National evaluation of the population-based colorectal cancer screening programme

2018–2021

National evaluation of the population-based colorectal cancer screening programme in the Netherlands

2018-2021

The second evaluation report
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National Evaluation Team for Colorectal Cancer Screening (LECO).

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Summary

A Dutch national colorectal cancer screening programme was launched in 2014 with the goal of reducing colorectal cancer mortality. The programme aims to detect, through a stool test, precursors of colorectal cancer (advanced adenomas), or colorectal cancers at an early stage. Better treatment is then possible than if colorectal cancer is detected by symptoms. This second evaluation report describes the main outcomes of the screening programme in the period 2018-2021.

After a five-year period of phased implementation, the screening programme has been fully implemented since 2019. The entire target population, persons aged 55 to 75, is invited to participate every two years. Due to the COVID-19 pandemic in 2020, the sending of invitations for the screening programme has been suspended for three months to reduce the pressure on the health care system. The resulting backlog was caught up without much delay. From 2018 to 2021, participation in the screening programme was high with a participation rate of 72% over the entire period. Despite the willingness of the overall target population to participate in the screening programme, the participation rate is decreasing slightly in recent years, especially among men younger than 60 years. It is still unknown what causes this decline.

Of those who returned a stool test from 2018 to 2021, 4.4% had a positive result and were referred for an intake interview for colonoscopy. About 85% of those with a positive result eventually underwent colonoscopy. The colonoscopies yielded a total of 70,526 advanced adenomas (precursors of colorectal cancer) and 12,156 colorectal cancers. It is important to detect colorectal cancer at an early stage because early stage cancers can be treated with less invasive treatment. The stool test proved successful in the early detection of colorectal cancers; two out of three cancers found through the screening programme were early-stage (stage I or II) colorectal cancers. The early detection of colorectal cancers is related to the high sensitivity of the stool test for colorectal cancers: 84.4% in the first round and 73.5% in the second round.

After the introduction of the screening programme in 2014, an increase in new colorectal cancer diagnoses was observed. This is because the screening programme has led to earlier detection of cancers that are not yet symptomatic, resulting in a temporary increase in early-stage colorectal cancer in particular. After 2015, the annual number of new cancer diagnoses decreased and in 2019 the number of new colorectal cancer diagnoses was lower than before the introduction of population-based screening for colorectal cancer.

If the screening programme continues to be succesful in the coming years, it is expected that in the long term (2034-2044) the screening programme might annually prevent over 4,300 cases of colorectal cancer and nearly 2,900 deaths from colorectal cancer.

1. Introduction

This evaluation report describes the main outcomes of the Dutch colorectal cancer screening programme over the period 2018-2021. This period was characterized by two important and partly unexpected developments: 1) the phased introduction of the population-based screening programme was completed; and 2) the programme was suspended temporarily due to the COVID-19 pandemic in 2020.

1.1 Phased introduction of colorectal cancer screening

Because the total target population is very large (about 4 million people at the start of the introduction), it was decided to introduce the screening programme in phases, starting in 2014. Each year, more people (per year of birth) were invited, so that the available capacity for the screening programme could be gradually expanded. Especially in the early years, there were problems with the available capacity for follow-up examination, thanks to great efforts from all parties involved, it was still possible to fully roll out the programme within the planned five years in 2019. As a result, there is currently a stable programme; all people in the target population (persons aged 55 to 75 years) are currently invited for the population screening programme every two years. See Chapter 2 for more information on the programme.

1.2 COVID-19

This achievement is all the more remarkable given the outbreak of the COVID-19 pandemic (COVID-19). Indeed, COVID-19 has had important implications for the organization of colorectal cancer screening. To keep health care capacity available for patients with COVID-19 infection, the Ministry of Health, Welfare and Sport (VWS) decided to temporarily stop inviting people to the screening programmes (for breast, cervical and colorectal cancer) on March 16, 2020. The colorectal cancer screening programme cancer was the first programme to be restarted. From mid-May 2020, people who were asked to wait to send in their stool test in March 2020 could again send in their stool test. From June 3, 2020, new invitations were sent out again. However, the available capacity for follow-up examination by means of a colonoscopy was still lower than normal. To be able to invite people in time for a colonoscopy after a positive stool test, fewer invitations were sent out. Moreover, the suspension had created a backlog in sending the invitations. It was therefore decided to temporarily extend the invitation interval for the screening programme from 24 months to a maximum of 30 months. Thanks to good coordination between the screening organization and the colonoscopy centres, it was possible to catch up with the backlog of invitations within due time. During the second and subsequent COVID-19 waves, the screening programme did not have to be suspended again.

Each of the individual chapters of this report addresses the impact of COVID-19 on the relevant colorectal cancer screening outcomes.

1.3 Reading guide

This evaluation report begins with a brief introduction to colorectal cancer and the population-based colorectal cancer screening programme (chapter 2). Next, the most important outcomes of the screening programme are presented, grouped by topic: participation (chapter 3), test characteristics and screening performance (chapter 4), stage, localization and treatment (chapter 5), colorectal cancer incidence and mortality (chapter 6), satisfaction with the colorectal cancer screening programme (chapter 7) and cost-effectiveness (chapter 8). Lastly, important and new developments in colorectal cancer screening are discussed (chapter 9).

2. Colorectal cancer and the national colorectal cancer screening programme

This chapter briefly describes how the disease colorectal cancer develops and the chances of cure after diagnosis of colorectal cancer. It then explains the purpose of screening, which is to detect colorectal cancer early in order to prevent death from colorectal cancer. The chapter ends with a detailed description of the target population, the design of the screening programme and the involved and responsible parties.

2.1 Colorectal cancer

Colorectal cancer is a common form of cancer in the Netherlands (Figure 2.1). The symptoms that people with colorectal cancer may experience are diverse: blood or mucus in the stool, changes in defecation patterns, decreased appetite for food, unintentional weight loss, abdominal discomfort and constant fatigue. However, not everyone with colorectal cancer develops symptoms.

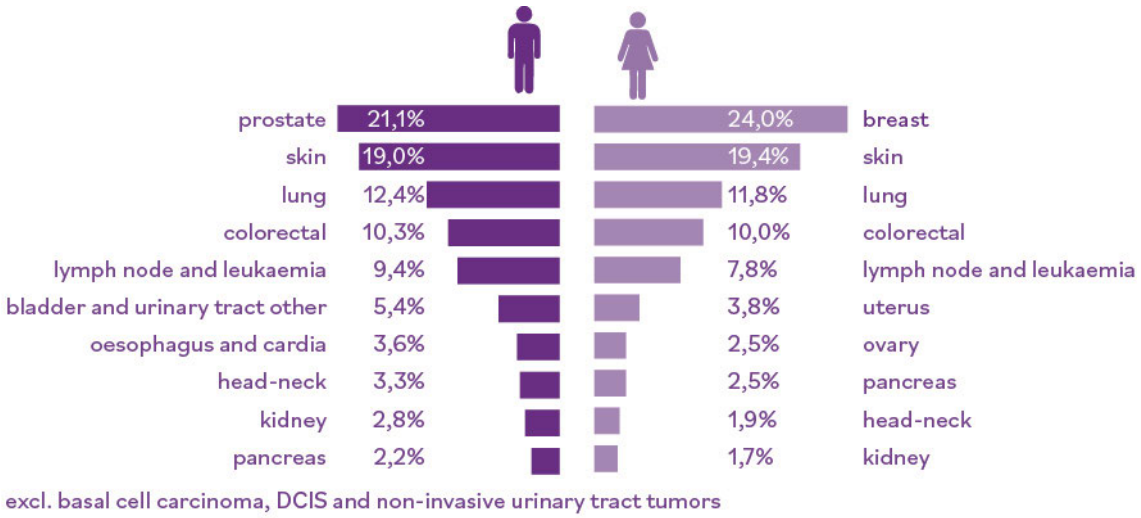

Figure 2.1: Ten most common cancer types in the Netherlands. *In percent in 2021. Source: Dutch Cancer Registry, managed by IKNL (1).*

2.1.1 Origin of colorectal cancer

Colorectal cancer usually begins as a benign polyp. A polyp is a lump on the inside of the bowel. It is estimated that 5-20% of people over the age of 50 have polyps in the colon (2). Most polyps are benign and remain so. Some polyps can become malignant. These polyps are called advanced adenomas. To determine whether an advanced adenoma is present, the tissue must be examined by a pathologist. Advanced adenomas are polyps larger than 1 centimetre and/or with specific features in the tissue. An advanced adenoma is a preliminary stage of colorectal cancer and is therefore counted as a relevant finding of the colorectal cancer screening programme. It takes approximately 15 years for a polyp to develop into colorectal cancer (3,4).

2.1.2 Stages of colorectal cancer

In colorectal cancer, four stages are distinguished. The different stages indicate how advanced the disease is. The stage is determined by how far the tumor has advanced into the bowel wall and whether there are metastases in the lymph nodes or anywhere else in the body. At stage I, the tumor is located only in the intestinal wall; at stage II, the tumor grows through the intestinal wall. At stage III, the tumor grows through the intestinal wall, and metastases in local lymph nodes are found as well. At stage IV the tumor grows through the intestinal wall and metastasizes to other organs in the body. Chapter 5 presents the results of the stage distribution of colorectal cancers found within the population screening programme.

2.1.3 Chance of survival

People with early-stage colorectal cancer (stages I and II) require less invasive treatment and are less likely to die than those with late-stage colorectal cancer. On average, of patients who developed colorectal cancer from 2010 to 2016, 66% were still alive after five years (1). This was 95% for patients with stage I colorectal cancer and only 12% for patients with stage IV colorectal cancer.

