

Overview of publications from the Bowel Cancer Screening in Norway (BCSN) pilot

(status per 1st November 2023)

2023

1. Kværner AS, Birkeland E, Vinberg E, Hoff G, Hjartåker A, Rounge TB, Berstad P. Associations of red and processed meat intake with screen-detected colorectal lesions. *Br J Nutr.* 2023 Sep 7;129(12):1-11. doi: 10.1017/S0007114522002860. Epub ahead of print. PMID: 36069337; PMCID: PMC10197083.

High intake of red and processed meat increases the risk of bowel cancer

The Norwegian National Bowel Screening Programme was formally launched 22 August 2022. Prior to this, there have been two major pilot projects testing screening methods – the first was in Telemark County and City of Oslo 1999-2001 and the second started in 2012 in Østfold County and Vestre Viken (now in its final phase). Both of these projects also included sub-projects on possible associations between lifestyle and cancer. The present study is from the most recent of these two pilot studies.

Among the screening participants who tested positive for invisible blood in their stools at screening, 1600 filled in a 14-page questionnaire about food- and drinking habits – in addition to lifestyle data (smoking and physical exercise). The questionnaire was filled in before colonoscopic work-up after screen-detected blood in the stools (colonoscopy is a flexible instrument inserted through the back passage for visualization of the large bowel). Only 2% of participants consumed less than the recommended upper limit of 21 G processed meat per week. 27% of those surveyed had "advanced lesions" in their large bowel, i.e. cancer or high-risk polyps – the latter carrying a high risk of developing into cancer.

Advanced lesions were associated with a high intake of red and processed meat – also when statistically corrected for gender, age, smoking and exercise habits. Low and moderate intake did not increase the risk. This is a large study with very good data collected before the participants were colonoscoped and made aware of any lesions in their large bowel. The findings are in line with previous studies that have also suggested a link between colorectal cancer and a high intake of red and processed meat.

This type of research should be embedded in ongoing screening programmes in order to obtain data FROM the target group to provide results which are tailored and optimally relevant specifically FOR the target group in the screening programme. Although bowel screening is about detecting cancer and possible precancerous conditions, it may also be a perfect window of opportunity to reach out with advice on primary lifestyle prevention measures against colorectal cancer.

2. Kirkøyen B, Berstad P, Hoff G, Bernklev T, Randel KR, Holme Ø, de Lange T, Robb KA, Botteri E. Type and severity of mental illness and participation in colorectal cancer screening. *Am J Prev Med* 2023;64:76-85

Poorer compliance for bowel screening among people with mental disorders.

The principle of equality for health services is important in Norway. We try to make arrangements for everyone to experience as much equality as possible in the health service.

In this study, we have looked at attendance at bowel screening among users and non-users of medication for mental disorders, e.g. anxiety, depression, psychosis. The persons were drawn randomly from the National Population Register to be offered screening using a home test for invisible blood in the stools or attendance at a hospital for sigmoidoscopy (an examination of

the lower approx. 50 cm of the large bowel by means of a thin, flexible "intestinal scope"). The national Prescription Register was used as a data source for information about medications prescribed.

Among 46,919 people invited for screening at age 50-74 years, 25% of the women and 13% of the men had been prescribed medication for psychiatric disorders. Regardless of the screening method, there was a greater dropout from screening for people who had been prescribed particularly anti-anxiety medication or anti-psychotic medication. There is a need for targeted efforts to facilitate the screening offer also for this part of the target group eligible for screening.

3. *Schult AL, Hoff G, Holme Ø, Botteri E, Seip B, Randel KR, Darre-Næss O, Owen T, Nilsen JA, Nguyen DH, Johansen K, de Lange T. Colonoscopy quality improvement after initial training: A cross-sectional study of intensive short-term training. Endoscopy International Open 2023;11:E117-E127*

Improved and more systematic training in the "Endoscopy school" for performing high-quality colonoscopies.

In Norway, approx. 100,000 colonoscopy examinations are performed every year. The quality of the examination is largely dependent on the person performing the colonoscopy. The aim is to perform "a painless, complete examination detecting everything". A colonoscopy school was established in 2011 for more systematic training of colonoscopists in the screening pilot studies and this was later made available as an option for all endoscopists in Norway ahead of the national screening program against bowel cancer which started in August 2022.

