
Executive summary

Conclusion

The Committee has concluded that there is sufficient evidence to justify starting a national bowel cancer screening programme. The most appropriate screening method is an immunochemical Faecal Occult Blood Test (iFOBT). The Committee recommends a programme based on the screening of people between fifty-five and seventy-five years old once every two years. People in the target group would be sent a faecal test sampling kit by the screening organisation. The faecal sample would have to be sent to a laboratory to be tested for invisible traces of blood. Persons with a 'positive' (i.e. abnormal) test result would be referred for colonoscopy, which would take place in an outpatient clinic under sedation and with the aid of pain management.

Recent trials in the Dutch cities of Nijmegen, Amsterdam and Rotterdam suggest that a 60 per cent participation rate may be expected. Under this assumption, modelling indicates that screening will in due course help to prevent an average of 1,428 bowel cancer deaths a year. In 2008, 4,843 people died from the disease in the Netherlands.

Bowel cancer is a serious health problem

Bowel cancer (colorectal cancer) is a common disease. In 2006, 11,231 cases were diagnosed in the Netherlands. In the general population, the lifetime risk of

bowel cancer is 4 to 5 per cent. The average five-year survival is 59 per cent, but an individual's chances of survival depend largely on how extensive the disease is when diagnosed. If the cancer is confined to the inner lining of the bowel (stage I), the five-year survival is 94 per cent; for patients with metastatic bowel cancer (stage IV), the five-year survival is limited to 8 per cent.

Bowel cancer is preceded by a prolonged adenomal state, which is relatively easy to detect and treat. Furthermore, a person who has bowel cancer is unlikely to notice any health problems for several years. These two facts mean that bowel cancer is an ideal 'candidate' for screening. From FOBT-based efficacy trials it has been known for some time that screening can reduce bowel cancer mortality by enabling early detection or prevention through the removal of adenomas. However, the implementation of a screening programme would be responsible only if other internationally recognised criteria are met, such as the availability of adequate manpower for diagnosis and treatment.

Research into possible screening methods

In trials held over the last few years, tens of thousands of Dutch people aged between fifty and seventy-five have been offered bowel cancer screening. Various recruitment strategies and screening methods have been used in these pilot trials, whose aim was to establish whether a national and organized population-based screening programme like those in England, Scotland and Finland would be desirable and feasible in the Netherlands.

In contrast to the situation with most other screenable diseases, there are several screening tests available for bowel cancer. The methods differ in various ways, including the participation rate and the sensitivity (in connection with which some tests need to be repeated annually, while others are needed only once every ten years). The four efficacy trials that have been conducted in other countries were all based on the guaiac (gFOBT) Haemoccult II test, which has been used with limited success for more than forty years. The test involves taking 2 samples from each of 3 consecutive stools. If blood is present, a dye (guaiac) reacts with the haem moiety in haemoglobin (the substance that gives red blood cells their colour), resulting in blue discoloration, which has to be visually assessed.

More recently, a test method has been developed, which involves the immunological analysis of faecal samples for occult blood (iFOBTs). The method has two advantages: the subject only has to provide a single faecal sample, and analysis can be automated, thus increasing quality control and reducing cost.

Another possible screening method is sigmoidoscopy: visual examination using an endoscope inserted through the anus into the distal (left-hand) portion of the large intestine. An enema is required prior to the examination.

A fourth option is colonography ('virtual colonoscopy'). This involves examination of the entire large intestine by means of CT or MRI scanning, preferably after limited bowel preparation (low-fibre diet, oral contrast agent). To achieve colonic distension carbon dioxide (CO₂) is delivered via a rectal catheter. Examinations are performed in both supine and prone position.

With all four methods described above, if any abnormalities are detected, the patient is referred for colonoscopy i.e. visual examination of the entire large intestine (Figure 1). Colonoscopy is a reliable way of detecting most abnormalities. Some screening programmes use colonoscopy as a screening method in its own right.

Finally, screening for molecular biomarkers is under development. Numerous biomarkers might theoretically be used for screening, but it is expected to be another five years before suitable ones can be identified. Even then, it will be necessary to conduct research in unselected populations to establish whether biomarker-based screening offers any advantages over the existing methods.

