Is it cost effective to introduce screening programmes for colorectal cancer? Illustrating the principles of optimal resource allocation

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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 Hemoccult test-II for the detection of colorectal cancer was compared to the use of the Pap smear test for the detection of cervical cancer.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
Inhabitants of Denmark.

Setting
Hospital. The economic study was carried out in Denmark.

Dates to which data relate
The main effectiveness data relating to colorectal cancer screening were derived from a Danish randomised controlled trial (RCT) initiated in 1985, the results of which were published in four papers between 1987 and 1996, and Danish national registry data published in 1993. The main effectiveness data on cervical cancer screening were derived from the literature between 1985 and 1993. The dates of the resource utilisation data were not specified. The price year for the cervical cancer screening study was 1992, and for colorectal cancer screening was 1993.

Source of effectiveness data
The main sources of effectiveness data relating to colorectal cancer screening were a Danish RCT, Danish national registry data, expert opinion, and a mathematical model. The evidence for the final outcomes relating to cervical cancer screening were derived from the literature, expert opinion, and a mathematical model.

Link between effectiveness and cost data
Costing was performed on the same patient sample as that used in the effectiveness analysis although it was not clear whether it was performed prospectively or retrospectively.

Study sample
In the Danish RCT on colorectal cancer screening, there were 30,976 individuals in the screening group against 30,966 subjects in the control (no screening) group. The age range for the study sample was 45 to 74 years. The subjects in the
test group were offered Hemoccult-II test (H-II) every 2 years. The rate of refusal to participate for first-time participants was 32.7%, and 6.5% at subsequent rounds.

**Study design**
Randomised controlled trial. The duration of the study period was 10 years.

**Analysis of effectiveness**
The principle (intention to treat or treatment completers only) of analysis of the effectiveness results was not specified. The main health outcome was the mortality rate for colorectal cancer, over a period of 10 years. Other health outcomes reported were the survival rate amongst patients whose cancers were detected, the rate of adenomas detected due to screening which would have otherwise gone undetected, and the percentage of large adenomas (greater or equal to 1 cm in diameter).

**Effectiveness results**
It was reported that the mortality rate for colorectal cancer, over a period of 10 years "was significantly reduced in the screening group (mortality ratio 0.82 (0.68-0.99))". The survival rate amongst the patients whose cancers were detected was 84.3% in the screening group versus 48.5% in the control group. The rate of adenomas detected due to screening which would have otherwise gone undetected was 60%, and the percentage of large adenomas in the study was 70%.

**Clinical conclusions**
"There was no statistical (significant difference) between the number of cancers occurring in the test group relative to the control group. Hence the improved survival is attributable to the early detection of cancers and not to the avoidance of cancers due to adenoma follow-up (although such an effect is likely to surface in the future)".

**Modelling**
A mathematical model was used to estimate the sensitivity of the tests and the average sojourn time, which in turn were used as inputs into a simulation process to calculate the cancer prevalence per screening round.

**Outcomes assessed in the review**
The outcomes relating to colorectal cancer screening were the cumulative risk of diagnosis of cancer at a large adenoma site and the relative risk of colorectal carcinoma due to detection and follow-up of adenomas. The outcomes relating to cervical cancer screening were screen-detected cases of dysplasia and cases of carcinoma in situ which would have regressed spontaneously, the false-positive rate, and the percentage of patients who would have survived in the case of no screening.

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

**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**
Number of primary studies included
Two primary studies provided data on colorectal cancer screening. Five published reports provided data on cervical cancer screening.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not stated.

Results of the review
The cumulative risk of diagnosis of cancer at a large adenoma site for 5, 10, and 20 year-follow-up was 2.5, 8 and 24%, respectively. The relative risk of colorectal carcinoma due to detection and follow-up of adenomas was 0.57. Screen-detected cases of dysplasia and cases of carcinoma in situ which would have regressed spontaneously were 80% and 60%, respectively. The false-positive rate was 0.62 and the percentage of patients who would have survived in the case of no screening was 57.8%.

Methods used to derive estimates of effectiveness
Assumptions were also derived based on the experience of a Danish project on colorectal cancer screening. Assumptions were also made on parameters relating to cervical cancer screening.

Estimates of effectiveness and key assumptions
The rate of false positive H-II tests was assumed to be 1%. The survival rate due to the early detection by the H-II test was assumed to be 30%. The key assumptions made relating to colorectal cancer screening were as follows: it was assumed that the age-dependent adenoma incidence was constant across screening intervals of 1, 2 and 3 years and that only the large adenomas were at risk of developing into cancers.

Assumptions made about cervical cancer screening were as follows: the participation rate was assumed to be 80% (70%-90%); screen-detected cases of dysplasia, carcinoma in situ or micro-invasive carcinoma were assumed to survive up to 99%; the rate of survival for screen-detected cases of unsymptomatic carcinoma was assumed to be 82%; and the sensitivity of the test was deemed to be independent of age as well as disease stage.