This study is based on a pilot project for the screening program where participants who tested positive for invisible blood in the stools were recommended to have a colonoscopy. In total, we evaluated 7,576 colonoscopies performed by experienced colonoscopists and recent graduates from the Endoscopy School. The newly graduated endoscopists examined the entire colon in 98% of their colonoscopies compared to 96% of the experienced colonoscopists.

Correspondingly, the newly trained discovered adenomatous polyps (possible precursors to later bowel cancer) more often than their experienced colleagues – in 58% versus 50% of the colonoscopies, respectively. The ability to perform painless examinations was similar for the newly trained and the experienced. There was great variation between the endoscopists, but as a group the newly graduated endoscopists from the Endoscopy School were fully up to the standards of their experienced colleagues.

4. *Nafisi S, Randel KR, Stær NC, Veierød MB, Hoff G, Holme Ø, Schult AL, Botteri E. Association between use of low-dose aspirin and detection of colorectal polyps and cancer in a screening setting. Dig Liver Dis 2023;55:1126-32*

Large study shows likely beneficial effect of aspirin on bowel cancer risk.

More than 4,000 individuals are diagnosed with bowel cancer in Norway each year and approx. 1,600 die each year from the disease. It is largely a lifestyle disease with a greater risk for those who smoke, have a high alcohol intake, are overweight and do little exercise. Changing lifestyle is often difficult. In the search for "a pill" that can reduce the risk, aspirin and other pills with acetylsalicylic acid have emerged as the most promising. But - the research results have not been unanimously in favor of aspirin and aspirin increases the risk of, among other things, bleeding ulcer. This has led to the US Preventive Services Task Force in 2016 initially recommending the use of some aspirin to reduce the risk of bowel cancer, but then they withdrew this recommendation in 2022. Many differences in the design of the previous studies may explain the varying results, i.e. that some show that aspirin is useful while others do not.

In this study, 64,889 persons aged 50-74 underwent a screening examination for bowel cancer in Norway and detection of possible precursors to bowel cancer. These possible precursors are adenomatous polyps (wart-like growths on the internal intestinal lining and although benign, a few of these lesions may develop into cancer). Long-term, continuous and regular use of aspirin tablets is in practice only feasible when one gets the tablets on prescription. We therefore linked screening data with data from the national prescription register. Occasional “over-the-counter” purchase of aspirin was not recorded in this study. The study showed that regular use of low-dose aspirin for at least 3 years was associated with a reduced risk of bowel cancer (34% reduction) and adenomatous polyps. This suggests that aspirin really does have a limiting effect on the risk of getting bowel cancer – consistent with findings in a pooled analysis from a number of smaller previous studies.

5. *Berstad P, Schult AL, Hoff G, Ursin G, Randel KR. Sosialer forskjeller i en pilotstudie på screening for tarmkreft. Tidsskr Nor Legeforen 2023;143:413-4*

Choice of screening method in a bowel screening program may affect social inequality in the screening service.

A project piloting the Norwegian national bowel screening program has been ongoing in Østfold County and Vestre Viken from 2012 to 2023. 140,000 women and men aged 50-74 were drawn from the National Population Register, and by drawing lots (randomization) they were offered either screening once with sigmoidoscopy (examination of the lower approx. 50 cm of the intestine with a flexible "intestinal scope") or four rounds of testing for invisible blood in the stools every two years. Those who tested positive for blood were recommended to have a full examination of the entire large bowel with a colonoscope.

The response rate was 60% at the first invitation in the group that was offered a stool test and 52% in the sigmoidoscopy group. Regardless of the screening method, participation was lower among those with the lowest income and education. Living without a partner, being born outside Norway and having a driving time of more than 20 minutes to the screening center also resulted in lower attendance. Other illnesses, especially diabetes and mental disorders, were associated with lower participation. Socioeconomics influenced participation to a greater extent in sigmoidoscopy than in testing for blood in the stools.

The results showed that the screening method affects social inequality in the bowel screening offer. Screening with a requirement to attend a screening center for an invasive screening examination created greater social differences in compliance than the stool home-test which required only to be mailed for analysis. The national bowel screening program started in 2022 with a stool test as the chosen screening method.

6. *Bhargava S, Botteri E, Berthelsen M, Iqbal N, Randel KR, Holme Ø, Berstad P. Lower participation among immigrants in colorectal cancer screening in Norway. Front Public Health 2023. (<https://www.frontiersin.org/articles/10.3389/fpubh.2023.1254905/full>).*

Immigrants have lower participation in bowel screening than Norwegian-born people.

