Effect of Flexible Sigmoidoscopy Screening on Colorectal Cancer Incidence and Mortality: A Randomized Clinical Trial

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IMPORTANCE Colorectal cancer is a major health burden. Screening is recommended in many countries.

OBJECTIVE To estimate the effectiveness of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality in a population-based trial.

DESIGN, SETTING, AND PARTICIPANTS Randomized clinical trial of 100,210 individuals aged 50 to 64 years, identified from the population of Oslo city and Telemark County, Norway. Screening was performed in 1999-2000 (55-64-year age group) and in 2001 (50-54-year age group), with follow-up ending December 31, 2011. Of those selected, 1415 were excluded due to prior colorectal cancer, emigration, or death, and 3 could not be traced in the population registry.

INTERVENTIONS Participants randomized to the screening group were invited to undergo screening. Within the screening group, participants were randomized 1:1 to receive once-only flexible sigmoidoscopy or combination of once-only flexible sigmoidoscopy and fecal occult blood testing (FOBT). Participants with positive screening test results (cancer, adenoma, polyp ≥10 mm, or positive FOBT) were offered colonoscopy. The control group received no intervention.

MAIN OUTCOMES AND MEASURES Colorectal cancer incidence and mortality.

RESULTS A total of 98,792 participants were included in the intention-to-screen analyses, of whom 78,220 comprised the control group and 20,572 comprised the screening group (10,283 randomized to receive a flexible sigmoidoscopy and 10,289 to receive flexible sigmoidoscopy and FOBT). Adherence with screening was 63%. After a median of 10.9 years, 71 participants died of colorectal cancer in the screening group vs 330 in the control group (31.4 vs 43.1 deaths per 100,000 person-years; absolute rate difference, 11.7 [95% CI, 3.0-20.4]; hazard ratio [HR], 0.73 [95% CI, 0.56-0.94]). Colorectal cancer was diagnosed in 253 participants in the screening group vs 1086 in the control group (112.6 vs 141.0 cases per 100,000 person-years; absolute rate difference, 28.4 [95% CI, 12.1-44.7]; HR, 0.80 [95% CI, 0.70-0.92]). Colorectal cancer incidence was reduced in both the 50- to 54-year age group (HR, 0.68; 95% CI, 0.49-0.94) and the 55- to 64-year age group (HR, 0.83; 95% CI, 0.71-0.96). There was no difference between the flexible sigmoidoscopy only vs the flexible sigmoidoscopy and FOBT screening groups.

CONCLUSIONS AND RELEVANCE In Norway, once-only flexible sigmoidoscopy screening or flexible sigmoidoscopy and FOBT reduced colorectal cancer incidence and mortality on a population level compared with no screening. Screening was effective both in the 50- to 54-year and the 55- to 64-year age groups.

TRIAL REGISTRATION clinicaltrials.gov Identifier: NCT00119912


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Flexible Sigmoidoscopy and Colorectal Cancer Incidence

Methods

Design and Participants
In November 1998, all men and women aged 55 to 64 years living in Oslo, Norway, or Telemark County, Norway, were identified through the Norwegian Population Register (study protocol is provided in Supplement 1). Equal numbers of men and women were randomly sampled from the birth cohorts of 1935-1945 and invited by mail for screening (screening group). Remaining individuals in the screening areas constituted the control group; control participants were never contacted and were not offered any screening. Participants in the screening group were further randomized (1:1) to receive an invitation for once-only flexible sigmoidoscopy or a combination of once-only flexible sigmoidoscopy and immunological fecal occult blood testing (FOBT; FlexSure OBT, Beckman-Coulter) (Figure 1). An independent body (IBM Norway) performed both randomization procedures using computerized algorithms.

At the end of the year 2000, the study funding bodies (Norwegian Government and Norwegian Cancer Society) decided to extend the study to also include all individuals aged 50 to 54 years in the same geographic areas to obtain more information about the ideal age to start screening. No power calculations were used for this extension of the trial. The randomization, invitation, and screening procedures were similar to those for the 55- to 64-year age group. To due to higher birth rates in the 50- to 54-year age group (born 1946-1950, after World War II), the ratios between the screening and control group were 1:3 in the 55- to 64-year age group and 1:5.4 in the 50- to 54-year age group. The screening interventions took place in 1999 and 2000 for the 55- to 64-year age group and in 2001 for the 50- to 54-year age group. During the course of the trial, there was no colorectal cancer screening program in Norway and there have been virtually no screening colonoscopies outside the trial. Thus, all cases of colorectal cancer in the control group were identified by work-up of gastrointestinal symptoms.