2.2 The colorectal cancer screening programme

A colorectal screening programme was launched in 2014. This programme aims to detect colorectal cancer at an early stage through a stool test. If colorectal cancer is found at an early stage, treatment is less invasive and the number of people who die from colorectal cancer may decrease. The screening programme also allows for removal of (advanced) adenomas in the colon or rectum as a precautionary measure, thus preventing colorectal cancer.

2.2.1 Target population

Based on the advice of the Health Council, it was decided at the start of the programme to offer the screening every two years to persons aged 55 to 75 years in the Netherlands. In order to formulate this advice, the Health Council carefully weighed the harms and benefits of screening at younger and older ages at the time (explanation: see box).

Considerations for defining the target population

The Health Council carefully weighed the harms and benefits of screening at younger and older ages before introduction of the nationwide colorectal cancer screening programme. If younger people (<55 years of age) were invited, more people would have to undergo a stool test to prevent a small number of colorectal cancers. These participants do become burdened by, for example, the uncertainty of the results. If older people (>75 years) were invited, colorectal cancer would be found more often, because the risk of colorectal cancer increases as people age. However, the chance of dying from something other than colorectal cancer (such as cardiovascular disease) also increases with age. Screening older people means that older people will receive (intensive) treatment for colorectal cancer. In some cases, colorectal cancer may not have been the cause of death. The treatment was then "unnecessary". Older people are also more likely to have complications from the colonoscopy or treatment (5).

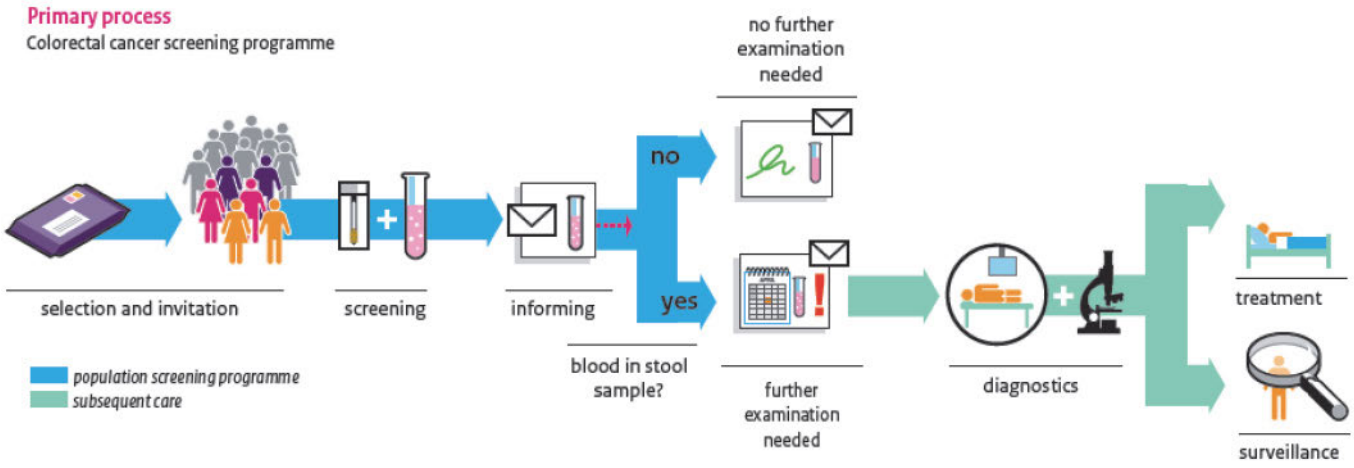

Figure 2.2: Flow chart colorectal cancer screening programme. *Source: RIVM*

2.2.2 The stool test

Figure 2.2 shows the different steps of the colorectal cancer screening programme. Everyone who is invited for the first time first receives a preliminary invitation and three weeks later an invitation set. All subsequent times one receives only the invitation set. The invitation set consists of an invitation letter, a leaflet, a stool test with instructions, a bag and a return envelope. People are asked to collect some stool, put some of it in a test tube and send that tube in the bag to the laboratory. There the stool is examined for the presence of haemoglobin (Hb), a blood protein. In fact, advanced adenomas and colorectal cancer can cause minor bleeding, which is not always visible to the naked eye. Thus, the presence of Hb may indicate the presence of colorectal cancer or an advanced adenoma. In the Netherlands, we speak of a positive result of the stool test with an Hb level exceeding 47 micrograms per gram (µg Hb/g) of stool (5).

All participants are sent the test result in writing. Participants with a positive result (Hb level exceeding 47 µg Hb/g stool) also automatically receive an appointment for an intake interview at a hospital or independent treatment centre. Of those who have communicated the details of their general practitioner (GP) by telephone or via the client portal, the GP also receives the positive result.

The first invitation is called invitation round one. Subsequent invitations are called follow-up rounds. In the period from the introduction of the screening programme through 2021, participants have been invited a maximum of four times. Therefore, this report presents data from a maximum of four rounds.

2.2.3 The follow-up examination: the intake interview and the colonoscopy

The purpose of the intake interview is to assess whether there are reasons not to perform a colonoscopy, to collect (medical) information relevant prior to the examination, and to inform the participant about the examination. At the intake interview, some people with a positive test result are advised not to have further examination, for example because they are already treated for a bowel disease or have other (serious) illnesses.

All other participants are offered a colonoscopy. During colonoscopy, a flexible tube with a light and a camera is inserted through the anus into the bowel and the doctor looks at the colon and rectum. There are then two options:

1. No relevant abnormalities or only small polyps are found. These small polyps are not considered a relevant finding in the context of the screening programme. Small polyps are removed immediately and the tissue is further examined by a pathologist. Participants receive the results of the colonoscopy after approximately one week.
2. Relevant abnormalities are found: colorectal cancer or an advanced adenoma. If possible, an early-stage colorectal cancer or advanced adenoma is removed immediately during the colonoscopy. In all other cases, a biopsy (piece of tissue) is taken. All the tissue taken is examined by a pathologist. Depending on the stage of colorectal cancer, the follow-up will be discussed with the client.

2.2.4 Organization of the population screening programme.

The Ministry of Health, Welfare and Sport commissioned the national colorectal cancer screening programme. The Ministry is advised by the Health Council of the Netherlands. Funding is provided by the Public Health Subsidy Scheme, which means that participation is free for everyone. The center for population-based screening, part of the National Institute for Public Health and the Environment (RIVM), is in charge of the implementation of the programme on behalf of the Ministry of Health, Welfare and Sport. The RIVM is responsible for the national monitoring of the screening programme and the connection to health care. The RIVM is also responsible for quality control and identifying bottlenecks in the programme's primary process.

The screening organization, *Bevolkingsonderzoek Nederland,* is responsible for the implementation of the colorectal cancer screening programme. This organization takes care of sending the invitations with the stool tests. *Bevolkingsonderzoek Nederland* uses data from the national *Basisregistratie Personen* (BRP). The screening laboratories, which analyse the stool samples, pass on the results to the screening organization, which then takes care of sending a result letter to the participants. The screening organization also makes the appointment for the intake interview. The hospitals and independent treatment centres involved conduct the intake interviews and colonoscopies. The pathology laboratories evaluate the tissue taken during the colonoscopy.

3. Participation in the colorectal cancer screening programme

This chapter discusses participation in the colorectal cancer screening programme. The participation rate is an important outcome, as it affects the effectiveness of the programme. At higher participation rates, higher decreases in disease burden and colorectal cancer mortality can be expected.

3.1 Invitations and participation in the screening programme (stool test)

Between 2018 and 2021, 8.6 million invitations were sent out. Of these, 6.1 million (72%) stool tests were returned. From 2014 to 2017, 3.9 million (73%) stool tests were returned.

Figure 3.1 shows participation rates by invitation round by calendar year for men and women. The participation rate differs for men and women, by age and by invitation round. Most striking is the higher participation of women compared to men. In addition, the participation rate is higher in the subsequent rounds than in the first round. This may be because people in the subsequent rounds are older; older people are more likely to participate in the screening programme than are younger people. Another explanation may be that people who in a previous invitation round permanently opted out of the programme are not invited again to participate.