In this study, participation in bowel screening was examined for approximately 117,000 persons invited to screening for bowel cancer with a stool sample to be taken at home once every two years or a once-only sigmoidoscopy (a camera examination of the lowermost part of the large bowel) in hospital. We compared participation for immigrants and those born in Norway. Immigrants had lower participation in bowel screening compared to the rest of the population. It turned out that participation in sigmoidoscopy screening, which required attendance at a hospital, was particularly low among immigrants compared to those born in Norway. The lowest

participation was observed among immigrants from non-Western countries. Compared to people born in Norway, attendance among immigrants was particularly low for work-up colonoscopy of screen-positives, i.e. even if the participant was informed about having blood detected in a stool sample.

7. *Kværner AS, Andersen AR, Henriksen HB, Knudsen MD, Johansen AMW, Hjartåker A, Bøhn SK, Paur I, Wiedeswang G, Smeland S, Rounge TB, Blomhoff R, Berstad P. Associations of the 2018 World Cancer Research Fund/American Institute of Cancer Research (WCRF/AICR) cancer prevention recommendations with stages of colorectal carcinogenesis. Cancer Med 2023*
A healthy lifestyle reduces the likelihood of finding cancer precursor lesions at bowel cancer screening.

Adherence to cancer prevention advice has been shown to reduce the risk of bowel cancer. In this research project among 1,486 FIT-positive participants from CRCbiome, we show that compliance with cancer prevention advice also reduces the probability of detecting potential cancer pre-stages (polyps) during the screening examination. Although some advice appeared to be more important than others (such as limiting alcohol intake and maintaining a healthy body weight), it appears that the cancer prevention gains are achieved by having an overall healthy lifestyle. This is also in line with previously published research on bowel cancer prevention.

2022

8. *Schult AL, Botteri E, Hoff G, Holme Ø, Bretthauer M, Randel KR, Gulichsen EH, El-Safadi B, Barua I, Munck C, Nilsen LR, Svendsen HM, de Lange T. Women require routine opioids to prevent painful colonoscopies: a randomised controlled trial. Scand J Gastroenterol. 2021 Dec;56(12):1480-1489. doi: 10.1080/00365521.2021.1969683. Epub 2021 Sep 17. PMID: 34534048.*

Colonoscopy is the most common method for examination of the large bowel (rectum and colon). A colonoscope is a thin, flexible tube with a camera on the tip to inspect the rectum, the entire colon and the lower part of the small intestine. The colonoscope is inserted through the back passage. Women are more likely than men to experience the examination as painful - probably due to gender differences in the pelvic anatomy.

In the present study, two morphine-like preparations (Fentanyl and Alfentanil) were used. 183 women aged 55-79 years and referred for a colonoscopy were allocated by lottery (randomization) to one of three groups: 1. Fentanyl administered immediately before the colonoscopy with possible top-ups if necessary (i.e. in case of pain during the examination), 2. Fentanyl only when needed (on-demand), 3. Alfentanil only when needed. The study showed that Fentanyl administered before the colonoscopy provided better pain control than Fentanyl or Alfentanil given only on demand.

9. *Knudsen MD, Kværner AS, Botteri E, Holme Ø, Hjartåker A, Song M, Thiis-Evensen E, Randel KR, Hoff G, Berstad P. Lifestyle predictors for inconsistent participation to fecal based colorectal cancer screening. BMC Cancer 2022;22:172*

Important to design bowel screening services especially for people with a poorly health-promoting lifestyle and thus an increased risk of bowel cancer, since it is precisely these people who more often choose not to make use of screening services.

In the years since 2012, 140,000 people in Østfold County and parts of the Vestre Viken region have been invited to participate in a project on screening for bowel cancer and possible

precursors to bowel cancer (i.e. polyps which are benign growths on the intestinal mucosa, but some of them may turn into cancer). The screening entails, among other things, testing for invisible blood in the stools every two years – adding up to a total of four screening rounds. Not everyone participate in all four rounds.

In this sub-study, we have looked at lifestyle (including smoking, exercise, diet) among those who have not taken part in all the screening rounds and the occurrence of polyps and cancer compared to those who have attended each screening round. Among those who did not attend all the screening rounds, there were more signs of an unhealthy lifestyle than among those who attended every time and they also more often had "advanced lesions" (ie cancer or a type of polyp with a particularly high risk of turning into cancer).

There is a risk that those who might benefit most from screening will opt out of participation in screening services. Such an offer should therefore be facilitated to attract especially individuals with a less health-promoting lifestyle.