The study entry date for participants in the screening group was the date of the screening examination as proposed in their invitation letter. For the control group, each participant was assigned an entry date evenly distributed throughout the screening period (January 1, 1999, to December 31, 2000, for the 55- to 64-year age group; January 1, 2001, to December 31, 2001, for the 50- to 54-year age group). The only exclusion criterion was prior history of colorectal cancer. We did not have any information on family history of colorectal cancer at the time of the random sampling. Details of the study design, baseline findings, and short-term follow-up have been published previously.9,10,11

All participants who attended the screening examination provided written informed consent. The study was approved by the Ethics Committee of South-East Norway and the Norwegian Data Inspectorate.

All screening examinations were performed at 3 dedicated centers (2 in Telemark and 1 in Oslo). Bowel cleansing was restricted to a 240-mL sorbitol enema administered at attendance at the screening center. All examinations were performed using standard colonoscopes (140 cm Olympus) with the exception of a small screening center in Telemark, where a disposable endoscopy sheath was used (Vision Sciences 60 cm disposable Endosheath). During flexible sigmoidoscopy, all visible lesions were biopsied and subjected to histopathological evaluation. The screening participant brought the fecal sample to the screening center and the FOBT was analyzed on site prior to undergoing flexible sigmoidoscopy. There was no option to be screened with FOBT only. Participants with a positive screen, defined as any polyp of 10 mm or greater (irrespective of histology), any adenoma, colorectal cancer, or positive FOBT, were referred for colonoscopy at the screening centers. During colonoscopy, all lesions were removed. Designated pathologists examined all specimens. Postpolypectomy surveillance recommendations followed Norwegian guidelines.12

The primary study end points were colorectal cancer incidence and mortality. We also analyzed incidence and mortality from colorectal cancer located distal and proximal to the descending sigmoid junction, stage-specific incidence, and all-cause mortality. All residents in Norway are assigned a unique personal identification number and all included participants were followed up through linkage to public registries. Date of diagnosis, stage, and localization of colorectal
cancer were obtained from the Cancer Registry of Norway (which has near complete registration of all cancers in Norway). Colorectal cancer was defined as adenocarcinoma of the colon or rectum and classified as localized (Dukes A or B) or advanced (Dukes C or D). Cases were also included if they were reported to the Cancer Registry of Norway as clinically diagnosed colorectal cancer without confirmatory histology (14 cases). Date and cause of death were obtained from the Cause of Death Registry. Socioeconomic data of all participants were obtained from Statistics Norway.

Statistics
The power calculation was conducted for the 55- to 64-year age group and for the 2 screening groups combined vs the control group. Assuming 70% adherence, a 30% intention-to-treat reduction in colorectal cancer incidence after 5 years with 90% power, and a significance level of 5%, 14 000 participants had to be included in the screening group and 42 000 in the control group. Half of the participants in the screening group were offered flexible sigmoidoscopy screening only, and the other half were offered screening with flexible sigmoidoscopy and FOBT (the effectiveness comparison of the 2 different screening groups was a secondary analysis).

The primary analytic approach for this study followed the intention-to-screen principle. Each participant was observed from entry date until diagnosis of colorectal cancer, death, emigration, or December 31, 2011, whichever occurred first. Age-standardized rates were computed using the screening group as the reference standard to adjust for a slightly higher mean age in the screening group than in the control group (56.9 vs 56.1 years). Age-adjusted hazard ratios (HRs) with 95% CIs were estimated for the screening group vs the control group by fitting Cox models adjusted for age. Two sensitivity analyses were performed: the ratio between the control group and screening group was higher in Oslo (6.2:1) than in Telemark (1.5:1) due to higher population numbers in Oslo, but the age-adjusted colorectal cancer incidence and mortality rates were comparable in the control groups in both areas. Consequently, in a sensitivity analysis when we included screening center in the Cox model, the results were unchanged. Analyses were also performed with follow-up restricted to 11 years in both the screening and control groups, taking into account the slightly different follow-up time (due to age differences), with comparable results.

