questions regarding screening for breast cancer [14]. The most important is to determine whether breast cancer screening in women aged under 50 reduces breast cancer mortality and, if so, by how much. There is also the need for more information to determine the extent to which older woman (aged 70 and older) are likely to benefit from screening programmes. The issue of the most appropriate screening interval is still live and there is a need to obtain quantitative estimates of the net gain in terms of deaths avoided in relation to the extra costs arising from more frequent mammographic examinations.

On the basis of current evidence, breast self-examination programmes are not an effective method of population screening and cannot be recommended as public health policy [14]. The majority of breast cancers are still found initially by the women themselves and, consequently, women should be advised to continue regular examination of their breasts. Every step taken to reduce the mortality from breast cancer is an important one.

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0959-8049(94)E0137-S

Colorectal Cancer Screening: Methods, Benefits and Costs

O. Kronborg and J. Wahrendorf

INTRODUCTION

FIVE YEARS after the diagnosis of a colorectal cancer, no more than one-third of patients are alive. The results of treatment are unsatisfactory, and prevention of the disease in the general population is difficult at present. Therefore, screening, which results in detection and removal of early cancers and precursors, will hopefully contribute to a reduction in this disease [1].

Colorectal cancer is one of the most frequent cancers in Europe, with about 130 000 new cases and 90 000 deaths every year in the EC countries. As for most cancers, incidence and mortality increase with age, with a steep rise at 50 years of age.

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METHODS FOR SCREENING

Digital rectal exploration

This results in detection of only 10% of colorectal cancers, and is an unpleasant experience; both of these factors make it unsuitable as a screening method.

Rigid sigmoidoscopy

This may result in detection of 25% of these cancers but is also unpleasant and carries a small risk of intestinal perforation, making it a poor method for screening although there is some evidence that sigmoidoscopic surveillance can reduce mortality from rectal cancer. Flexible sigmoidoscopy (60 cm) is more attractive than the rigid type because more than half of these cancers are located within reach of this instrument. Even though it is less unpleasant than rigid sigmoidoscopy, however, preliminary figures have shown low acceptability, and the economic costs are substantial.

Full colonoscopy

This is the most sensitive and specific for neoplasia but fulfils no other criterion as a screening method.

Double-contrast barium enemas

These have less diagnostic accuracy than colonoscopy and all the drawbacks of the latter.

Tumour markers

Tumour markers like carcinoembryonic antigen and Ca19-9 are too insensitive, and their specificity is too low for screening purposes. Other antigens and enzymes have been studied, but none have been found to be suitable.

Guaiac tests

These tests for faecal occult blood fulfil many of the criteria for screening tests, being easy to perform and inexpensive. Although the specificity is satisfactory for screening purposes when no rehydration is used, even the widely used Hemoccult-II cannot detect more than 50–70% of colorectal cancers, depending on how often it is used. Several factors are responsible for the relatively low sensitivity of these tests for detecting cancer. Bleeding varies, and the blood may not be equally distributed in faeces; furthermore, the test is not specific for human haemoglobin.

Immunochemical tests

Tests have been developed which are specific for human haemoglobin and may be more sensitive, but processing is complex and much more expensive. The same is true for the Haemoquant test, based on fluorescence of haem-derived porphyrins; furthermore, this test has lower sensitivity for cancer than Hemoccult-II.

EVALUATION OF SCREENING

Many data indicate that colorectal cancer cases detected by screening are generally found at an earlier stage of the disease and that patients in whom cancer is detected at these stages have a favourable prognosis. In order to demonstrate that offering colorectal cancer screening by occult blood tests to the general population does represent a benefit, it must be demonstrated that both an artificial decrease in the time to diagnosis and a measurable gain in age-specific mortality are achieved. Therefore, the ultimate end-point to be evaluated in colorectal cancer screening programmes is a difference in mortality from this cancer between the two study arms of a prospective randomised trial or between deaths from colorectal cancer and appropriate controls in a case–control evaluation.

During the 1980s, four randomised population trials with Hemoccult-II were initiated in Europe, following two major studies of selected groups in the U.S.A. The four studies are presented in Table 1. The rate of positive tests was highest in Gothenburg (Sweden), because rehydration was used in that study and not in the others. Rehydration resulted in a considerable decrease in specificity, and thereby an increase in the number of further colorectal examinations made in persons without neoplasia. Flexible sigmoidoscopy and double-contrast barium enemas were used for further examination in this study, whereas colonoscopy was used in the other three studies. Recently, the number of subjects was doubled.

Larger studies from Nottingham (U.K.) and Funen (Denmark), with screening intervals of 2 years, were based on random sampling of individuals, whereas the study in Burgundy (France) was based on towns and administrative districts. Acceptability was highest in the Scandinavian studies (Table 1).