10. Botteri E, Hoff G, Randel KR, Holme Ø, de Lange T, Bernklev T, Aas E, Berthelsen M, Natvig E, Kirkøen B, Knudsen MD, Kværner AS, Schult AL, Jørgensen A, Berstad P. Characteristics of non-participants in a randomized colorectal cancer screening trial comparing sigmoidoscopy and faecal immunochemical test. *Internat J Cancer*, 2022;151:361-71

Some key factors must be considered in the national bowel screening program to ensure equal access for everyone in the target group.

In Bærum and Moss municipalities in 2012, a trial of two possible screening methods was launched to pilot a Norwegian national bowel cancer screening programme. 140,000 men and women aged 50-74 were drawn by randomization from the population register and invited to either being tested for invisible blood in the stools every two years for 10 years or a once-only examination of the lower approx. 50 cm the large bowel using a flexible "bowel scope" (sigmoidoscopy). Both methods are considered to be good methods for reducing death due to bowel cancer. Support in the population and high attendance are crucial for the usefulness of a screening programme.

In this sub-study, we investigated characteristics of those choosing not to make use of the screening offered. Men, younger age, low education and income levels, retired or unemployed, living alone, immigrant, long journey to screening center and using psychiatric or diabetes medication showed an association with low participation rates for both screening methods. Low socio-economic status, immigrant and long journey to the screening center mattered more in the sigmoidoscopy group than among those invited to be tested for blood in the stools. Attendance was 51.5% in the sigmoidoscopy group and 58.5% among those who were invited to be tested for blood in the stools.

Testing for blood in the stools has now been chosen as the current screening method in the national screening program which started in May 2022 - possibly with a gradual transition to primary colonoscopy screening (examination of the entire large bowel) when the capacity for this has been built up satisfactorily. This sub-study has provided an insight into which groups need more facilitation to ensure an equal health service provision for all.

11. Berthelsen M, Berstad P, Randel KR, Hoff G, Natvig E, Holme Ø, Botteri E. The impact of driving time on participation in colorectal cancer screening with sigmoidoscopy and faecal immunochemical blood testing. *Cancer Epidemiol* 2022;80:102244

Travel distance to screening centers matters for bowel screening attendance.

In Norway, each year there are approx. 4,500 new cases of bowel cancer and approx. 1,600 deaths due to bowel cancer. Early detection improves post-treatment recovery and survival. Bowel cancer is well suited for screening, which provides the opportunity for early detection before the disease has produced symptoms. The effect of a screening program is completely dependent on good compliance. We already know that the people who most often make use of an offer of bowel screening are older, well-educated, they are in a relationship and do not belong to ethnic minority groups. Those who have relatives with bowel cancer also attend screening more often.

In this study, we looked at accessibility to the nearest screening centre. We have measured this as estimated time spent by car from home to the screening center for approx. 115,000 people living in Østfold and Vestre Viken. By drawing lots, these were offered either screening with a short, flexible "intestinal scope" (sigmoidoscope) requiring attendance at the local screening center or by mailing a stool sample to be analyzed for invisible blood. When detecting certain types of polyps at sigmoidoscopy screening (polyps are possible precursors to bowel cancer) and if blood was detected in the stool sample, a colonoscopy examination of the entire colon (colonoscopy) was recommended, which also required attendance at the screening centre. The hospital in Moss was the screening center for Østfold County and Bærum hospital for Vestre Viken. For those who were offered screening with sigmoidoscopy, the attendance rate fell by 7% for every 10-minute increase in travel time to the screening centre. In the group who submitted a stool sample which tested positive for blood, there was poorer attendance for subsequent work-up colonoscopy if travel distance was more than a 20-minute drive to the screening centre. These findings are important for planning screening programs suggesting to consider making screening transport arrangements (screening buses?) in certain areas.