To test for heterogeneity, product (interaction) terms were included (between sex and study group and between age group and study group) in the Cox model. Colorectal cancer incidence and mortality were computed using age-standardized cumulative probability. Furthermore, the yearly age-standardized risk ratios after randomization were calculated in the screening group and in participants who were screening adherent relative to the control group. The number needed to invite for screening to prevent a single colorectal cancer case or death within 10 years was calculated as the inverse of the age-standardized risk difference at 10 years (all participants were observed for at least 10 years). The incremental cost-effectiveness ratios (expressed in terms of prevented colorectal cancer cases and colorectal cancer deaths

Figure 1. Flowchart of Norwegian Colorectal Cancer Prevention trial (NORCCAP)
Flexible Sigmoidoscopy and Colorectal Cancer Incidence

Original Investigation Research

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Table 2. Findings at Screening and Endoscopy

<table>
<thead>
<tr>
<th>Group</th>
<th>No. (%)</th>
<th>Flexible Sigmoidoscopy (n = 6692)</th>
<th>Flexible Sigmoidoscopy + FOBT (n = 6263)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Any adenomaa</td>
<td>Advanced adenomab</td>
<td>Colorectal cancer</td>
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<tr>
<td></td>
<td></td>
<td>(17.3)</td>
<td>(4.6)</td>
<td>(0.3)</td>
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<tr>
<td></td>
<td></td>
<td>1156</td>
<td>304</td>
<td>21</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1054</td>
<td>278</td>
<td>20</td>
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<tr>
<td></td>
<td></td>
<td>(16.9)</td>
<td>(4.5)</td>
<td>(0.3)</td>
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<tr>
<td></td>
<td></td>
<td>.50</td>
<td>.78</td>
<td>&gt; .99</td>
</tr>
</tbody>
</table>

Abbreviations: FOBT, fecal occult blood test.

a Reported results include findings at flexible sigmoidoscopy and colonoscopy of screen-positive participants among those who were screening adherent.

b Individuals with screen-detected colorectal cancer were excluded. Advanced adenoma was defined as an adenoma of 10 mm or larger, with villous histology or with high-grade dysplasia.

c Refers to participants with perforations (n = 6) and admittance to hospital for postpolypectomy bleeding (n = 4).

Results

Of 100,210 randomized participants, 1415 (1.4%) were excluded due to diagnosis of colorectal cancer, death, or emigration before study entry (Figure 1) and 3 could not be traced through the population register. Thus, our analyses include 78,220 participants in the control group and 20,572 in the screening group. A total of 10,283 participants were randomized to undergo screening with flexible sigmoidoscopy only and 10,289 were randomized to undergo screening with flexible sigmoidoscopy and FOBT. Baseline characteristics are reported in Table 1. End of follow-up was December 31, 2011.

Of 20,572 participants invited to undergo screening, 12,955 (63%) attended the screening examination. Adherence was 60.9% in the combined screening group and 65.1% in the group invited for flexible sigmoidoscopy screening only (P < .001). Screening findings and key endoscopy figures are reported in Table 2. There were no complications after flexible sigmoidoscopy. A total of 2816 colonoscopies were performed in 2520 participants (19.5% of those who attended screening). Perforation occurred during colonoscopy in 6 participants, and 4 participants were admitted to the hospital for postpolypectomy bleeding following snare polypectomy. Two patients had complications after surgery. No screening-associated deaths occurred.

