Sigmoidoscopy and faecal occult blood test – a comparative screening trial

Colorectal cancer is a major health issue, both globally and in Norway. Bowel cancer screening is perhaps the most effective method to mitigate the consequences of the disease for patients and society. Large-scale randomised trials show that screening with sigmoidoscopy and faecal occult blood tests reduce colon cancer mortality. A systematic programme of continuous assessment of the benefits and possible harms of alternative screening methods will ensure the best possible effect. In accordance with recommendations from the Norwegian National Council for Priority Setting in Health Care, a pilot for a national screening programme was launched in 2012. The project is designed as a randomised comparative effectiveness study. The two screening methods, sigmoidoscopy and faecal occult blood tests, were compared 1:1 in a group of 140 000 people. Until now, more than 100 000 have been invited. Preliminary experiences from the pilot project for colorectal cancer screening demonstrate the potential to design and implement a regional screening programme without imposing an undue burden on clinical capacity. A regional centre for endoscopy training has been established, and it is expected that the added burden of subsequent surveillance endoscopies can be offset by the increased number of endoscopists resulting from the focus on screening and training.

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Colorectal cancer (CRC) or bowel cancer is one of the most common cancers for both sexes. The incidence in Norway has nearly tripled since the 1950s (1). The cumulative risk of developing CRC is respectively 5.9 % in women and 7.7 % in men (2). Clinically detected CRC is often advanced and has a poor prognosis. The five-year relative survival rate is about 65 % (2). Consequently, it is important to find solutions to improve outcome and possibly reduce the incidence of CRC. In Norway, three comparative studies on bowel cancer screening have been initiated. The most recent in 2012 is a pilot for a national screening programme. The Norwegian National Council for Priority Setting in Health Care has recommended establishing a national screening programme – much of it based on knowledge gained from these studies.

Rationale

CRC screening has been implemented in several countries (3). Randomised controlled trials have shown that screening using faecal occult blood test (FOBT) or sigmoidoscopy reduces colorectal cancer mortality (4). Sigmoidoscopy may also reduce CRC incidence (4). In recent years, FOBT has been replaced by more specific and sensitive immunochemical tests, immunochemical (i) FOBT (5). Sigmoidoscopy and FOBT have not previously been compared head to head in a screening setting (4). Thus, we do not know which of these methods is the most cost-effective. Although the premises for screening is that the benefits should outweigh any possible harms, this has not been sufficiently investigated (6). It is possible to obtain the required knowledge through the introduction of screening programmes implemented as a series of comparative effectiveness studies.

Hypothesis

It is possible to establish a national programme for bowel cancer screening that entails significantly greater benefit than harm. A programme will have a positive effect on training and treatment quality in clinical practice.

Methods

Participants and inclusion

In January 2012, the population cohort born between 1 January 1938 and 31 December