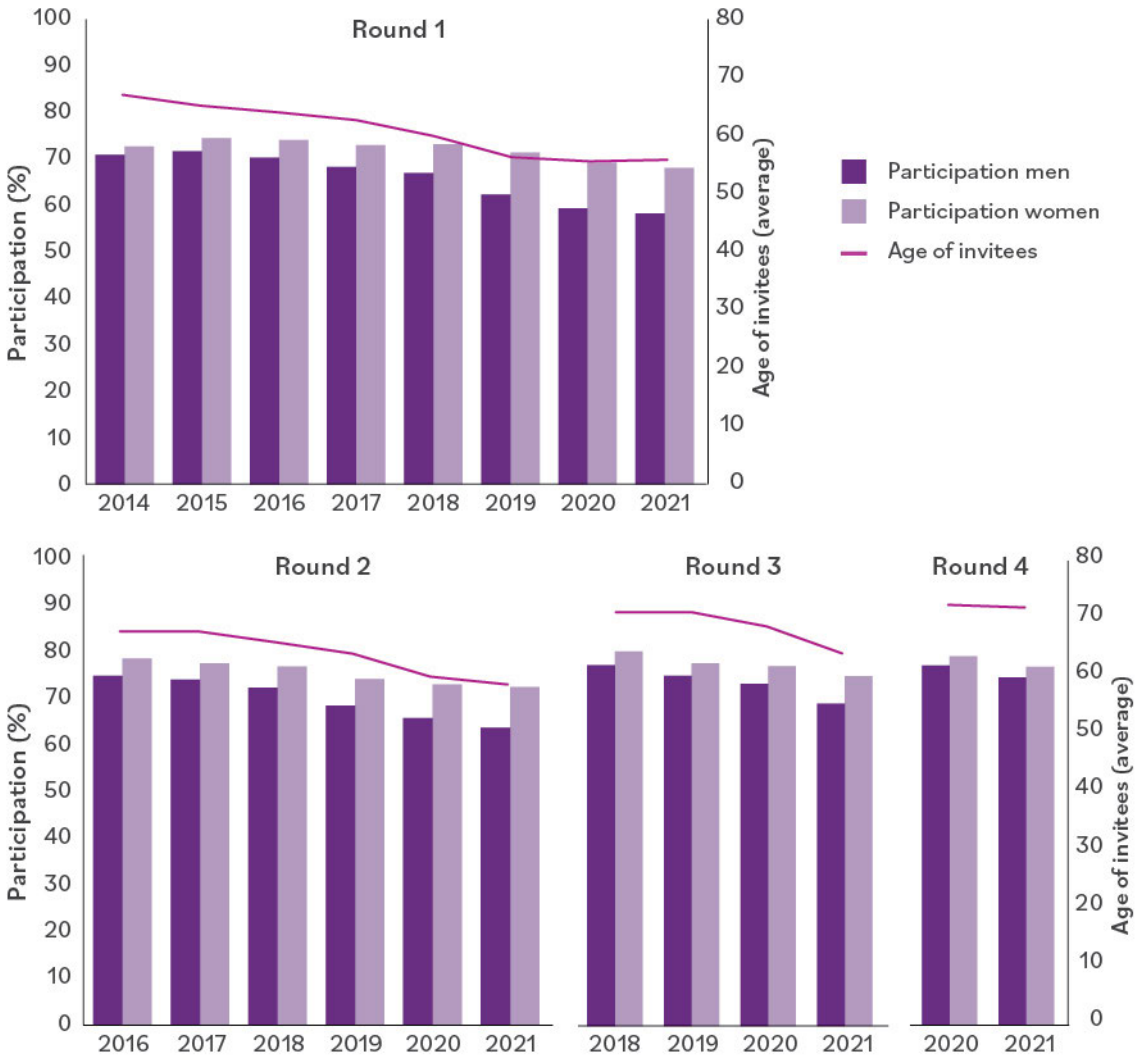

Figure 3.1: Participation and mean age of men and women by invitation round by calendar year

The most recent invitation years show a decrease in participation (Figure 3.1). This decrease can only be partially explained by the fact that the average age of those invited was lower. The real reasons causing this decrease are currently unknown. The decrease in participation was mainly visible in the first round; in 2021, participation decreased to 58.2% for men and to 68.0% for women. However, overall participation in the screening programme still meets the European guideline: at least 65% of the target population participates (6). Only for men in round 1, participation has been lower than the recommended 65% since 2019: 62% in 2019, 59% in 2020 and 58% in 2021.

3.2 Repeat participation

The majority of people who participate in one of the invitation rounds also participate in the next round; this is around 93% (Figure 3.2). We call this 'repeat participation.' Like initial participation, repeat participation has been declining in recent years (Figure 3.2). The reason for the lower repeated participation rate is not clear.

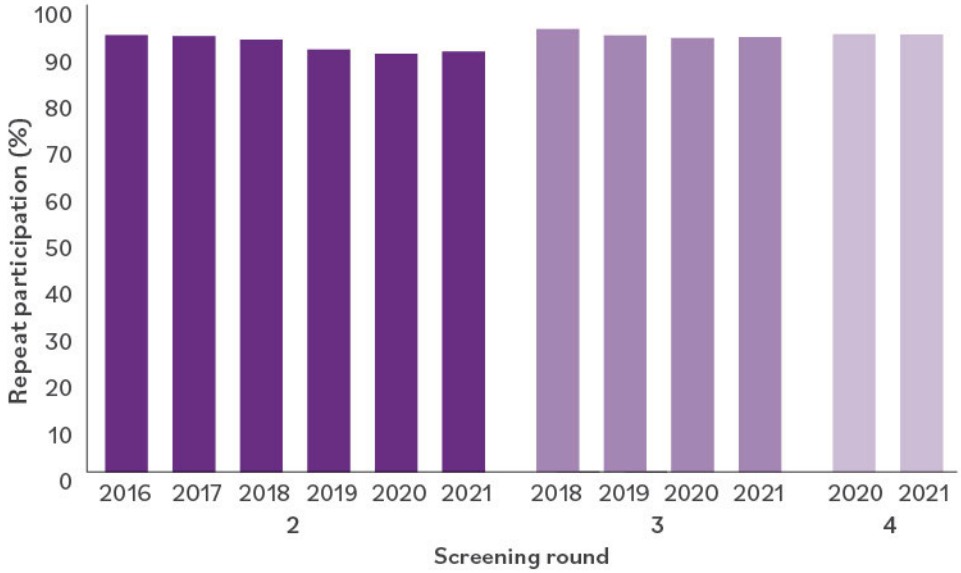

Figure 3.2: Repeat participation by invitation round by calendar year. *Bars represent the % of people who participated in the given round who also participated in the previous round.*

3.3 Participation in colonoscopy

Before participants undergo a colonoscopy, they are first invited for an intake interview. At the intake interview, in 4.7% of cases, the gastroenterologist advises against undergoing a colonoscopy because of comorbidity (the presence of other diseases). In addition, 1.0% of participants with a positive stool test were found to already have (had) colorectal cancer and/or had recently undergone a colonoscopy. These are reasons not to perform a colonoscopy. This group of people actually should not have participated in the screening programme. To limit this, the invitation leaflet was modified in January 2021. It is now explained that in some cases it may be less beneficial to participate in the screening programme, and people are advised to discuss this with their GP.

From 2018 to 2021, about 230,000 (85%) of people with a positive stool test underwent a colonoscopy. The percentage was slightly higher than that from 2014 to 2017, when 81% had a colonoscopy performed. This is partly due to a change in the registration of colonoscopy findings, which means that from 2019 more colonoscopies are being counted in, leading to higher participation rates for colonoscopy. In addition, people were younger than in the 2014 to 2017 period. Younger people are more often eligible for a colonosocpy compared to older people, as older people are more likely to have comorbidities.

If people undergo a colonoscopy at a hospital that is not connected to the national information system of the colorectal cancer screening programme, this colonoscopy is not registered in the national screening database and therefore not included when calculating the participation rate. With the help of the national pathology database (PALGA), it was investigated how many people nevertheless underwent a colonoscopy that was not registered in the national screening database. This turned out to be the case for about 2.5% of the people with a positive stool test. Thus, in reality, about 87.5% of the people with a positive stool test participate in the colonoscopy. With this, the participation rate approaches the European guideline of 90% (8).

3.4 Effects of COVID-19 on participation

The effect of COVID-19 was also visible in the willingness to participate in colorectal cancer screening or colonoscopy. During the first COVID-19 wave (March 2020 to June 2020), fewer people participated in the screening programme than before the first COVID-19 wave, both in the first round (decrease from 68.5% to 63.2%) and the repeated participation in the subsequent rounds (decrease from 92.3% to 89.3%). After the first COVID-19 wave, repeated participation recovered again (92.0%). Participation in the first round remained below pre-COVID-19 levels (65.9%).

Participation in colonoscopy decreased slightly during the first COVID-19 wave, from 89.4% to 88.7% for those with a positive stool test in the first round and from 87.4% to 86.8% for those with a positive stool test in a subsequent round. Like participation in the stool test, participation in the colonoscopy recovered for people in the subsequent round (87.9%) but not for people in the first round (86.4%).

3.5 Motives for (non-)participation

3.5.1 Motives for (non-)participation in stool test

A customer satisfaction survey was conducted in 2020 to understand the motives for participation in the Dutch colorectal cancer screening programme (8). People participate because they find it important that colorectal cancer is detected early, because they like being checked to make sure everything is fine, and because family members or loved ones suffer or have suffered from cancer. Only limited data are available on people who do not participate. In a very small group of 26 non-participants who took part in the customer satisfaction survey, it turned out that about half of them consider colorectal cancer screening important, but do not participate because they are already under treatment or have recently undergone a colonoscopy (8).

Section 3.1 describes that men and younger people are less likely to participate in the screening programme. Other factors associated with non-participation in the stool test were previously unknown. To gain more insight into this, data of invitees were linked to demographic data in the register of Statistics Netherlands (CBS). This showed that people are less likely to participate in screening if they have a lower income, they do not live with a partner, or if they have a migration background (Figure 3.3). People with a Moroccan migration background are the least likely to participate. People with lower levels of education and those receiving benefits also participate less likely.

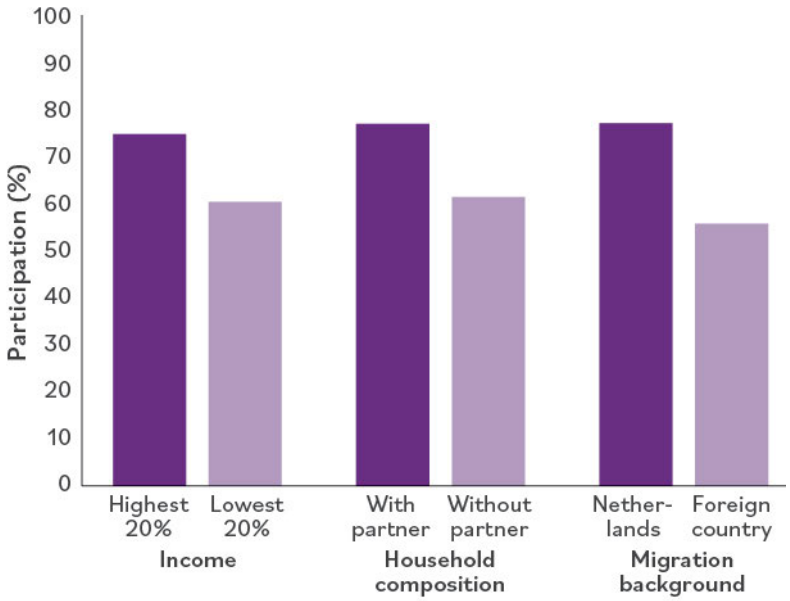

Figure 3.3: Participation by demographic characteristic

3.5.2 Motives for (non-)participation in colonoscopy

The reason for (non-)participation in colonoscopy was also studied using a questionnaire survey. Factors associated with participation in the colonoscopy were the GP's conviction and knowledge, a previous colonoscopy experience, concerns about cancer, confidence in the stool test and the screening organization, and a recommendation from someone else (medical or non-medical) to have the colonoscopy done (7).