Colorectal Cancer Incidence

Median follow-up time was 11.2 years in the screening group and 10.9 years in the control group. The age-standardized colorectal cancer incidence rate (per 100,000 person-years) was 112.6 in the screening group and 141.0 in the control group; the absolute rate difference was 28.4 (95% CI, 12.1-44.7), and the HR was 0.80 (95% CI, 0.70-0.92) (Table 3; Figure 2A). In the 50- to 54-year age group, the HR was 0.68 (95% CI, 0.49-0.94) and in the 55- to 64-year age group, the HR was 0.83 (95% CI, 0.71-0.96) (P value for heterogeneity = .27). In men, the HR was 0.73 (95% CI, 0.60-0.89) and in women, the HR was 0.87 (95% CI, 0.72-1.06) (P value for heterogeneity = .26). For distal colorectal cancer, the HR was 0.76 (95% CI, 0.63-0.92; Figure 2C) and for proximal colorectal cancer, the HR was 0.90 (95% CI, 0.73-1.10) (Table 3). For
flexible sigmoidoscopy screening only, the HR was 0.72 (95% CI, 0.59-0.87) and for flexible sigmoidoscopy and FOBT, the HR was 0.88 (95% CI, 0.74-1.05) (*P* value for heterogeneity = .11). Screen-detected colorectal cancer was more often diagnosed at an earlier stage than non–screen-detected colorectal cancer (Table 4). The relative risk of colorectal cancer was lower each year after screening in the screening group compared with the control group, except for the first year after randomization due to screen-detected cancers (Figure 3A and Figure 4A and B). The number needed to invite for screening to prevent a single colorectal cancer case over 10 years was 498 (incremental cost-effectiveness ratio, $58 448; eTable 7 in Supplement 2).

**Colorectal Cancer Mortality**

The age-standardized colorectal cancer mortality rate (per 100 000 person-years) was 31.4 in the screening group and 43.1 in the control group, the absolute rate difference was 11.7 (95% CI, 3.0-20.4), and the HR was 0.73 (95% CI, 0.56-0.94) (Table 3 and Figure 2B). In the 50- to 54-year age group, the HR was 0.74 (95% CI, 0.40-1.35) and in the 55- to 64-year age group, the HR was 0.73 (95% CI, 0.55-1.09) (P value for heterogeneity = .10). For distal colorectal cancer mortality, the HR was 0.79 (95% CI, 0.55-1.11) and for proximal colorectal cancer mortality, the HR was 0.73 (95% CI, 0.49-1.09) (Table 3). For flexible sigmoidoscopy screening only, the HR was 0.84 (95% CI, 0.61-1.17) and for flexible sigmoidoscopy and FOBT, the HR was 0.62 (95% CI, 0.42-0.90) (P value for heterogeneity = .20). Figure 3B shows the yearly risk ratio for colorectal cancer mortality in the screening group relative to the control group. The number needed to invite for screening to prevent a single colorectal cancer death over 10 years was 1547 (incremental cost-effectiveness ratio, $226 002; eTable 7 in Supplement 2).

<table>
<thead>
<tr>
<th>Table 3. Colorectal Cancer Incidence and Mortality in the Screening and Control Groups</th>
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<tbody>
<tr>
<td><strong>Group</strong></td>
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<tr>
<td><strong>Colorectal Cancer Incidencea</strong></td>
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<tr>
<td>Overall</td>
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<td></td>
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<tr>
<td>Location</td>
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<tr>
<td>Distal</td>
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<td>Proximal</td>
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<td>Sex</td>
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<td>Men</td>
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<tr>
<td>Women</td>
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<tr>
<td>Age group, y</td>
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<tr>
<td>50-54</td>
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<tr>
<td>55-64</td>
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<tr>
<td>Screening modality</td>
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<tr>
<td></td>
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<tr>
<td><strong>Colorectal Cancer Mortalityb</strong></td>
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<tr>
<td>Overall</td>
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<tr>
<td></td>
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<tr>
<td>Location</td>
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<td>Age group, y</td>
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<td>50-54</td>
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<td>55-64</td>
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<tr>
<td>Screening modality</td>
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<tr>
<td></td>
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<tr>
<td>All-cause mortality</td>
</tr>
</tbody>
</table>

Abbreviations: FOBT, fecal occult blood test; HR, hazard ratio.

* Person-years of observation: for the screening group, 221 429; and for the control group, 828 207.

* Person-years of observation: for the screening group, 222 677; and for the control group, 832 003.
There were no differences in all-cause mortality between the screening and control groups (HR, 0.97; 95% CI, 0.93-1.02).

**Adherence-Adjusted Analysis (Per-Protocol Effect)**

The intention-to-screen 10-year risk absolute difference (risk in the screening group minus risk in the control group) was −0.22% (95% CI, −0.38% to −0.06%) for colorectal cancer and −0.06% (95% CI, −0.14% to 0.03%) for colorectal cancer death in the entire study population. After adjustment for nonadherence, the corresponding 10-year risk differences were −0.42% (95% CI, −0.69% to −0.15%) for colorectal cancer and −0.10% (95% CI, −0.25% to 0.05%) for colorectal cancer death (eTable 2 in Supplement 2).

