Cost-utility of one-time colonoscopic screening for colorectal cancer at various ages
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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 examined one-time colonoscopic screening for colorectal cancer (CRC) at different initial screening ages.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
This was a reference population of 40 to 64 year-old men and women with life expectancies based on USA norms, subdivided into cohorts covering a 5-year range (i.e., 45 - 49).

Setting
The setting was that for performing colonoscopy and excision of any adenoma.

Dates to which data relate
Effectiveness data were established from literature published between 1961 and 1997. Resource costs were estimated in the same way from studies published between 1995 and 1996. The price year was 1998.

Source of effectiveness data
Effectiveness data were derived from a review of the literature.

Modelling
A discrete event simulation model was used to imitate a real world system of development, diagnosis and treatment of colorectal neoplasms in order to determine the cost-effectiveness of different age dependent screening strategies. Separate male and female models were constructed due to gender differences in natural life expectancy and colorectal neoplasia incidence. The structure and workings of the model were very well described within the paper and justified by reference to relevant literature.

Outcomes assessed in the review
The review assessed the following outcomes:

Colonoscopic sensitivity to detect:

CRC, Large polyps (larger than 1cm), intermediate polyps (6-9mm), small polyps smaller than 5mm.)
Colonoscopic complication rates for:
postpolypectomy haemorrhage, perforation, mortality and utilities.

The natural history of colorectal neoplasia was identified using relevant literature and used to inform the model.

**Study designs and other criteria for inclusion in the review**
Not stated.

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

**Criteria used to ensure the validity of primary studies**
Not stated.

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

**Number of primary studies included**
At least 25 primary studies were used to inform the model.

**Methods of combining primary studies**
It was not stated how the studies were combined in order to ascertain the parameter estimates used within the model.

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

**Results of the review**
The results of the review were as follows:

Colonoscopic sensitivity to detect:

CRC, 95%;

large polyps (larger than 1cm), 85%;

intermediate polyps (6-9mm), 80%; and

small polyps (smaller than 5mm), 75%.

Colonoscopic complication rates were:

postpolypectomy haemorrhage, 0.3%;

perforation, 0.1%;

mortality, 0.02%; and
utilities (comprehensively reported in the paper).

Lifetime risk of CRC was represented by a bounded Johnson distribution; mean value for men 6% and mean value for women 5.5%. The mode of the Johnson distribution was set to 0.5%, close to zero to represent the low risk attached to developing CRC in a patient's lifetime. Incidences of adenomas were assigned to 'fast-progressing' or 'slow progressing' groups in a proportion that was age dependent. The assumption was made that less than 2.5% of adenomas become CRC within the first ten years. The time of transition from one state to another was determined by random allocation to one of two different bounded Johnson distributions representing the progression rate. Fast progressing adenomas transition to CRC had a mean period of 26 years. Slow progressing adenomas transition to CRC had a mean period of 52 years.

Whilst transitioning from adenoma to CRC the model allows adenomas to simultaneously make transitions in size from small, to intermediate and on to large. These parameters were again represented individually by bounded Johnson distributions that were dependent upon gender, rate of progression (fast versus slow) and the size transition taking place (small to intermediate or intermediate to large), thus allowing all adenomas the possibility of making the transition to CRC whilst favouring those which are more likely to do so.

Asymptomatic CRC progressed towards symptomatic CRC using a normal distribution with a mean value of 4.8 years. Asymptomatic CRC was initially assigned to the 'local' stage. CRC could then make the transition to 'regional' stage (mean value 5.2 years) or 'distant' stage (mean value 5.55 years) using a normal distribution. This method allowed transition from 'local' to either of the other transition stages. Once the transition to 'distant' stage had been made the patient would remain in this transition state until death.

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

Quality adjusted life years (QALYs) were used as an outcome measure in the economic analysis. It was stated that they were based on societal preferences from a published study.

**Direct costs**

All direct costs of treatment and diagnosis were stated to have been included within the model. Cost categories were: colonoscopy, polypectomy, pathology and CRC costs as initial, continuing (less than or equal to 4 years) and terminal. Resource quantities and unit costs were only reported separately for number of colonoscopies and price of colonoscopy. Costs related to colonoscopy were derived from Medicare reimbursement rates and published studies, costs relating to the treatment of cancer were assigned to initial, continuing, or terminal care dependent on whether or not they occurred within 6 months of diagnosis or death. The price year was given as 1998 and all direct cost were discounted at the rate of 3%.

Estimation of costs and quantities were derived from modelling 100,000 simulated patients from birth to death whilst matching CRC incidence based on published literature. Direct non-health care costs relating to diagnosis and treatment were not included, and were clearly stated as excluded by authors.

**Statistical analysis of costs**

Costs were not treated in a stochastic manner.

**Indirect Costs**

Indirect costs were not included.