2021

12. *Randel KR, Schult AL, Botteri E, Hoff G, Bretthauer M, Ursin G, Natvig R, Berstad P, Jørgensen A, Sandvei PK, Olsen ME, Frigstad SO, Darre-Næss O, Norvard ER, Bolstad N, Kørner H, Wibe A, Wenaas K-A, de Lange T, Holme Ø. Colorectal cancer screening with repeated fecal immunochemical test versus once-only sigmoidoscopy: baseline results from a large randomized trial. Gastroenterology, 2021;160:1085-96*

This is the first report from the large pilot study on a national screening program against bowel cancer in Norway that has been ongoing since 2012 in Østfold County and parts of Vestre Viken. 140,000 men and women aged 50-74 were drawn from the Population Register to receive an offer of screening either by once-only sigmoidoscopy screening or up to four rounds of examination for invisible blood in the stools every two years. Sigmoidoscopy is an examination of the lower approx. 50 cm of the colon using a flexible "intestinal scope". In this article, results are shown after the sigmoidoscopy screening and after three rounds of testing for invisible blood in the stools (FIT testing). Attendance was 52% for sigmoidoscopy, 58% for the first FIT round, but accumulated over three rounds, 68% had attended at least once. Bowel cancer was detected as frequently during one FIT round as during the once-only sigmoidoscopy (0.25% of the approx. 70,000 invited). So-called advanced adenomas (polyps with an increased risk of progressing to cancer) were detected more often during one round of sigmoidoscopy (2.4%) than during one round of FIT (1.4%), but overall after 3 rounds of FIT more cases of advanced adenomas were detected in this group (2.7%). It will take a few years before it is possible to say which of these two screening methods may be the most suitable screening method in Norway. For the time being, it has been decided that the national screening program will start using only

FIT (FIT stands for "faecal immunochemical test". The FIT immunochemical methodology only detects human blood in the stools, not dietary blood from e.g. a juicy steak.

13. *Knudsen MD, Botteri E, Holme Ø, Hjartåker A, Song M, Thiis-Evensen E, Hoff G, Berstad P. Association between lifestyle and site-specific colorectal lesions in screening with faecal immunochemical test and sigmoidoscopy. Dig Liver Disease, 2021;53:353-9*

A national bowel cancer screening program is planned to start in 2022. Since 2012, we have had a study running in Østfold County and Vestre Viken to pilot such a program. 140,000 participants have been drawn from the population register and offered screening with sigmoidoscopy (a flexible «viewing tube» to inspect the bottom approx. 50cm of the intestine) or examination for invisible blood in the faeces (FIT, i.e. "Fecal Immunochemical Test", which only gives results for human blood - not, for example, bloody beef).

This part of the pilot study includes all 14,842 people who were invited for screening in the period November 2012 to September 2013. They also filled in a questionnaire about lifestyle, including smoking, alcohol, exercise, diet. This provided the basis for a score for "unhealthy lifestyle". The objective was to see if any factors and "lifestyle scores" could have predicted findings at colonoscopy of those who had a positive screening test and whether the findings (polyps and cancer) could be expected to be found far down or far up in the colon (e.g. out of reach of sigmoidoscopy) and whether this can provide a basis for a more individualized and tailored screening offer. "Advanced lesions", i.e. cancer or polyps with an increased risk of turning into cancer, were found more frequently in the upper parts of the colon in those who smoked, had a high intake of alcohol and were overweight. This study suggests that an examination of the entire large bowel with colonoscopy (not just sigmoidoscopy) may be a cost-effective screening method for people with a high score for "unhealthy lifestyle". However, larger studies with a slightly different design are needed before conclusions can be drawn.

14. *Schult AL, Botteri E, Hoff G, Randel KR, Dahlen E, Eskeland SL, Holme Ø, de Lange T. The role of bowel symptoms in colorectal cancer screening participants: a cross-sectional study. BMJ Open 2021;11:e048183*

Many people reject attendance to bowel cancer screening if they have no symptoms - which is understandable. But - the basic idea of screening in general is to offer examinations with a view to detect diseases that are common, serious and often do not produce symptoms until the disease has developed far and the prospects for being cured are reduced. Bowel cancer is one such disease.

In this study, the incidence of cancer and "advanced adenomas" (polyps in a stage thought to be just before they can tip over into cancer) was examined among a total of 42,554 individuals who participated in a screening project in southern Norway 2012-2019. Further investigation with a "full colonoscope examination" (colonoscopy) was carried out in the event of a positive screening test for invisible blood in the stools (6495 persons) or when advanced lesions (in 3297 persons) had been detected at screening by sigmoidoscopy (reaching only half-way up the large bowel when compared to colonoscopy). In the group that was screened for blood in the stools, 65% of 299 with screening-detected bowel cancer had no symptoms. It was similar in the sigmoidoscopy group: 60% of 120 people with bowel cancer had no symptoms. Absence of symptoms should not be what determines whether you wish to opt out of an offer of bowel cancer screening.