Measure of benefits used in the economic analysis
The main benefit measure was life-years gained. Other intermediate outcomes estimated by the models employed were the sensitivity of the tests and average sojourn time.

Direct costs
Costs were discounted. Quantities in the study on colorectal cancer screening were reported separately from the costs, but not in the cervical cancer screening study. The costs included were the direct costs of the screening programme, such as costs of screening tests, diagnostic tests, mailing costs, test analysis, offices, inventory, manpower and net treatment costs. Costs were estimated from costs incurred by programmes running in the Funen county in Denmark and these were varied according to different screening intervals and/or different target groups. The cost analysis was performed from the perspective of the Danish health care system. 1992 price data was used for the costs incurred in the cervical cancer programme, and 1993 costs were used for the colorectal cancer screening. Future diagnosis and treatment costs saved due to the screening were included in the cost analysis.
Indirect Costs
Not stated.

Currency
Danish Kroner (DKr). A conversion was not performed.

Sensitivity analysis
A set of one-way sensitivity analyses was undertaken on the following variables; the discount rate for effects was varied to 0%, an increase in the cost of smear tests, parameter values including the cost of the Hemoccult-II test, colonoscopy (assuming no cancers were avoided by polypectomy) and a reduction in the survival rate amongst screen detected colorectal cancers, and finally the inclusion of future health care costs due to added life years.

Estimated benefits used in the economic analysis
Life-years gained were estimated for 60 hypothetical colorectal cancer screening programmes, and were plotted in the form of a possibility frontier curve. The life-years gained for the six efficient programmes had a range from 974 years for the target population of 65-74 year olds (with a screening interval of every two years) to 3,081 years for 50-74 year olds, every year. The estimated rate of sensitivity of the H-II test was 62.1%. The average sojourn time was estimated to be 2.1 years. The rate of sensitivity of Pap-smear, and the average sojourn time for the cervical cancer screening were not reported. Life-years gained for the cervical cancer screening ranged from 2,910 years for the screening programme of "every five years for 30-59 years old" to 4769 years for "every 3 years 20-69 years old". The discount rate used was 5%. The duration of the benefit was assumed to be 36 years.

Cost results
The total costs for the two different screening types varied according to the groups targeted and screening intervals adopted. For the cervical cancer screening programme the total cost varied from DKr61 million to DKr182.5 million. For the colorectal cancer screening programme the total cost varied from DKr16.5 million to DKr80 million. A discount rate of 5% per year was used for both screening types. The duration of the costs was assumed to be 36 years.

Synthesis of costs and benefits
The average and marginal cost per life-year gained were calculated. For the cervical cancer screening programme the average cost per life-year ranged from DKr20,940 (screening programme every five years for those aged 30-59) to DKr38,240 (every 3 years for those aged 20-69 years). The corresponding values for the marginal cost per life-year was from DKr20,940 to DKr113,510. For the colorectal cancer screening programme the average cost per life-year varied from DKr17,000 (every two years for 65-74 year olds) to DKr26,000 (every year for 50-74 year olds). The corresponding values for the marginal cost per life-year were from DKr17,000 to DKr42,500. A comparative analysis between the colorectal and the cervical cancer screening programmes was performed according to the different assumed values for the budget constraint. Summary findings were that "colorectal cancer screening (60-74 year olds every 2 years) should be introduced before implementing any of the cervical cancer screening programmes included in the analysis. Moreover it is optimal" to target 55-74 year olds every year for the colorectal cancer screening programme (with a marginal cost per life-year gained of DKr35,471) before implementing a cervical cancer screening programme with screening intervals of less than five years (the marginal cost per life-year gained of introducing a cervical cancer screening programme of less than 5 years is DKr38,080). Added to this, it was suggested that the colorectal cancer screening programme should be extended to the "50-54 year-olds every 4 years before the cervical cancer screening programme is extended beyond the 25-59 year-olds every 4 years".

Authors' conclusions
The paper concluded that "colorectal cancer is a cost-effective option relative to cervical cancer screening when health is seen as the only outcome of the screening programs. However, further insights into consumer preferences and
inclusion of intangible costs and benefits is necessary in order to guarantee optimal resource allocation”.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator is clear.

**Validity of estimate of measure of benefit**
The benefit results from colorectal cancer screening are likely to be internally valid since their estimation was mostly based on the results of a large Danish RCT. However, in the case of benefit results relating to cervical cancer screening, the internal validity is likely to be weakened by the lack of randomisation.

**Validity of estimate of costs**
Resource quantities were not fully reported separately from prices. Adequate details of the methods of cost estimation were not given.

**Other issues**
As acknowledged by the author, some intangible costs and benefits of the screening programmes were not incorporated in the study. The issue of generalisability to other settings or countries was not addressed.

**Source of funding**
None stated.

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