**Discussion**

In this study, flexible sigmoidoscopy screening reduced colorectal cancer incidence by 20% and colorectal cancer mortal-

There were no differences in all-cause mortality between the screening and control groups (HR, 0.97; 95% CI, 0.93-1.02).

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**Conclusion**

Flexible sigmoidoscopy screening reduced colorectal cancer incidence by 20% and colorectal cancer mortal-

### Table 4. Colorectal Cancer Stages*

<table>
<thead>
<tr>
<th>Stage</th>
<th>No. (%)</th>
<th>Adherents (n = 12 955)</th>
<th>Nonadherents (n = 7 617)</th>
<th>Total (n = 20 572)</th>
<th>Control Group (n = 78 220)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Screen-Detected</td>
<td>Post-Screen-Detected</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized</td>
<td>29 (2.2)</td>
<td>48 (3.6)</td>
<td>40 (5.4)</td>
<td>117 (5.7)</td>
<td>470 (6.7)</td>
</tr>
<tr>
<td>Advanced</td>
<td>10 (0.8)</td>
<td>49 (3.7)</td>
<td>62 (8.3)</td>
<td>120 (5.8)</td>
<td>562 (7.8)</td>
</tr>
<tr>
<td>Unclassified</td>
<td>2 (0.1)</td>
<td>4 (0.3)</td>
<td>9 (1.2)</td>
<td>16 (0.8)</td>
<td>54 (0.8)</td>
</tr>
<tr>
<td>Total</td>
<td>41 (3.1)</td>
<td>101 (7.6)</td>
<td>111 (15.0)</td>
<td>253 (12.3)</td>
<td>1086 (15.3)</td>
</tr>
</tbody>
</table>

* Number of localized and advanced colorectal cancers (age standardized/1000 participants) by randomization group status and by mode of detection.

Cumulative probability for colorectal cancer incidence (panels A and C) and mortality (panels B and D), for the colorectum overall and for the distal colon.
Younger participants aged 50 to 54 years seemed to benefit at least as much from the screening intervention as older participants aged 55 to 64 years.

Three other large randomized trials of flexible sigmoidoscopy screening with comparable length of follow-up have been published. In the trials from the United Kingdom (Flexi Scope trial) and Italy (SCORE), offering once-only flexible sigmoidoscopy examination to participants aged 55 to 64 years, colorectal cancer incidence was reduced by 23% and 18% and colorectal cancer mortality by 31% and 22%, respectively.5,7 In the US trial (PLCO), which included participants aged 55 to 74 years and offered flexible sigmoidoscopy screening at 2 occasions, colorectal cancer incidence was reduced by 21% and colorectal cancer mortality by 26%.6

Our results are in accordance with those reported from the previous trials and extend them in 3 important ways. First, unlike the other trials, the estimates of this trial were not affected by screening contamination in the control group. Second, this study’s population-based design with random sampling directly from the population registry allowed estimation of the effectiveness of a national screening program with similar adherence. The study populations of the other trials consisted of volunteers. Therefore, the findings in other trials may not be generalizable to their national populations if participants included in the trial had a different risk of colorectal cancer diagnosis or death than the background population. Indeed, in the Italian SCORE trial, the colorectal cancer mortality rate was 46% lower in the control group than in...
the background population. Third, our estimates show, for the first time, the effectiveness of screening in participants aged 50 to 54 years.

The ideal age to start screening for colorectal cancer has not been firmly established and national screening recommendations vary accordingly. As yet no study has reported on effectiveness of flexible sigmoidoscopy screening in participants younger than 55 years. This study shows that participants aged 50 to 54 years benefit as much from flexible sigmoidoscopy screening as those older than 55 years, with respect to colorectal cancer incidence.

The 4 flexible sigmoidoscopy trials had important differences in the threshold for referral to colonoscopy. In the present study, a low referral threshold was adapted, meaning that any adenoma (irrespective of size) qualified for colonoscopy. The PLCO trial referred all participants with any detected lesion or polyp to follow-up, while only participants with advanced or multiple adenomas were offered colonoscopy in the UK trial. The Italian trial adopted the recommendation from the UK trial, but in addition, referred participants with adenomas 6 to 9 mm in size. These differences led to widely varying colonoscopy rates (19.5% in NORCCAP, 5.0% in the United Kingdom, 7.8% in Italy, and 21.9% in the US trial). Despite these differences, reported reductions in colorectal cancer incidence were similar (18%-23%). This observation may infer that the least extensive referral approach could be sufficient, implying that only participants with advanced adenomas at flexible sigmoidoscopy should be referred to colonoscopy.