15. Kværner AS, Knudsen M, Hjartåker A, Henriksen HB, Blomhoff R, Hoff G, Randel KR, Ursin G, Berstad P. *Kost, livsstil og tarmscreening. Norsk Tidsskrift for Ernæring. 2021, nr. 3, s. 12-18*
About 6% of all residents in Norway are diagnosed with bowel cancer during their lifetime. In 2022, a nationwide bowel screening program will be rolled out. Extensive research is ongoing at the Cancer Registry on how to achieve the best possible bowel screening program. In this article, we will give an insight into the ongoing research that deals with dietary and lifestyle habits. We are also discussing the possibility of starting a nationwide health survey among screening participants to follow developments in diet, lifestyle and health in all age cohorts.

16. Randel KR, Botteri E, Romstad KMK, Frigstad SO, Bretthauer M, Hoff G, de Lange T, Holme Ø. *Effects of oral anticoagulants and aspirin on performance of fecal immunochemical tests in colorectal cancer screening. Gastroenterology 2019;156:1642-1649*

A national screening program against bowel cancer in Norway is imminent. Participants will be screened for invisible blood in the stools using an immunochemical test (FIT) which may only give a positive test results on human blood, and not on dietary blood, for example from a bloody beef. Use of blood thinners (anticoagulants) is expected to give more positive test results using FIT. Such medicines are increasingly being used – in 2016 they were used by 5% of Norwegians aged 65-69 and 12% in the 75-79 age group. In addition comes the consumption of Aspirin, which also has a blood-thinning effect.

This study is based on submitted stool samples from 4908 people in the ongoing project piloting a national screening programme. 1,008 of these individuals used Aspirin, 147 warfarin (Marevan), 212 used DOAC (a relatively new group of blood thinners that are supposed to be equivalent to Marevan) and 3,541 did not use any blood thinners. The study showed that in relation to detecting cancer and polyps with a high risk of cancer development, there were more "false positive" test results in the group that used Aspirin or DOAC. Screening program participants should be informed of this increased risk of false positives if they use these types of blood thinners.

2018

17. Knudsen MD, Hjartåker A, Olsen MK, Hoff G, Lange TD, Bernklev T, Berstad P. *Changes in health behavior 1 year after testing negative at a colorectal cancer screening: a randomized-controlled study Eur J Cancer Prev. 2018 Nov 7. [Epub ahead of print] CRISTIN-16 1400423*

A possible disadvantage of screening programs as a health service is that they can give an excessive feeling of security and reduce a conscious or unconscious motivation to take responsibility for one's own health through a healthy lifestyle. As part of an ongoing screening project for bowel cancer in Østfold County and Vestre Viken, 14,842 people aged 50-74, were drawn from the Norwegian Population Register and offered screening for invisible blood in the stools (iFOBT) or flexible sigmoidoscopy (FS). They were asked to fill in a lifestyle form before the screening examination and one year after. 7,000 people of the same age and gender and living in neighboring municipalities with a similar socio-economic profile were asked to fill in the same form and repeat it after a year.

Contribution to fill knowledge gap: One year after screening, there was no unfavorable change in lifestyle habits among screening participants compared to the control group. On the contrary, there was some change in a favorable direction. The iFOBT screening is repeated every 2 years and the long-term impact of screening on lifestyle is still unclear - especially in the iFOBT group.

Consequences and transfer value: Compared with other studies, there is still uncertainty with regard to possible adverse long-term effects of screening in relation to lifestyle.

Screening programs should consider the time of screening as a good opportunity to promote the importance of a healthy lifestyle in relation to the restricted, disease-specific benefit (limited to one condition/disease). A single screening method in a programme does not embrace all lifestyle diseases. The project has transfer value to the planning of screening programmes.

18. Knudsen MD, Hjartåker A, Robb K, de Lange T, Hoff G, Berstad P. *Improving cancer preventive behaviors: A randomized trial of tailored feedback in colorectal cancer screening. Ca Epidemiol Biomarkers Prevention* 2018;27:1442-9 doi:10.1158/1055-9965. EPI-18-0268

Bowel cancer is one of several lifestyle diseases. Bowel cancer screening is to be introduced as a nationwide option in Norway starting in 2019 [later delayed, but started in 2022]. This could be a good opportunity to remind people of the importance of a healthy lifestyle. We are in the midst of testing bowel cancer screening in a so-called pilot study in the municipalities Bærum and Moss. This lifestyle project is part of this pilot project.