The main reason for not undergoing a colonoscopy was doctor's advice not to participate because of comorbidities (7). Other factors associated with non-participation included feeling at low risk for colorectal cancer, difficulty in making decisions, advice from a non-medical person not to have a colonoscopy, and referral to an unfamiliar hospital to have the colonoscopy. The less knowledge people had about colorectal cancer, colorectal cancer screening and colonoscopy, the more often people had unjustified certain beliefs or fears, such as believing they could feel colorectal cancer themselves (7).

4. Test characteristics and screening performance

This chapter is an evaluation of the performances of the stool test and colonoscopy. It also discusses the effects that the COVID-19 pandemic has (had) on these outcomes.

4.1 Referrals for follow-up examination

Chapter 2 described that participants with positive stool test results (≥ 47 µg Hb/g stool) were referred for colonoscopy. From 2018 to 2021, 270,547 (4.4%) participants had a positive stool test. In the period of the previous evaluation report (2014 to 2017), this was 223,043 (6.0%) participants. The referral rate decreased from 2018 to 2021 as relatively more participants were invited to a subsequent round. A decrease in the referral rate in the subsequent round is explained by the fact that some of the participants with colorectal cancer or advanced adenoma, or with blood in the stool from another cause (e.g., chronic colitis) were already detected in the first round. Participants that underwent a colonoscopy will not be invited back to the screening programme (for 10 years). Because colorectal cancer is more common in men than in women and the sensitivity of the test is higher for men, the referral rate for men is higher than for women: 5.3% for men and 3.6% for women for all invitation rounds.

The referral rate differed for people who participated in the first round or a follow-up round. In the first round, the referral rate was 4.7%; the referral rate was higher for men (5.7%) than for women (3.7%). The referral rate in the first round for the period 2018 to 2021 was lower than the referral rate of 6.1% in the period 2014 to 2017. This is because first-round invitees were on average younger in the 2018 to 2021 period than in the 2014 to 2017 period. At younger ages, blood in the stool is less likely to be found. The referral rate in the subsequent rounds was 4.3%, with again a higher referral rate for men (5.2%) than for women (3.6%). The referral rate in the subsequent rounds for the period 2018 to 2021 was also slightly lower than the 4.5% referral rate in the period 2014 to 2017. In 2021, the referral rate was higher than that in previous years in both the first round and subsequent rounds (Figure 4.1). It is still unclear what caused this.

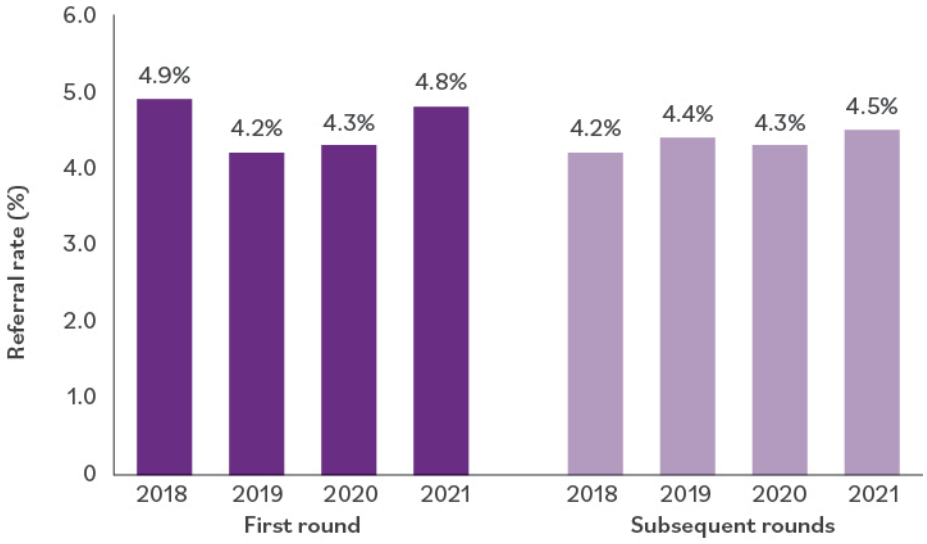

Figure 4.1: Referral rates

4.2 Positive Predictive Value and Detection Rate

The goal of the colorectal cancer screening programme is to detect colorectal cancer at an earlier stage or precancerous stage. The detection and removal of advanced adenomas can prevent colorectal cancer. From 2018 to 2021, colorectal cancer was found in 12,156 participants and advanced adenoma in 70,526 participants. Thus, a total of 82,682 participants had a relevant finding, i.e., colorectal cancer and/or advanced adenoma, at colonoscopy. The positive predictive value (PPV), the percentage of people with a colonoscopy in whom a relevant finding was found, was 36%. The detection rate, the number of participants in whom a relevant finding was found, thus came to 13 per 1,000 participants.

The PPV and detection rate were lower in the period 2018 to 2021 than in the period 2014 to 2017. The main reason for this is that the participants were younger. Like the referral rate, the PPV and detection rate were also lower in the subsequent rounds than in the first round (Table 4.1).

Table 4.1: Detection rates and Positive Predictive Value for colorectal cancer and advanced adenomas.

	Detection rate (per 1,000 participants)		Positive predictive value	
	2014 - 2017	2018 - 2021	2014 - 2017	2018 - 2021
Total	25	13	52%	36%
First ronde	29	17	53%	42%
Subsequent rounds	16	13	41%	34%

4.3 Interval cancers and sensitivity stool test

4.3.1 Interval cancers

Because the stool test is not perfectly sensitive – in other words, it is not 100% sensitive – it may happen that participants with a negative test are found to have developed colorectal cancer before the next invitation round. We call these cancers interval cancers. The interval cancers can only be identified through a link between the Dutch Cancer Registry (NKR) and the national screening database. This causes some delay, which results in reporting over a different time period.

Of the more than two million participants between 2014 and October 2017 with a negative result in the first screening round, 2,256 participants developed colorectal cancer before the second round of invitations. Thus, the risk of interval cancer was 9.8 per 10,000 participants. This can be compared to the colorectal cancers found after a positive stool test. In the first round, 12,183 colorectal cancers were found after a positive result; 52.9 colorectal cancers per 10,000 participants. Of the 703,895 participants with two consecutive negative stool test results, 675 participants developed colorectal cancer before the third round. Thus, the risk of an interval cancer was slightly lower in the second round than in the first round: 9.6 interval cancers per 10,000 participants. In the second round, 1,874 colorectal cancers were found after a positive result; 26.6 colorectal cancers per 10,000 participants found through the screening programme (9).

4.3.2 Sensitivity of the stool test

With the information on interval cancers and colorectal cancers found through the screening programme, it can be determined how well the stool test is able to detect colorectal cancer. This is the sensitivity of the stool test. The sensitivity of the stool test was 84.4% in the first screening round and 73.5% in the second screening round (Figure 4.2). It is also known from previous research that the sensitivity of the stool test decreases after the first screening round (10,11). The decrease in sensitivity most likely has to do with the fact that relatively more colorectal cancers will be found in the first screening round than in the subsequent screening rounds, while the proportion of interval cancers among participants with a negative stool test remains the same. Regarding the effectiveness of the national colorectal cancer screening programme, it is important that the sensitivity of the stool test be well monitored over time.

The sensitivity of the stool test is higher in men than in women. This difference was evident in the first round, with a sensitivity of 86.6% in men and 81.0% in women (Figure 4.2). In the second round, the difference between men and women decreased, with a sensitivity of 74.4% in men and 73.0% in women.

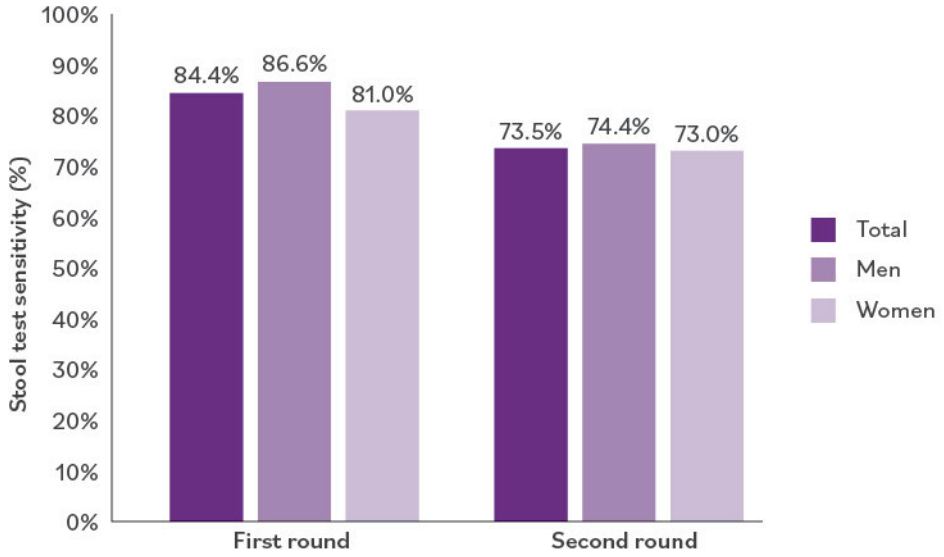

Figure 4.2: Stool test sensitivity. *Results based on data from participants between 2014 and October 2017.*

4.4 Effect of COVID-19 pandemic on test characteristics and screening performance

The first COVID-19 wave hardly affected the referral rate, both in the first round and in the subsequent rounds. There was, however, a small decrease in the PPV of colorectal cancer and advanced adenomas due to the COVID-19 pandemic. In the first round, the PPV decreased from 40.0% before the first COVID-19 wave to 35.3% during and 37.6% after this wave. In the subsequent rounds, the PPV decreased from 34.7% before the first COVID-19 wave to 31.8% during and 32.0% after. The number of interval cancers did not differ between the periods before, during and after the first COVID-19 wave. Temporarily extending the invitation interval from 24 months to a maximum of 30 months did not affect the referral rate, the PPV and the number of interval cancers.