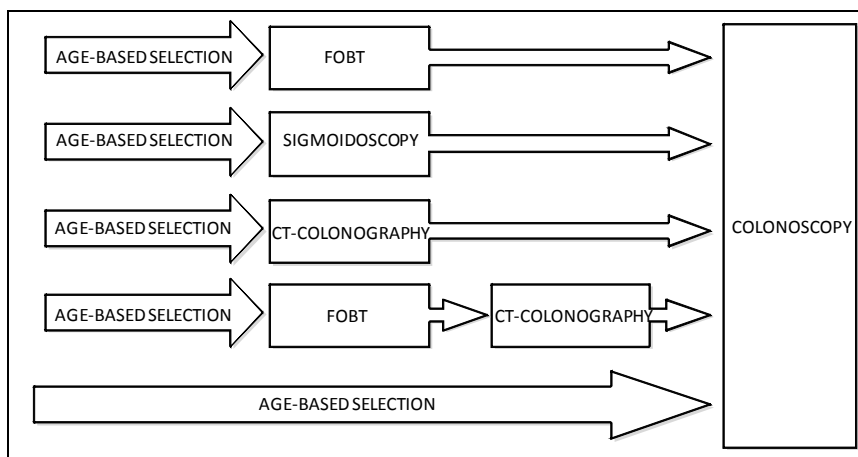


Figure 1 Colonoscopy is the final common pathway of all CRC screening.

Careful assessment is required before introduction of a national screening programme

Assessment of the possible screening methods against the criteria for responsible screening – serious health problem, proven value, suitable screening test, acceptance, cost-effectiveness – reveals the following picture.

As indicated above, it is evident that bowel cancer is a serious health problem. However, it is less obvious which screening method best satisfies the other criteria. It has been demonstrated that gFOBT screening can reduce bowel cancer mortality by 15 per cent. On the other hand, the method is not a very sensitive means of detecting bowel cancer (less than 40 per cent of cases are picked up at first screening). Furthermore, the participation rate is low (47 per cent in the trials).

iFOBT screening is based on the same principle as gFOBT screening: the detection of blood in faecal samples. However, the randomized trials in Amsterdam, Nijmegen and Rotterdam demonstrated convincingly that iFOBT screening yielded better participation and detection rates than gFOBT screening. Furthermore, despite what is often assumed, the cost of iFOBT screening did not prove to be higher. In other words, iFOBT screening is significantly more effective and efficient as a means of reducing both the incidence of bowel cancer and the associated mortality.

The participation rate was significantly higher with iFOBT screening (60 to 62 per cent) than with gFOBT screening (47 to 50 per cent). Moreover, on an intention-to-screen basis (i.e. relative to the number of invitations sent), the number of cases of bowel cancer and advanced adenoma detected was 2.5 times as great. The higher participation and positivity rates do mean that colonoscopy is needed more often (35 cases per thousand invitations). Nevertheless, iFOBT screening is substantially more cost-effective than gFOBT screening.

Compared with a single iFOBT screening, sigmoidoscopy is roughly equally sensitive for bowel cancer, but significantly more sensitive for advanced adenomas. Some studies suggest that re-screening with this method at intervals of five years would be sufficient. However, the level of participation in the Rotterdam trial was low: only 32 per cent. No data are currently available regarding the effectiveness of sigmoidoscopy screening as a means of reducing bowel cancer mortality. It is therefore difficult to draw conclusions regarding its cost-effectiveness. Furthermore, even allowing for a low participation rate, sigmoidoscopy screening requires a great deal of endoscopy capacity (327 sigmoidoscopic

examinations plus twenty-seven coloscopic examinations per thousand invitations). The results of sigmoidoscopy trials in England and Italy are expected in 2010. If they are encouraging, they should be taken into account in modelling of the Dutch situation.

CT colonography is almost identical to colonoscopy in terms of its sensitivity for bowel cancer and polyps measuring ten millimetres or more. However, it is less unpleasant for the subject and less likely to have serious complications. Furthermore, re-screening might not be required for five or ten years. On the other hand, the participation rate associated with colonography is not known, there is no evidence that CT colonography reduces bowel cancer mortality, and it involves exposure to radiation. Colonoscopy is likely to be needed in more than twenty cases per thousand invitations (assuming a 35 per cent participation rate and a referral threshold of ten millimetres).