**Currency**

US dollars ($).
Sensitivity analysis
Selected variables were varied within 'plausible' ranges, using one-way sensitivity analysis, to assess the effect on cost-effectiveness. The ranges were stated.

Estimated benefits used in the economic analysis
The number of QALYs per person were, for men:

never screened = 18.933;
screened at age 60-64 = 18.978;
screened at age 55-59 = 18.991;
screened at age 50-54 = 18.999;
screened at age 45-49 = 19.000;

and, for women,:

never screened = 20.551;
screened at age 60-64 = 20.600;
screened at age 55-59 = 20.661;
screened at age 50-54 = 20.616;
screened at age 45-49 = 20.616.

QALYs were discounted at a rate of 3%.

Cost results
Estimated cost per person varied dependent on gender and age group.

Male:
age 45-49 total cost per person $731;
age 50-54 total cost per person $662;
age 55-59 total cost per person $654;
age 60-64 total cost per person $640; and
no screening total cost per person $749.

Female:
age 45-49 total cost per person $935;
age 50-54 total cost per person $625;
age 55-59 total cost per person $581;
age 60-64 total cost per person $574; and
no screening total cost per person $676.

All costs were discounted at 3%.

**Synthesis of costs and benefits**
Dominated strategies (cost more and less effective) were identified and excluded from further interpretation, as they would never be chosen. Those that were dominated were: no screening for both men and women, screening at age 60-64 for men and 45-49 for women. Additional cost per QALY (marginal cost-utility) was then calculated by comparing one clinical strategy to another. A summary of the results obtained follows. Further detailed results can be found in the paper.

For males compared to screening at 55-59, screening at 50-54 had an additional cost per QALY of $3,625. Likewise screening at 45-59 had an additional cost per QALY of $69,000 compared to screening at 50-54 years of age.

For females compared to screening at 60-64 years, screening between 55-59 had an additional cost per QALY of $636. Comparing to screening at 55-59, screening between 50-54 had an additional cost per QALY of $8,800.

**Authors' conclusions**
One-time colonoscopic screening in men aged under 60 and women aged under 65 dominates no screening and screening at older ages. One-time colonoscopic screening between 50-54 years of age is cost-effective when compared to a strategy of no screening or screening within older age groups. Dependent on societies willingness-to-pay screening in men age 45-49 may also be a cost-effective strategy when compared to screening between 50-54 years of age.

**CRD COMMENTARY - Selection of comparators**
The selection of age ranges was determined by preliminary analysis, but the choice of no screening was not explicitly justified. There was also no mention of standard practice and it is, therefore, unclear whether the no screening option is a viable choice of comparator.

**Validity of estimate of measure of effectiveness**
The authors undertook a review of the literature to determine effectiveness estimates, which were then used to inform the model. Although this seems appropriate, and the authors stated that it is reproducible, they did not state the methods used to conduct the review. In particular, we do not know how the estimates from several sources were combined or how the ranges for sensitivity analysis were determined. Some validation of the model was undertaken but its usefulness was not clear.

**Validity of estimate of measure of benefit**
The estimations of benefits were derived from the effectiveness analysis through the process of discrete-event modelling. Utility values were supposedly taken from societal preferences, although the precise methods and population were not stated.

**Validity of estimate of costs**
The original source of cost estimation was clearly stated although generally resource quantities and unit costs were not reported separately, thus reducing transparency and generalisability. The price year was given. As the study was conducted from the societal perspective it could have been expected that indirect costs were reported. However, this was not the case and it is not clear that they were accounted for in any way. Sensitivity analysis (apparently one-way) was quite extensively conducted, but the source of the ranges was not given and not all the results were reported.

**Other issues**
The paper was very detailed, extensively reporting its methods and effectiveness results. However, costs and sensitivity analysis results were reported selectively. The authors clearly stated the limitations of generalisability due to the base case assumptions; they also made reference to some validation of the model they had conducted. They attempted to validate the model's construct validity and criterion validity. Construct validity is ascertained by running the model, comparing the results derived with those obtained from the 'SEER database', and then adjusting the model to approximate the 'SEER database'. Criterion validity was assessed by modelling a population of 100,000 patients with demographic characteristics and initial endoscopic findings as reported in a comparator study. The model produced 3 cancers compared to the 5 reported by the comparator study. The confidence interval from the model was reported as 0 - 6. Although the authors have attempted to validate their model it is not clear exactly what the validation methods show. Their conclusions were in keeping with the study population.

**Implications of the study**
The findings from the study suggest that one-time colonoscopic screening between 50-54 years is cost-effective when compared to no screening or screening at older ages. Screening within other age cohorts may be cost-effective but is dependent upon society's willingness-to-pay. This appeared to be a generally well-conducted study, although somewhat lacking in transparency. No reference was made to current practice with regard to screening, hence it is not known if no screening is a valid comparator.

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