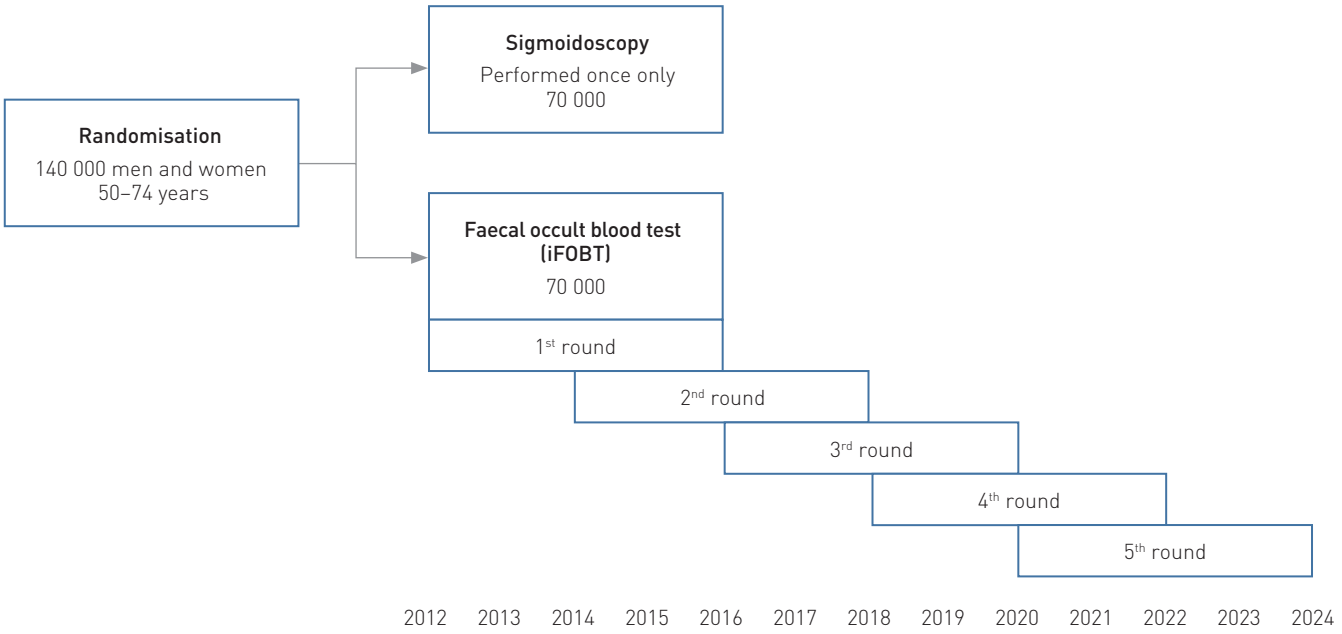

Figure 1 *Overall study design: 140 000 women and men in the age group 50–74 years are randomised 1 : 1 to screening with either sigmoidoscopy performed once only or to five rounds of faecal occult blood tests (immunochemical faecal occult blood test, iFOBT). Relevant participants are invited to the first screening test in the period 2012–18. Inclusion for sigmoidoscopy will be completed in 2018 and the 5th round of faecal occult blood tests will be undertaken during 2024*

1962 and living in south-eastern Norway was randomised 1:1 to either iFOBT every second year for 10 years (5 screening rounds) or sigmoidoscopy performed once only (Figure 1).

Ethics

The study was conducted in accordance with the Declaration of Helsinki and approved by the Regional Ethics Committee for South East Norway (REF approval no 2011/1272). The study has been registered at ClinicalTrials.gov (Identifier: NCT01538550).

Outcome measures

The main endpoint is CRC mortality after ten-year follow-up. Secondary endpoints at ten-year follow-up are: other disease-specific mortality, total mortality, CRC incidence, cost-effectiveness, sensitivity and specificity for each of the screening methods, attendance rate, detection rate of CRC and high-risk adenomas (more than two adenomas, adenomas with high-grade dysplasia or villous components, adenomas greater than or equal to 10 mm), CRC stage at diagnosis, endoscopic and surgical complications.

Screening method: immunochemical faecal occult blood test (iFOBT)

The iFOBT OC-Sensor Diana™ (Eiken Chemicals Co. Ltd., Tokyo, Japan) system was chosen to test stool samples. A positive test is defined as a haemoglobin concentration of more than 75 ng /mL buffer. This was considered to be most cost-effective and based on previous studies, this cut-off was expected to give a 5 % positivity rate (7).

Screening method: sigmoidoscopy

Sigmoidoscopy is performed immediately after administration of a 250 ml sorbitol enema. A sigmoidoscopy is considered positive when polyps greater than or equal to 10 mm, high-risk adenoma or colorectal cancer is detected. A positive screening test with either iFOBT or sigmoidoscopy qualifies for a work-up colonoscopy with endoscopic or possibly subsequent surgical removal of lesions. The Olympus Excera III system™ (Olympus Co Ltd (Tokyo, Japan)) were used both for screening sigmoidoscopy and work-up colonoscopies.

Sample size calculation

The sample size calculation was based on the «intention-to-screen» comparison of CRC mortality between the sigmoidoscopy and iFOBT groups. Compared to the general non-screened Norwegian population, we assumed a CRC mortality reduction of 30 % in individuals invited to participate in the sigmoidoscopy arm (8) and 15 % in those invited to participate in the FIT arm compared to no screening (9). Based on the 2010–2012 Norwegian age-specific rate of CRC deaths, 70 000 individuals in each arm give 80 % power to detect the assumed 15 % difference in CRC mortality reduction. The risk of type I error (?) was set to 0.05. Based on demographics in Norway, two screening centres at the hospitals in Bærum and Moss were established in order to achieve an uptake area of 140 000 persons aged 50–74 years.

Status of the project

By 10 November 2016, a total of 111 224 persons had been invited for screening, 42 782 for sigmoidoscopy, 68 442 for round 1 iFOBT, 29 490 for round 2 iFOBT and 1 392 for Round 3 iFOBT, respectively.