4.5 Interval cancers after colonoscopy

Participants with no polyps or one small polyp at colonoscopy (a negative colonoscopy result) are invited by protocol to return for colorectal cancer screening after 10 years. Of the more than 35,000 participants who had a colonoscopy between January 2014 and April 2017, 24 were diagnosed with colorectal cancer after their negative colonoscopy. When the risk of colorectal cancer in participants with a negative colonoscopy was compared with the risk in participants with a negative stool test result, the risk of colorectal cancer after a negative colonoscopy after about 2.5 years appeared to be the same as the risk of interval cancer within two years after a negative stool test (Figure 4.3). This estimate is surrounded by a wide margin of uncertainty because the number of participants who developed colorectal cancer after a negative colonoscopy was small, and participants with a negative colonoscopy were followed for a mean of only 1.6 years. A planned study will investigate whether participants with a negative colonoscopy should perhaps be invited back for colorectal cancer screening earlier than 10 years. The planned study is explained in more detail in Chapter 9 .

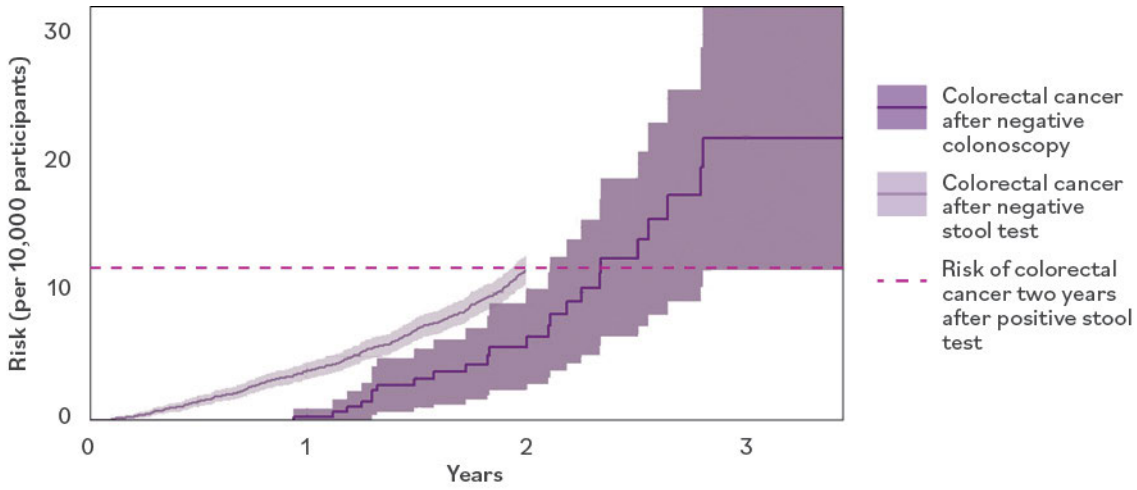

Figure 4.3: Risk of colorectal cancer after negative colonoscopy or negative stool test

4.6 Complications and other disadvantages of the screening programme

4.6.1 Complications after colonoscopy

As with any other medical examination, complications may occur during a colonoscopy. Complications that occur within 30 days of the colonoscopy are considered complications related to the colonoscopy. Complications are defined by severity and type of complication. Severity can be represented as mild, moderate or severe. If there was no hospitalization, or an admission of less than 4 days, it is called a mild complication. Moderate complications require hospitalization from 4 to 10 days. A complication is severe if the complication resulted in hospitalization longer than 10 days. A fatal complication is one that has resulted in the death of the patient. In the Netherlands, a national registry of complications after colonoscopy is kept, the Dutch Registration of Complications in Endoscopy (DRCE).

From 2018 to 2021, each year an average of 321 colonoscopy complications were registered. This is equivalent to 56 complications per 10,000 colonoscopies. The most common complication, accounting for almost 75% of all complications, is bleeding. Most complications from 2018 to 2021 were mild (53%) or moderate (40%). The numbers of mild and moderate complications cannot be compared with those in the period 2014 to 2017 because complications were registered differently then. For 80 colonoscopies severe complications were registered in the period 2018 to 2021. This is equivalent to 3.5 serious complications per 10,000 colonoscopies. The number of serious complications has decreased compared to 2014 to 2017. Then, 7.4 in 10,000 colonoscopies were associated with a severe complication. The reason for this is not well understood, but the decrease may be due to fewer adenomas being found during colonoscopy, and these adenomas being smaller.

From 2018 through 2021, there were eight fatal complications (0.3 per 10,000 colonoscopies). From 2014 to 2017, there were four fatal complications (0.3 per 10,000 colonoscopies). It is not clear whether a death after colonoscopy is always recorded because the death is not always linked to the colonoscopy. Therefore, additional information was used to calculate the risk of having a fatal complication. This showed that the risk of a fatal complication is estimated at 0.23 to a maximum of 0.91 per 10,000 participants undergoing a colonoscopy within the screening programme (12).

4.6.2 Concerns after colonoscopy

Over half of the participants who underwent a colonoscopy were found to have no abnormalities or only small polyps in the bowel. Although this is a reassuring result, undergoing the colonoscopy still appears to have an impact on this group of participants. It was found that one in six participants were still very concerned about cancer six months after the stool test; however, they generally did not appear to regret their participation (13).

5. Stage distribution, localization and treatment of colorectal cancers

The national colorectal cancer screening programme aims to reduce colorectal cancer mortality and the burden of disease for people with colorectal cancer. To achieve this, it is important that colorectal cancers are found early. People with early-stage colorectal cancer have a lower chance of dying from the disease than those with late-stage colorectal cancer. In addition, treatment for early-stage colorectal cancer is less invasive.

5.1 Stage distribution

Information on the stage distribution of colorectal cancer can be obtained from the Netherlands Cancer Registry (NCR), which requires a link between the NCR and the national screening database. This causes some delay, as with the registration of interval cancers. This evaluation report therefore reports the stage distribution of colorectal cancers found from 2014 to 2019.

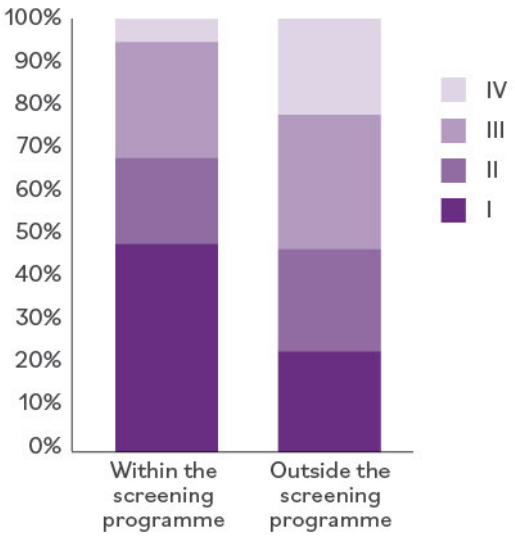

Figure 5.1: Stage distribution of colorectal cancers Netherlands. *2014 to 2019*

The screening programme showed to be effective in detecting colorectal cancer at an early stage. Of colorectal cancers found through the programme from 2014 to 2019, 67% were detected in early stages (stages I and II). Of colorectal cancers detected outside the colorectal cancer screening programme, 46% were detected at an early stage (Figure 5.1) (14). The explanation for this is that colorectal cancers are usually found when there are symptoms and, unfortunately, colorectal cancer often does not cause symptoms until a late stage. The proportion of early-stage colorectal cancers detected through the screening programme is approximately the same in the first, second and third rounds (Figure 5.2).

A colorectal cancer detected between two invitation rounds is called an interval cancer (see Chapter 4). These interval cancers are more often diagnosed at a later stage than the colorectal cancers found through the colorectal cancer screening programme. In the first round and the second round, 43% of interval cancers were found at an early stage (Figure 5.2).