Approximately 1,000 participants with normal bowel screening findings filled in a lifestyle questionnaire before the screening examination and after one year. They were divided into three groups by lottery (randomization): One group received a brochure on standard lifestyle advice, one group received individual feedback (encouragement and advice for improvement when justified) based on the first round of questionnaire responses and a third group received no lifestyle advice. Those who received individual feedback had a slight improvement in their intake of fruit and vegetables – best among overweight people. The other two groups showed no changes.

2017

19. de Lange T, Randel KR, Schult A, Knudsen M, Kirkøen B, Jørgensen A, Botteri E, Berstad P, Ursin G, Bretthauer M, Hoff G. *Sigmoidoskopi og testing for blod i avføringen – en sammenlignende screeningstudie. Tidsskr Nor Lægeforen* 2017;137:727-30

Norway is one of the countries in the world with the highest incidence of large bowel cancer. It has tripled since the 1950s. About 6% of women and 8% of men now get this form of cancer. 5-year survival is approx. 65%. Compared to many European countries with a much lower incidence of bowel cancer, Norway has been slow to introduce bowel cancer screening, but we appear to have been in the lead when it comes to research into bowel cancer screening. This article describes the piloting of a national screening programme.

The pilot is designed as a randomized comparison of screening every second year for invisible blood in the stools and once-only sigmoidoscopy (examination of the bottom approx. 50 cm of the intestine with a flexible "intestinal scope"). The first screening round started in 2012 and is expected to be completed during 2018. By then, 140,000 people aged 50-74 will have been offered either sigmoidoscopy once or at least one round of a total of 5 rounds of screening for invisible blood in the stools every two years. The article does not present any results, but refers to useful experiences, the need for quality assurance and that a school for doctors and nurses has been established to improve the quality of the endoscopy service in Norway - not just the part of the service that has to do with screening.

20. Kirkøyen B, Berstad P, Botteri E, Dalén E, Nilsen JA, Hoff G, de Lange T, Bernklev T. *Acceptability of two colorectal cancer screening tests: Pain as a key determinant in sigmoidoscopy. Endoscopy 2017;49:1075-86*

It is planned to introduce a national screening program against bowel cancer in Norway from 2019 [later delayed till 2022]. In a "pilot" of such a program, two relevant methods have been tested: One is examination for invisible blood in the stools with a method that only gives positive test results for human blood (not bloody beef) and the use of a flexible, thin scope (a sigmoidoscope) to inspect the lower approx. 50cm of the intestine. 3,257 individuals aged 50-74 were offered one of the screening methods by drawing lots (randomization) from the population register to find out which method appeared least troublesome and most acceptable to be repeated for the target groups.

After one year, 90% were willing to repeat the test for blood in the stools compared to 80% for sigmoidoscopy. This was due to the women's preference for testing for blood in the stools and more pain experienced with the sigmoidoscopy method for women. 22% of women reported pain during sigmoidoscopy compared to 5% of men. It is already known that more women than men experience pain during colonoscopy, probably due to gender differences in the pelvic anatomy. If sigmoidoscopy or similar internal visualization methods are to be offered to women as a screening method, more consideration must be given to expected pain during the examination.

21. Knudsen MD, Berstad P, Hjartåker A, Gulichsen EH, Hoff G, de Lange T, Bernklev T, Botteri E. *Lifestyle predictors for non-participation and outcome in the second round of faecal immunochemical test in colorectal cancer screening. Br J Cancer 2017;117:461-9*

There may be many reasons why some may not want to participate in screening examinations, e.g. in the ongoing bowel cancer screening project in Østfold County and Vestre Viken. Since bowel cancer is considered a lifestyle disease, it would be very unfortunate if the screening is rigged so that those with the most "unhealthy lifestyle" are the ones who choose NOT to participate. Then the offer should be rigged in a different way - if possible.

In this study, approx. 7,000 of those who took part in the first screening round in Østfold and Vestre Viken for examination of invisible blood in the stools were also asked to fill in a questionnaire about smoking, exercise, diet etc.. 3,114 individuals filled in the form. 17% of these chose not to participate in the 2nd screening round two years later. Smokers, overweight people and those who exercised little were the ones who more often chose not to participate in the second round of the screening - i.e. precisely those who have a slightly increased risk of bowel cancer.