Colonoscopy is the most sensitive means of detecting bowel cancer (more than 97 per cent) and advanced adenomas (90 to 98 per cent). This form of testing is therefore regarded as the reference standard. Evidence for the timing of colonoscopy screening is limited, suggesting that screening would be needed only once every ten years. No data are available regarding the participation rates and detection rates associated with colonoscopy in the Netherlands. Limited evidence exists on the efficacy of colonoscopy screening on colorectal cancer incidence and mortality. Consequently, it is not possible to calculate its cost-effectiveness. In one of the Dutch pilots, the COCOS trial, the anticipated participation rate is 20 to 25 per cent. Several other factors argue against using colonoscopy as a primary screening method: it is unpleasant for the subjects, there is a risk (albeit a small one) of serious complications and considerable colonoscopy capacity would be required (even assuming a participation rate of 25 per cent, 250 examinations per thousand invitations).

iFOBT screening meets the criteria for responsible screening

A single round of iFOBT testing will pick up 65 per cent of all bowel cancer cases – about the same as five or six rounds of gFOBT testing. The (programme) sensitivity is further boosted by the fact that iFOBT screening is repeated every two years. Assuming that the participation rate associated with iFOBT screening is 60 per cent, while the rate associated with sigmoidoscopy screening is 30 per cent, the effect of iFOBT screening will be one and a half times as great. Screening based only on sigmoidoscopy is not therefore desirable in the Netherlands. In

terms of simplicity, acceptance, performance and safety, iFOBT testing is the best screening method for use in the Netherlands.

Bowel cancer screening is desirable and possible, provided that the required capacity (e.g. colonoscopy) can be realised in the years ahead

The Committee recommends iFOBT-based screening (OC-Sensor, one faecal sample) once every two years for men and women between fifty-five and seventy-five years old. Modelling indicates that a programme designed on that basis would be cost-effective. Assuming a participation rate of 60 per cent, it would be possible to prevent 1,428 bowel cancer deaths each year. This works out at 2,200 euros per life year gained. This is more advantageous than in other cancer screening programmes in the Netherlands – the cost per life year gained being 11,300 euros for cervical cancer screening. For every bowel cancer death prevented, 785 people would need to complete iFOBT tests and 40 would need to undergo follow-up colonoscopy.

If the Committee's recommended screening strategy and the proposed introduction scheme were adopted, the colonoscopic capacity required for full introduction would be no more than 78,000, not 129,000 as previously calculated. The capacity needs can be further limited by updating the surveillance guidelines soon, partly in line with the availability of a screening programme, which will result in the detection of numerous small adenomas.

Alignment of screening with curative care is vital for quality

Experience has shown that the benefits of screening-related early detection are not fully utilised, because referral does not always lead to (prompt) diagnosis and treatment. Furthermore, there are major variations in the quality of colonoscopy among endoscopists. The Committee therefore recommends direct referral by the screening organisation to colonoscopy providers, with GPs playing a supporting role and always being informed. Appropriate arrangements should be made with the health insurers. Such a system would allow for preferential referral to the centres whose colonoscopy services meet the highest quality standards, and which maintain dedicated teams of certified endoscopists and other specialists.

Staged introduction

The implementation of a national screening programme is a major undertaking. The target population would amount to 3.5 million people, who would need to be

invited for screening every two years. Phased introduction is essential; it is expected to take five years to build up the necessary endoscopic capacity. The Committee makes the following recommendations:

- A bowel cancer screening programme should be introduced in phases, with a gradually expanding invitation scheme, as described in subsection 14.8.
 - An organisational structure as described in subsection 14.2 should be adopted, with a view to assuring quality and – if the iFOBT test method is used – sustainability.
 - If it is decided that a screening programme is to be set up, clear arrangements should be made with the relevant professions and care providers regarding:
 - the development of integrated (multidisciplinary) guidelines covering the entire chain from screening to diagnosis, treatment, follow up and surveillance, together with updating the guidelines on surveillance;
 - ways of assuring the quality of colonoscopy, including direct referral by the screening organisation and the creation of a system for on-site audits by a national reference centre; in this context it would seem appropriate for the Centre for Population Screening, as the national supervisory body, to play a supporting role;
 - the provision of data for quality control and evaluation of the screening programme, together with regular reporting;
 - public accountability for work-up, treatment and surveillance within the *Visible Care* programme.
 - From the outset, budgetary provision should be made for monitoring and evaluation, for a reference system and for the promotion of knowledge and innovation-oriented scientific research (necessary to keep the screening programme up to date).
 - The introduction of service screening for bowel cancer should be accompanied by a national public information campaign.
 - To enable people to make informed choices, a system of basic information and supplementary information should be developed, similar to those established in connection with screening for breast cancer and cervical cancer. In this context, particular attention should be given to the national uniformity of information provision in the various phases of the screening process.
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