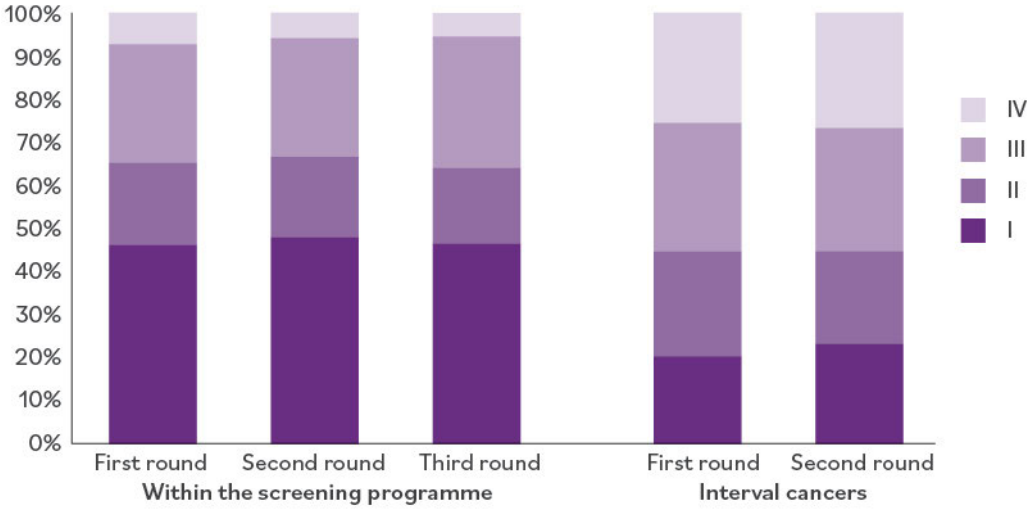

Figure 5.2: Stage distribution of colorectal cancers within the colorectal cancer screening programme vs. Interval cancers

5.2 Localization

The cancers found through the colorectal cancer screening programme were more often located on the right, and less often on the left side of the colon than colorectal cancers found by other means (Figure 5.3). This may be because colon cancers in the right part of the colon are further away from the anus (the exit). Blood that originates here is more likely to be degraded before it is excreted. This blood is then not detected by the stool test. In addition, certain polyps are more common in the right part of the intestine, which are less likely to bleed (1,2). A consequence of this is that interval cancers are more often located on the right side of the colon than colorectal cancers found through screening (Figure 5.4).

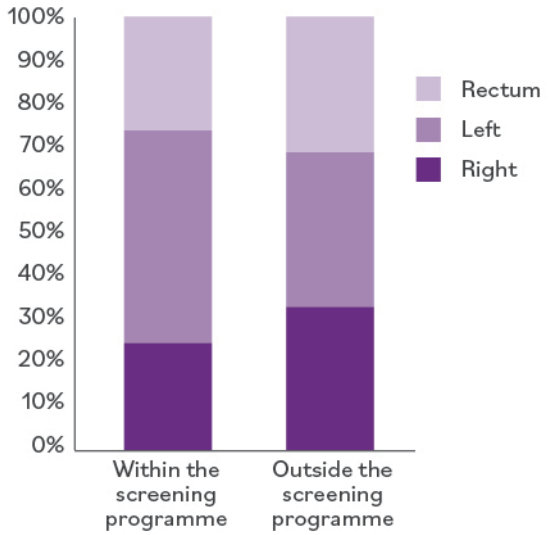

Figure 5.3: Localization of colorectal cancers Netherlands. *2014 to 2019*

The proportion of colorectal cancers on the left side of the colon decreased in the second and third rounds of the colorectal cancer screening programme, while the proportion of colorectal cancers on the right side of the colon increased (Figure 5.4). A large part of the colorectal cancers on the left side of the colon were probably found in the first round because they are easier to detect than colorectal cancers in the right side of the colon.

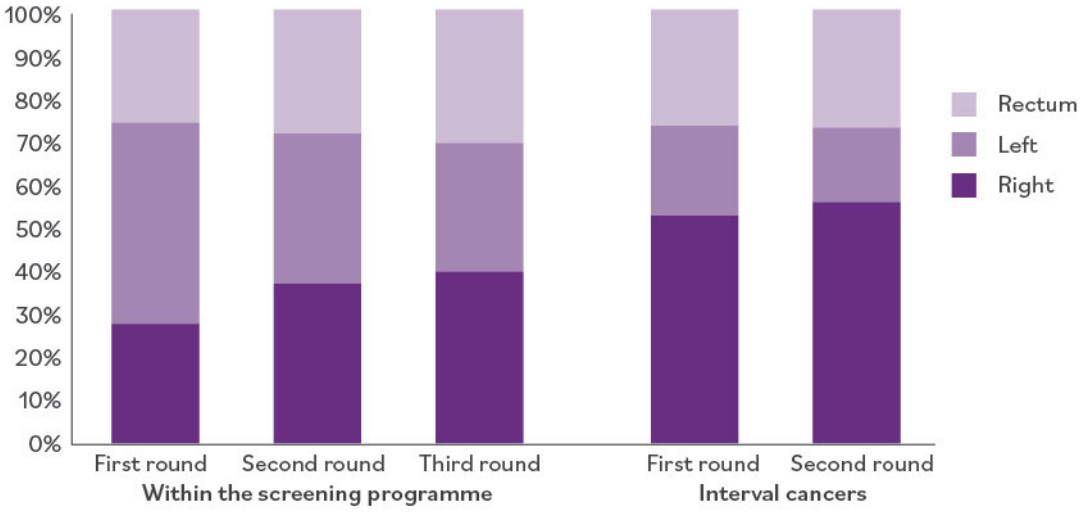

Figure 5.4: Localization of colorectal cancers within screening programme vs. Interval cancers

5.3 Treatment

Early-stage colorectal cancers require less invasive treatment than late-stage colorectal cancers. Local excision (i.e., during a colonoscopy) is the least invasive treatment for colorectal cancer. Removal by surgical resection is more invasive because part of the colon is removed. Late-stage colorectal cancer usually requires a combination of systemic therapy and/or radiotherapy and/or surgical resection. If surgical resection is not possible because of distant metastases, then usually only systemic therapy is given. Examples of systemic therapy include chemotherapy, targeted therapy or immunotherapy. Colorectal cancers found through the colorectal cancer screening programme could be removed by local excision in 17.4% of cases. For colorectal cancers found outside the screening programme, this was 4.9%. Local excision was also more often possible for rectal cancers found through screening: 22.1% compared to 9.1%. Figure 5.5 shows that additional treatment was less often needed for colorectal cancers detected through screening.

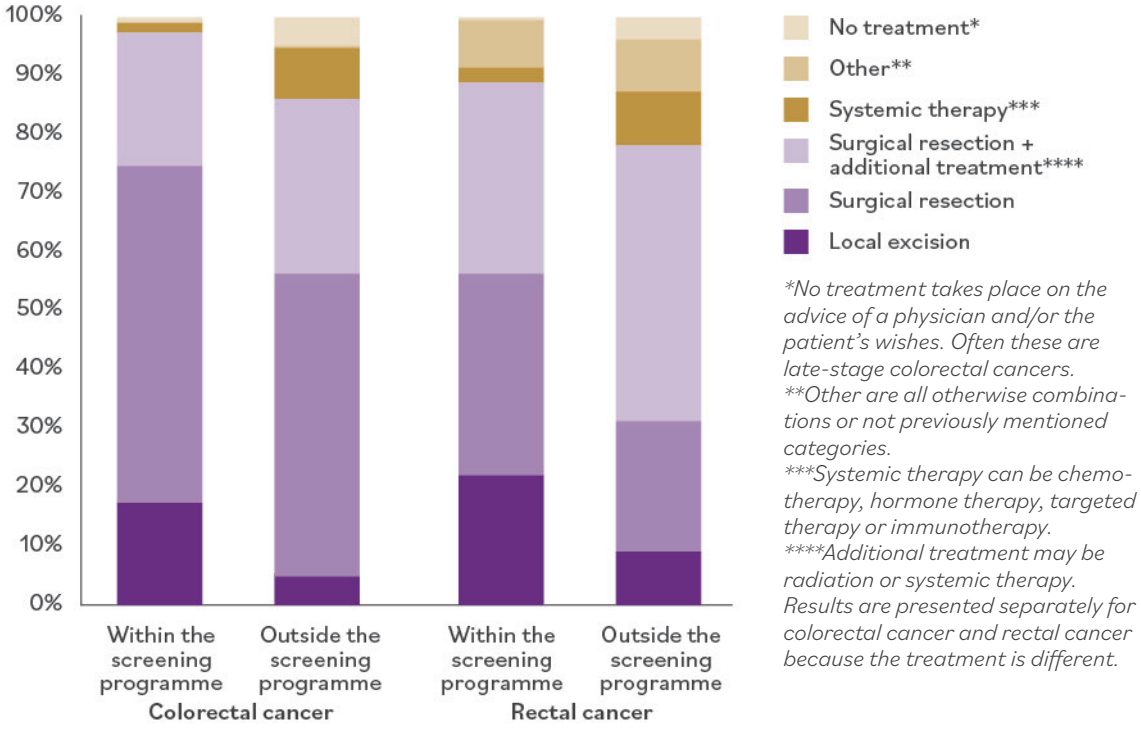

Figure 5.5: Treatment of colorectal cancers

When only considering cancers at the same stage, less invasive treatment is more often required when the colorectal cancer is detected through the screening programme(14,17). Stage I colorectal cancers are more often removed by local excision when detected through the screening programme compared to cancers detected outside screening the screening programme (34.4% compared to 20.0% for colorectal cancers and 48.1% compared to 38.5% for rectal cancers) (Figure 5.6). The reason for this cannot be analysed based on current information and needs further investigation.