2016

22. Kirkøyen B, Berstad P, Botteri E, Åvitsland TL, Ossum AM, de Lange T, Hoff G, Bernklev T. *Do no harm: no psychological harm from colorectal cancer screening. Br J Cancer 2016;114:497-504, CRISTIN -16 1362535*

The psychological consequences of receiving a message about a positive screening test are explored in this study where 3,213 individuals aged 50-74 years were screened either with a test for invisible blood in the stools or flexible sigmoidoscopy (intestinal scope). The participants' reaction to the results of the screening was recorded using validated questionnaires (HADS and SF-12) before screening and repeated after the results had been communicated to the participants. A positive screening test (suspicion of something being wrong) did not lead to increased anxiety or depression measured with the HADS form and no reduced quality of life

measured with the SF-12. A negative screening test (no suspicion of anything wrong) gave a somewhat reduced anxiety level and a better score for quality of life in the SF-12 form.

Contribution to fill in knowledge gap: None of the observed changes were considered to be of clinical significance, but in particular the positive effect on screening negatives (reduced anxiety) may have an unwanted effect on lifestyle if it leads to feeling «invincible» with reduced motivation for maintaining a healthy lifestyle (diet, exercise, non-smoking - cf. article by Paula Berstad et al, Long-term lifestyle changes after colorectal cancer screening. *Gut* 2015;64:1268-76)

Consequences and transfer value: Important awareness of psychological reactions to screening. Useful in planning screening studies and programmes. The study has transfer value to screening planning.

23. Knudsen MD, de Lange T, Botteri E, Nguyen DH, Evensen H, Steen CB, Hoff G, Bernklev T, Hjartåker A, Berstad P. Favorable lifestyle before diagnosis associated with lower risk of screen-detected advanced colorectal neoplasia. *W J Gastroenterol* 2016;22:6276-86. CRISTIN -16 1385719

In this study, lifestyle factors associated with the risk of bowel cancer (smoking, alcohol intake, physical activity, body mass index and components of the diet) were examined in individuals who participated in bowel cancer screening. Data were collected before participating in the screening. The sum of healthy lifestyle factors that the participants stated to have according to recommendations was inversely associated with the risk of having advanced colorectal neoplasia (high-risk adenoma or large bowel cancer) detected in the screening. The risk was 59% lower in participants who reported following at least five out of six lifestyle advices compared to participants who stated that they follow none or only one lifestyle advice. The factors with the strongest association with high-risk adenoma were smoking and a high alcohol intake (at least 14 and 21 units per week for women and men, respectively).

Contribution to fill knowledge gap: Modifiable lifestyle factors can be used in risk stratification of participants in bowel cancer screening, for example by those with the greatest risk being given preference for invitation in a possible screening programme.

Consequences and transfer value: The study has transfer value to screening planning.

24. Kirkøen B, Berstad P, Botteri E, Bernklev L, El-Safadi B, Hoff G, de Lange T, Bernklev T. Psychological effects of CRC screening: Participants vs/ individuals not invited. *World J Gastroenterol* 2016;22:9631-41 CRISTIN -16 1448433

A possible disadvantage of screening programs as a health service is that they may enhance a feeling of security and lead to a consciously or unconsciously reduced motivation for responsibility for one's own health through a healthy lifestyle. Many submit a positive screening test. There is limited knowledge about the long-term consequences of the anxiety that this can be expected to trigger. In this study, the psychological reactions one year after screening were examined, including the use of a questionnaire that measures anxiety and depression (HADS) and quality of life (SF-12).

Contribution to fill knowledge gap: One year after screening, there was no clinical psychological harm from having received (and investigated) a positive screening test. Among those who were screened with sigmoidoscopy (but not by screening for blood in the stool), scores for anxiety (subclinical) were marginally higher than before screening.

Consequences and transfer value: No transfer value to routine clinics.

Completed PhD's:

25. Benedicte Kirkøyen. Does colorectal cancer screening cause psychological harm? Results from the randomized trial "Bowel Cancer Screening in Norway". University of Oslo 2017. ISBN 978-82-8377- 125-1
26. Markus Dines Knudsen. Lifestyle and colorectal cancer screening by fecal immunochemical test and sigmoidoscopy in a Norwegian pilot study. University of Oslo 2017. ISBN 978-82-8377-129-9
27. Kristin Ranheim Randel. Faecal testing or sigmoidoscopy for colorectal cancer screening? Baseline results from a randomized trial. University of Oslo 2021. ISBN 978-82-8377-859-5
28. Anna Lisa Schult. Performance of two screening tests and barriers to colorectal cancer screening. University of Oslo 2022. ISBN 978-82-8377-992-9