The lowest positivity rate was seen in the Danish study, which may be due to the dietary restrictions used and the exclusion of all subjects with known colorectal neoplasia before randomisation.

More early cancers and precursors (adenomas) were found in the test groups in all four studies compared to controls (Table 2); however, no significant reduction in the number of more advanced cancers has yet been seen, and the number of interval cancers is high. Final mortality figures cannot be expected from any of the trials before 1996. The designs of the Danish and U.K. trials are very similar and will allow a meta-analysis to be conducted.

The faecal occult blood test has been offered for screening purposes to the general population of Germany since 1977 in the framework of the statutory health insurance system. Attendance rates are approximately 14% for eligible men, aged 45 years and above, and 25% for women. Thus, 1.2 million men and 3.1 million women are screened each year. In 1986, participation was 11% of the men and 40% of the women in the age group 50–54 years, 16 and 23% in the age group 60–64 years and 14 and 13% of people over 65 years of age. Approximately 1% are found to have faecal occult blood.

Although the overall annual attendance rates may appear low, the cumulative proportion of people in each age range who have ever participated is considerably higher, estimated to be in the order of 50%. This high prevalence of 'exposure' to the faecal occult blood test in the general population indicated that a case–control approach might be used to assess the efficacy of this screening programme. This evaluation would address the question of whether individuals who die of colorectal cancer have a less dense average screening history than appropriate healthy controls. The study which is under way in Germany [2] requires access to the death certificates of people who have died of colorectal cancer in the given population, to appropriate controls and to the complete screening histories of cases and controls.

Table 1. *Randomised trials with Hemoccult-*II *in four European cities*

City	Age group (years)	Test group	Control group	Performed Haemoccult-II		Positive rate (%)	
				1st screen	2nd screen	1st screen	2nd screen
Gothenburg	60–64	13759	13744	9040	7770	3.8	6.4
Nottingham	50–74	78000	78000	27651	7344	2.3	1.7
Funen	45–74	30970	30968	20672	18779	1.0	0.8
Burgundy	45–74	47000	47000	24562		2.1	NA

Table 2. Cancers detected by screening and among controls in four European cities

City	Cancers detected per 1000 screened		Cancers detected by screening (%)	Cancers among controls (%)
	1st screen	2nd screen	Dukes' A	Dukes' A
Gothenburg	1.9	2.4	34	15
Nottingham	2.3	1.5	51	12
Funen	1.8	0.7	51	9
Burgundy	1.6		52	

COST-BENEFIT ANALYSIS

A cost–benefit analysis cannot be made with any certainty before the final data on mortality are available. The Danish experience with the randomised trial, which began in 1985, suggests that the total cost for screening the Danish population aged 45–74 years (total population, 5 million) every 2 years using Hemoccult-II will be about 800 000 U.S. dollars per year.

Other costs must also be considered, however. A small risk exists of diagnostic and therapeutic colonic perforation, which may be lethal in a very small number of cases. False negative results may result in interval cases, or people may be treated unnecessarily for cancer that would not have been lethal. These drawbacks indicate that a reduction in mortality from the disease must be demonstrated before population screening with Hemoccult-II can be introduced. If no reduction is demonstrated, more complex strategies like flexible sigmoidoscopy with Hemoccult-II may be considered; furthermore, better markers for colorectal cancer must be found both in faeces and in urine and blood. On the basis of the indirect data on colorectal cancer screening so far available, a mathematical model has been used to identify optimal screening strategies in a cost–benefit analysis [3].

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0959-8049(94)E0139-U

Economics of Cancer Screening: Total Costs and Benefits in Economic Terms

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INTRODUCTION

THE MAIN objective of an economic appraisal of a screening programme is to assist the relevant decision makers in making the best use of the resources available in the health care sector, e.g. screening programmes versus new treatments or, more narrowly, choice of a specific screening programme.

Economics is the study of how to allocate scarce resources to competing ends. Economic appraisals — cost–benefit analysis on the one hand and cost-effectiveness or cost–utility analysis on the other — are useful, relevant tools, as they bring together the two sets of information necessary to evaluate any health-care programme: net consumption of resources and relevant clinical and epidemiological evidence about health-related effects.

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An economic appraisal is often added to clinical trials as a last thought, in an attempt to convince decision makers that a screening programme is worthwhile. It should, however, be an integral part of the trials, as it combines results on clinical effectiveness with the resource dimension. It also provides a clear picture of the practical details necessary for the organisation of a 'real life' screening programme, i.e. not only screening frequency and target group but also, for instance, whether a mobile screening unit is to be used in a screening programme for breast cancer and how the screening unit is to be staffed. Such detail is necessary to provide an idea of the expected resource consumption in an actual programme, rather than the often idealised circumstances under which a clinical trial is carried out.

An increasing number of economic appraisals are published and (to a much lesser degree) used when advocating a particular (screening) programme or (even more rarely) for actual decision