Auxiliary studies

A negative screening test may be perceived as a health certificate and reduce the motivation to follow lifestyle recommendations (10). This may reduce the effect of screening, by increasing mortality due to lifestyle diseases (11). Invitation to and participation in colorectal cancer screening may potentially expose the individual to anxiety that influences quality of life (12). Such effects may offset the benefits of reduced cancer mortality. Therefore, we conducted studies on a randomised selection of screening participants and non-screened control groups in neighbouring municipalities. These studies assess whether participation in screening is associated with lifestyle changes, anxiety or health-related quality of life. The participants' satisfaction with their choice to attend is also investigated in a randomised selection of screening participants.

Screening centres

Screening centres for the project were established at the hospitals in Moss and Bærum.

New personnel were employed at the start of project. The hospitals decided on the changes required on the premises. Endoscopy equipment was procured in consultation with the Secretariat of the Cancer Registry within given budgetary constraints.

Quality assurance system

All endoscopic procedures are prospectively recorded in a dedicated database. Key results and the following quality indicators are continuously available to staff and project management: caecum intubation rate (CIR) for colonoscopy, level reached at sigmoidoscopy, and for both examinations: adenoma detection rate (ADR), polyp detection rate (PDR), high risk adenoma (HRA) rate, CRC detection rate, quality of bowel preparation and complications. Patient-reported experience measures (PREM) are prospectively recorded in the National Quality Registry «Gastronet» (13). For participants referred for surgery, the outcome of the intervention and any complications until 30 days after surgery are recorded in the same database.

Endoscopy training

Training of new personnel was provided under the direction of the project to avoid draining resources from clinical services (14). In collaboration with the South Eastern Regional Health Authority (RHF), the Cancer Registry of Norway, the two screening centres and Oslo University Hospital (OUH), a regional centre for endoscopy training was established at OUH. Six new positions for registrars were established for the project's endoscopy service. These were later extended to eight positions in order not to place a strain on clinical activities. The recruited doctors who systematically trained full-time under intensive supervision for six months had little or no prior endoscopy experience.

This endoscopy training system was gradually extended to train experienced endoscopists to become competent and certified colonoscopy trainers through «Train the Colonoscopy Trainer courses». The courses were organised in collaboration with British and Canadian faculties with more than ten years of experience.

Eight nurses began training to become endoscopy assistants two months ahead of the pilot project. Due to an increase in their work tasks, ten nurses are currently working at the two screening centres. In all, 19 endoscopy nurses have been trained in the course of the pilot project.

Discussion

We have established an infrastructure for population-based colorectal cancer screening that compares two screening modalities in a randomised design. We have also established a structured training system for endoscopy that is also extendable to endoscopy training for clinical practice.

The BCSN pilot project aims to generate important new knowledge about colorectal cancer screening. It may also measure the effects of systematic endoscopy training. The project will help to indicate the best screening test for the Norwegian population, based on solid methodology in the form of a randomised comparative effectiveness study. Four papers from sub-studies on lifestyle and psychological reactions have already been published (1518).

The design of the project was based on the political decision that long-term implementation of bowel cancer screening should be evidence-based. This may strengthen Norway's leading international role in research on colorectal cancer screening.

The preliminary results from this pilot project and the preceding Norwegian Colorectal Cancer Prevention (NORCCAP) project (8), have formed the basis for the recommendation by the Norwegian National Council for Priority Setting in Health Care on implementation of a national programme for bowel cancer screening (19).

New colorectal cancer screening tests are evolving and need testing as part of a population-based programme in the years to come. A future screening programme should be an arena for systematic testing of new methods (20).

We also plan to test other population-oriented prevention measures as part of the bowel screening programme, such as information and advice on beneficial lifestyle. This may reduce the incidence of several lifestyle diseases. We have fulfilled the requirements of the Norwegian National Council for Priority Setting in Health Care (14) by avoiding placing an undue burden on regular clinical practice. On the contrary, the pilot project entailed recruitment of new gastroenterologists and endoscopy nurses by establishing a regional centre for structured endoscopy training. In total, 22 endoscopists from 13 hospitals in South-Eastern Norway Regional Health Authority were trained and certified as colonoscopy trainers and will cover much of the need for endoscopy training in the region. International experience indicates that the need would probably have been met had half of the endoscopists taken the course.

Conclusions

The pilot project has provided valuable experience in terms of implementing an evidence-based programme for bowel cancer screening with continuous generation of new knowledge. Hitherto, the pilot project has been implemented with limited impact on clinical practice and has served as a platform to recruit new specialists in digestive diseases, as well as a platform for more systematic endoscopy training

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