but the impact of using alternative discount rates was not investigated. Statistical analyses of the costs were not performed and the use of different cost estimates was not tested in the sensitivity analysis, in which only the potential inclusion of future health care costs was investigated.

Other issues
The authors did not compare their findings with those from other studies. They did not explicitly address the issue of the generalisability of the study results to other settings. Only limited sensitivity analyses were carried out. The authors stated that the published decision model used to simulate clinical and economic outcomes in unscreened and screened populations had already been validated. Thus, this represented a strength of the analysis. The study referred to healthy individuals and this was reflected in the authors' conclusions.

Implications of the study
The study results suggest that widespread CRC screening beginning at age 50 represents a national priority in the USA.

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