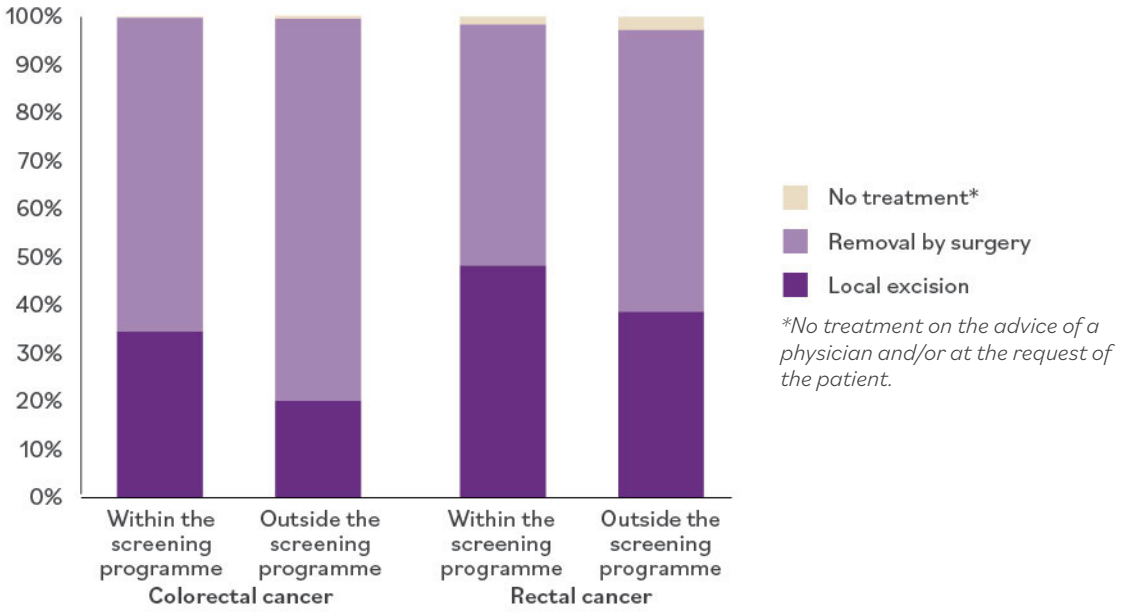

Figure 5.6: Treatment of stage I colorectal cancers

6. Colorectal cancer incidence and colorectal cancer mortality

The colorectal cancer screening programme detects and removes advanced adenomas before colorectal cancer develops. In addition, colorectal cancer is detected at an earlier stage. As a result, mortality from colorectal cancer is expected to decrease. However, this will not be seen for many years after the introduction of screening. In the meantime, the annual number of new cases of colorectal cancer (the incidence) and mortality predictions give an indication of what can be expected in the long term.

6.1 Incidence of colorectal cancer

The incidence of colorectal cancer is defined as the number of new cases in a specific time period, often a 1-year period. Shortly after the introduction of the colorectal cancer screening programme, there was a temporary increase in the incidence of colorectal cancer in persons aged 55 years and older, due to the fact that through the programme colorectal cancers were detected that did not cause symptoms at that time (Figure 6.1). Thereafter, the incidence declined from 14,557 new colorectal cancer diagnoses in 2015 to 11,440 new colorectal cancer diagnoses in 2019 (1). This is slightly lower than the incidence before the introduction of colorectal cancer screening: 11,658 colorectal cancers in 2013. For men, the incidence dropped by 27% between 2015 and 2019; for women, the incidence dropped by 14%. This difference is perhaps explained because the stool-based test is more sensitive for detecting colorectal cancer in men than in women (see **Chapter 4**). In 2020, the programme was suspended for some time because of the COVID-19 pandemic. Some of the colorectal cancers that would normally have been found in 2020 were therefore probably not diagnosed until 2021, which can be seen in the slight increase in incidence in 2021. In 2020, the colorectal cancer incidence was 9,947 and in 2021, the colorectal cancer incidence was 11,424.

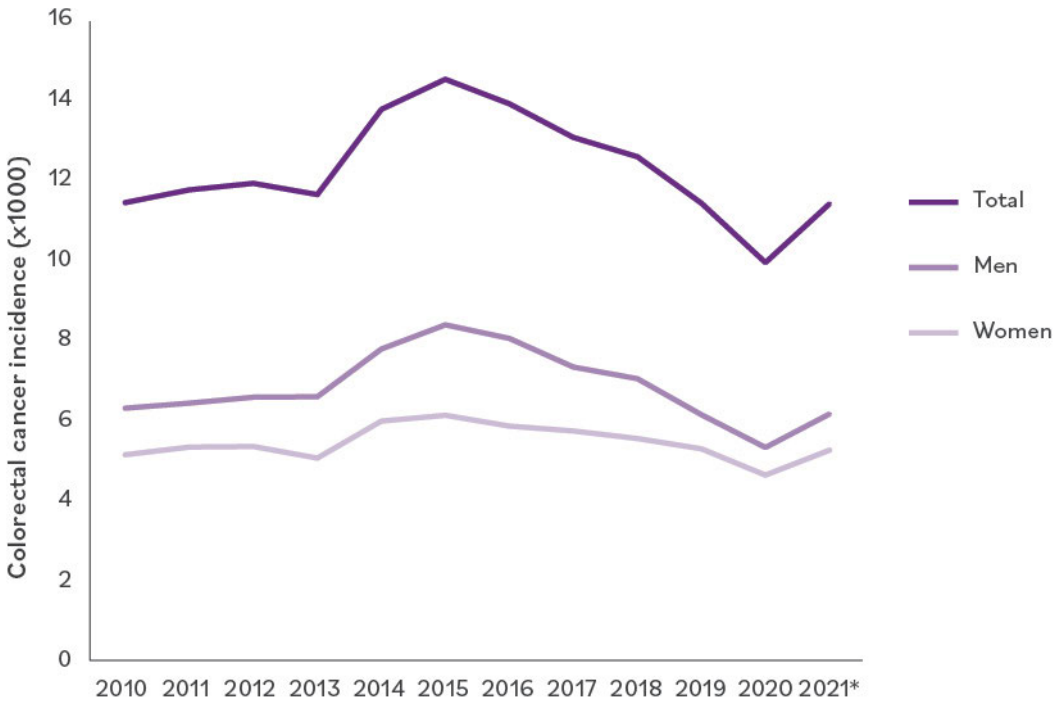

Figure 6.1: Observed colorectal cancer incidence in the Netherlands.
**2021 refers to preliminary results (1).*

A special trend analysis, a Join point regression analysis, was used to evalaute at what point in time there was a significant change in incidence. Figure 6.2 shows that after the introduction of the colorectal cancer screening programme, a significant change in incidence was observed from 2013; i.e., an increase in the colorectal cancer incidence due to the colorectal cancer screening programme. After that, another significant change is visible from 2015, with a decrease in the colorectal cancer incidence. The above

findings show that colorectal cancer screening most likely contributes to a decrease in the incidence of colorectal cancer, which should be confirmed in the coming years.

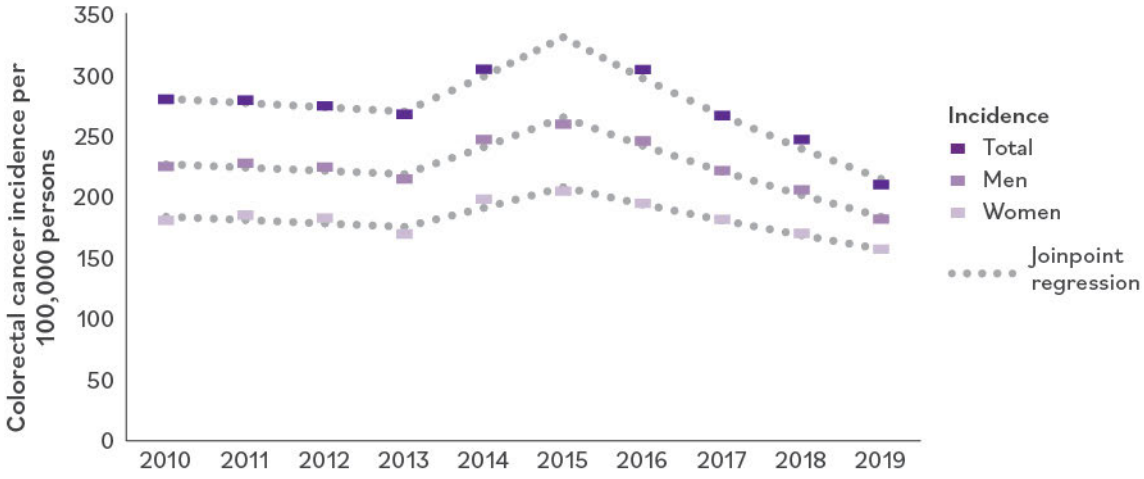

Figure 6.2: Trend analysis of colorectal cancer incidence 2010-2019. *Joinpoint regression analysis of colorectal cancer incidence per 100,000 persons aged 55 years and older for the period 2010 - 2019.*

People with late-stage colorectal cancer are more likely to die from the disease than those with early-stage colorectal cancer. Therefore, the goal of the colorectal cancer screening programme is also to detect early-stage colorectal cancers. Again, joinpoint regression analysis was used to determine any change in incidence for early-stage (stages I and II) and late-stage (stages III and IV) colorectal cancers (Figure 6.3). The incidence of early-stage colorectal cancer followed the same pattern as the overall colorectal cancer incidence; an increase in incidence was seen from 2013 and a decrease in incidence from 2015. The incidence of late-stage colorectal cancer showed a different pattern; the incidence increased slightly until 2015, after which a significant decrease was seen.