Adoption of this recommendation would have great impact on costs of flexible sigmoidoscopy screening programs but would also reduce the number of advanced adenomas detected in the proximal colon. We have previously reported that the number of colonoscopies would have been reduced by 66% if only participants in the NORCCAP trial with advanced adenomas were referred to colonoscopy. But, as a consequence, 38% of proximal advanced adenomas would not have been detected. Other trials have confirmed that approximately half of proximal advanced adenomas did not have a synchronous distal lesion and would thus have been missed due to normal findings at flexible sigmoidoscopy. In our trial, a 10% reduction in proximal colorectal cancer incidence was found, which is in accordance with the PLCO trial in which a 14% reduction in proximal colorectal cancer incidence was found with a similar colonoscopy referral rate. The optimum threshold for colonoscopy referral in a screening program should be weighed against costs and available endoscopy resources.

Adding one-time FOBT did not lead to additional screen-detected cancers or the detection of more advanced adenomas. This is in keeping with previous results. To reduce colorectal cancer mortality, FOBT has to be repeated. In fact, the combined screening approach led to lower adherence in our trial and could thus have a negative impact on a screening program. No reduction in all-cause mortality was observed. This was not unexpected because only 4% of all deaths in the NORCCAP population were due to colorectal cancer and the trial was not powered to detect any difference in all-cause mortality.

Even if underpowered for subgroup analyses, the results of this study may suggest a stronger effect of the screening intervention in men than in women. Colorectal cancer incidence and mortality were reduced by 27% and 42% in men and 13% and 9% in women, respectively. A larger benefit for men was also evident in the PLCO and the UK trials. Possible explanations, supported by previous studies, may be that more women than men have proximal advanced adenomas without distal lesions, which would have triggered a full colonoscopy, and more women than men have proximal sessile serrated lesions, which may be more difficult to detect.

In this article, we use observed data for prevented colorectal cancer incidence and colorectal cancer deaths as a measure for clinical cost-effectiveness in a 10-year perspective. Hence, the findings of this study are not comparable with most other cost-effectiveness analyses, which are model-based and apply a lifetime perspective. Our estimate of the costs per prevented colorectal cancer case shows that screening in the 50- to 54-year age group is at least as cost effective as in the 55- to 64-year age group, despite lower baseline risk of colorectal cancer.

Estimating the per-protocol effect under full adherence is important to quantify the maximum benefit of the screening intervention that may be achieved in a screening program. The results of this study show that in case of full adherence, the absolute reduction in 10-year colorectal cancer risk would be twice as high as in the intention-to-treat analysis (−0.42% vs −0.22%) if the adherents were approximately representative of the general population. The colorectal cancer incidence rate in nonadherents was equal to that in the control group (eFigure 1 in Supplement 2), which supports the generalizability of these estimates to the entire population. Figure 4A and B approximately quantifies the effectiveness of a flexible sigmoidoscopy screening program on colorectal cancer incidence under perfect adherence.

A possible limitation of this trial is that mortality estimates were based on public registries and did not include a death review committee or expert coder to perform an additional review of death certificates. However, using a death review committee did not significantly alter the number of deaths attributable to colorectal cancer in 2 previous colorectal cancer screening trials. Even if an expert coder found more colorectal cancer deaths in the UK flexible sigmoidoscopy trial than were obtained from public registries, the added yield was similar in both the screening and control groups and therefore did not change the effect estimates of the screening intervention.

Conclusions

Compared with no screening, once-only flexible sigmoidoscopy screening or flexible sigmoidoscopy with FOBT reduced colorectal cancer incidence and mortality in a population-based trial in Norway. Screening effects were similar in 50- to 54- and 55- to 64-year-old participants.
Flexible Sigmoidoscopy and Colorectal Cancer Incidence

ARTICLE INFORMATION

Author Contributions: Drs Holme and Løberg had full access to all data and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Holme and Løberg contributed equally.

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Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Holme.

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