Health technology
Using unhydrated Hemoccult (H-II) test for the colorectal cancer (CRC) screening of individuals between 45 and 75 years old every 2 years during a 10-year follow-up period.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
Individuals between 45 and 75 years old.

Setting
Community and hospital. The economic study was carried out in Denmark.

Dates to which data relate
The main effectiveness data were collected between August 1985, and August 1995. The data on the incidence of colorectal cancer by sex and gender were obtained from the Danish national registry, data from the period 1983-87 and published in a study in 1993. The date of the resource use data was not explicitly reported. The fiscal year was 1993.

Source of effectiveness data
A published study and Danish national registry data provided effectiveness data.

Link between effectiveness and cost data
It is not entirely clear whether the costing was performed on the same patient sample as that used in the effectiveness analysis. The authors mentioned that the calculation of fixed costs per year was based on the average yearly costs incurred over the initial 8 years of the trial. It is not clear whether the costing was performed prospectively or retrospectively.

Study sample
Power calculations were used to determine the sample size (a total of 30,000 subjects in each study group was needed to satisfy a power of 0.70 with a significance level of 0.05 to be able to detect a 25% reduction in CRC mortality). All 140,000 inhabitants of Funen, Denmark, in August 1985, aged 45-75, were regarded as eligible for inclusion in the study. A total of 2,515 inhabitants were excluded, and the remaining 137,485 were randomly allocated to the screening group (30,967 subjects), control group (30,966 subjects), or were not enrolled (75,552). The study had a participation
rate of 67.3% for first-time participants and 93.5% at subsequent screening rounds.

**Study design**
The study was a randomised controlled trial, carried out in a Danish county. The duration of the follow-up was 10 years. A total of 1,149 subjects from the 49,402 people alive at the end of the follow-up moved away from the study county. The randomisation was performed in blocks of 14; three were assigned to screening, three to the no-screening group, and eight not enrolled.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness was intention to treat. The health outcome measures used were cases of diagnosed CRC, and the number of deaths attributable to CRC. The groups were comparable in age, sex, and mortality from causes other than CRC.

**Effectiveness results**
At the end of 10-year follow-up, the screening group had 481 cases of detected CRC versus 483 in the control group (not significant). The screening group experienced 205 cases of death attributable to CRC including death caused by complications of CRC treatment as opposed to 249 deaths in the control group. The mortality ratio was 0.82 (95% CI: 0.68 - 0.99), p=0.03.

**Clinical conclusions**
The study findings indicate that biennial screening by faecal occult blood tests can reduce mortality. This study was to be continued to improve its statistical power and to assess the effect on CRC incidence of removing more precursor adenomas in the screening-group participants than in controls.

**Modelling**
A mathematical model (details of which were not provided in the paper) was used to estimate the sensitivity of the test and the average time period during which the asymptomatic cancer was detectable by the test (the average sojourn time). The sensitivity and average sojourn time plus age- and gender-specific incidence rates were used as inputs to the model to estimate the prevalence of colorectal cancer per screening round, which in turn were employed, together with excess survival rate and age-specific life expectancy, to calculate life years gained and costs associated with each screening programme.

**Methods used to derive estimates of effectiveness**
Assumptions about effectiveness were also made by the authors.

**Estimates of effectiveness and key assumptions**
The following assumptions were made:

(1) early detection due to screening alone was the cause of survival improvement;

(2) sensitivity was independent of disease stage;

(3) excess survival rate was estimated to be 30% (despite it being 35.8% in the clinical trial) and to be constant and independent of screening interval;

(4) only the large adenomas (1cm or more in diameter) were at risk of developing into cancers (70% in the clinical trial).
Measure of benefits used in the economic analysis
Life-years gained was the benefit measure adopted in the study. To calculate the life-years gained, the sensitivity of the test and the average sojourn time were estimated as intermediate measures.

Direct costs
Costs were discounted. Quantities were reported separately from the costs. The cost items were reported separately. The cost analysis covered the running and set up costs of the screening programmes considered in the study. The cost calculations were performed from the perspective of the national health care sector, while in the sensitivity analysis it was extended to cover the perspective of society. The sources of resource use and cost data were not clearly specified. 1993 price data were used. The cost of CRC treatment was excluded.

Indirect Costs
Not considered.

Currency
Danish kroner (DKK). The exchange rate was DKK1 = US$0.15.

Sensitivity analysis
One-way and multi-way sensitivity analyses were performed on cost of H-II test, cost of colonoscopy, effect of adenoma follow-up, excess survival rate, discounting rate, and the scope of the analysis (considering the social perspective) to assess the robustness of the results.

Estimated benefits used in the economic analysis
The sensitivity of the test was estimated to be 62.1% and the average sojourn time was 2.1 years. The life-years gained resulting from 6 efficient screening programmes ranged from 974 years, for a programme in which screening is performed every 2 years for the age group 65-74 years old, to 3,081 years for a programme with a screening interval of one year and a target group aged 50 to 74. Life-years gained were discounted at a rate of 5%. The duration of the screening programmes was assumed to be 36 years.

Cost results
The discount rate was 5%. The total costs associated with 6 efficient screening programmes ranged from DKK16,558,000 for a programme in which screening is performed every 2 years for the 65-74 age group to DKK80,106,000 for a programme with screening interval of one year and target group aged 50-74 years old. The duration of the screening programmes was assumed to be 36 years (a permanent programme).

Synthesis of costs and benefits
The costs and benefits were combined by computing incremental cost per life-year gained. The incremental cost per life-year gained for 6 efficient screening programmes ranged from DKK17,000 for a programme in which screening is performed every 2 years for the 65-74 age group to DKK42,500 for a programme with a screening interval of one year and a target group aged 50-74. The study established the robustness of the cost-effectiveness results except to discounting rate and the inclusion of future unrelated health care costs.

Authors' conclusions
The analysis identified a range of efficient programmes with incremental cost-effectiveness ratios lying in the range DKR17,000-42,500. All efficient screening programmes are cost-effective health care interventions.
CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear.

Validity of estimate of measure of effectiveness
The estimates of effectiveness are likely to be internally valid given the sample size, duration of follow up, and the study design (a randomised controlled trial).

Validity of estimate of costs
The sources of cost and resource utilisation data were not clearly specified. Sensitivity analysis was used to explore the uncertainty of the data.

Other issues
The issue of generalisability to other settings was addressed and appropriate comparisons with other studies were made by the authors.

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None stated.

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Other publications of related interest

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