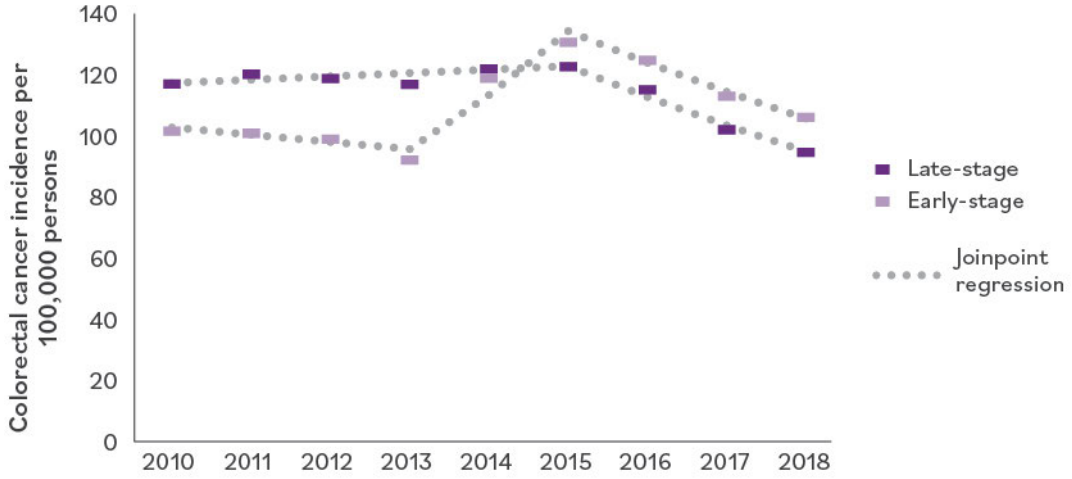

Figure 6.3: Trend analysis incidence of early- and late-stage colorectal cancer from 2010-2018. *Joinpoint regression analysis of colorectal cancer incidence per 100,000 persons aged 55 years and older for the period 2010 - 2018 for early (I and II) and late (III and IV) stage colorectal cancers.*

6.2 Colorectal cancer mortality

The annual number of colorectal cancer deaths for persons aged 55 years and older was lower in 2019 (4,473) and 2020 (4,249) than in the period before the introduction of national colorectal cancer screening programme (4,629 in 2013) (Figure 6.4). However, it is still too early to conclude that this is an effect of the screening programme. Indeed, after the introduction of the colorectal cancer screening programme, it will take several years (expectedly, at least 7 years) before an effect on colorectal cancer mortality can be seen.

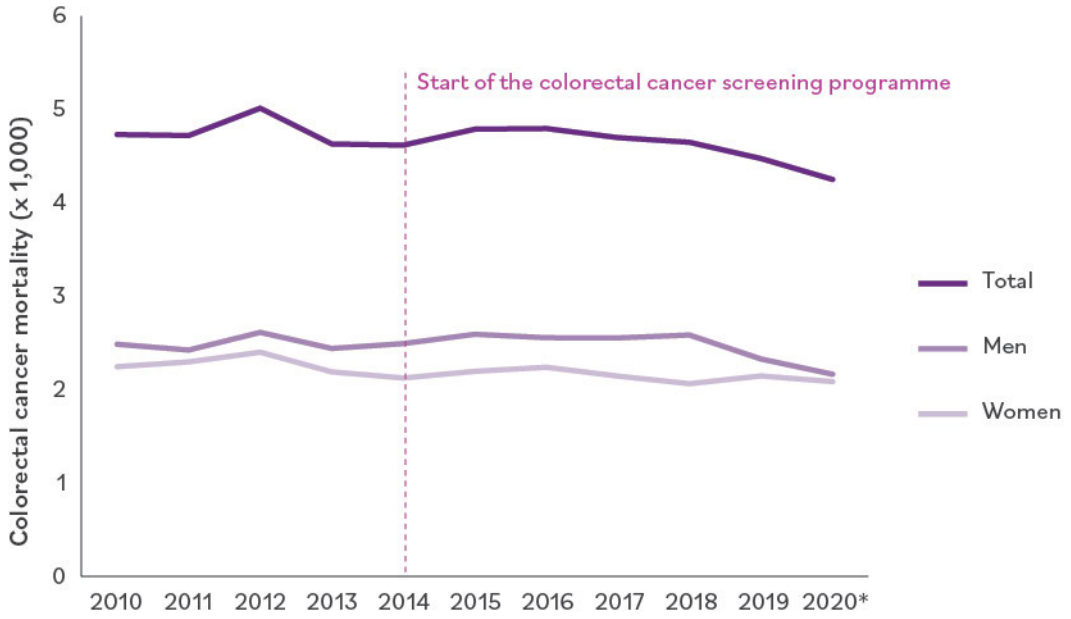

Figure 6.4: Colorectal cancer mortality
** 2020 refers to preliminary results. No data are yet available from 2021 (1).*

6.3 Predictions of colorectal cancer incidence and colorectal cancer mortality rates

To predict the long-term effect of population screening on colorectal cancer incidence and mortality, a computational model was used: the MIcrosimulation SCreening ANalysis-Colon model for colorectal cancer (MISCANColon).

6.3.1 The MISCAN-Colon model

The MISCAN-Colon model mimics the Dutch population in terms of age structure and life expectancy. Within that population, this mathematical model also simulates the development of colorectal cancer. Data from national and international studies are used to make the model as realistic as possible. The model is used to estimate short- and long-term effects of (adjustments to) the colorectal cancer screening programme.

6.3.2 Predictions of prevented incidence and mortality

The number of colorectal cancer cases predicted by MISCAN-Colon and the colorectal cancer mortality of the situation with and without colorectal cancer screening were compared. Figure 6.5 shows the predicted number of colorectal cancer cases and colorectal cancer deaths in the situation without and with population screening. If the programme continues to perform as it does now in the coming years, 3,550 colorectal cancer cases and 2,330 colorectal cancer deaths are expected to be prevented by the colorectal cancer screening programme in 2030. In the long term (2034-2044), an average of over 4,300 colorectal cancer cases and nearly 2,900 colorectal cancer deaths are expected to be prevented annually through the colorectal cancer screening programme. Thus, it is expected that the colorectal cancer mortality rate will decrease.

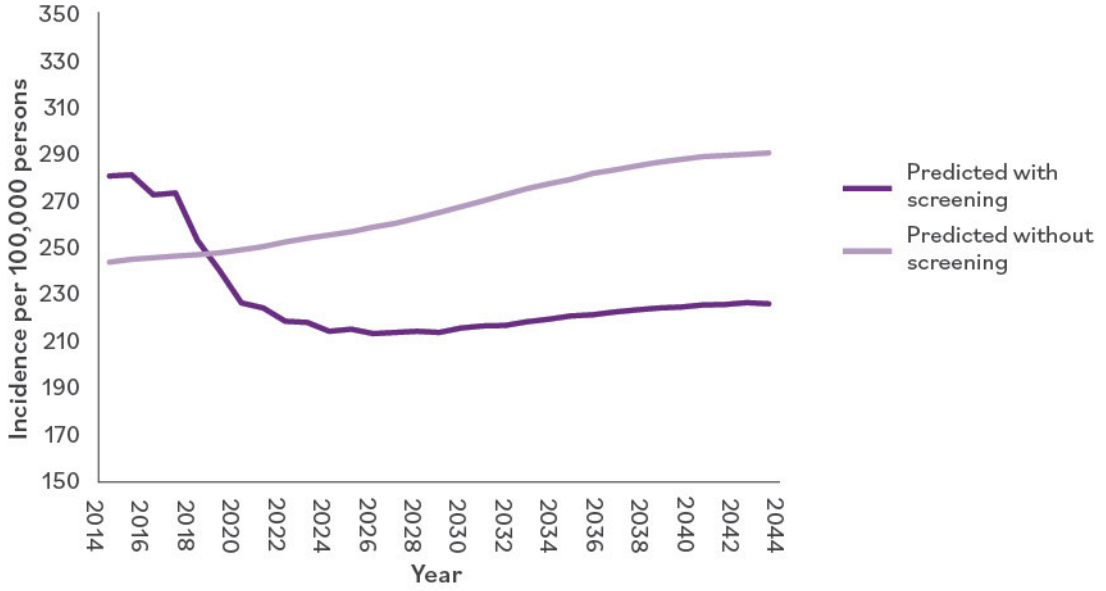

Figure 6.5a: Predicted colorectal cancer incidence

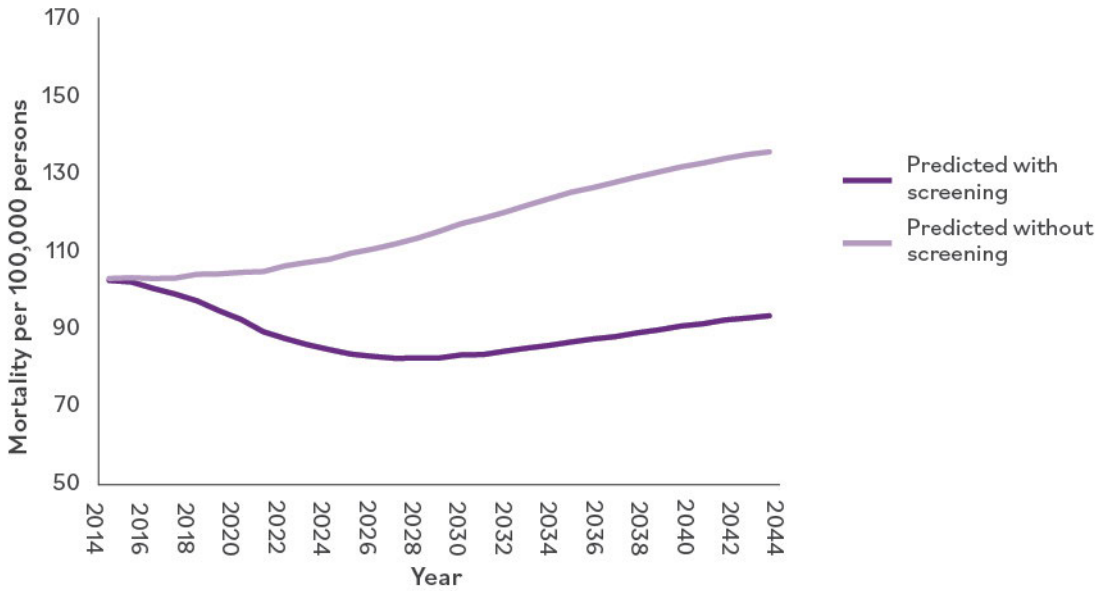

Figure 6.5b: Predicted colorectal cancer mortality rate

7. Satisfaction with colorectal cancer screening

To keep the barrier for participation in the colorectal cancer screening programme as low as possible, it is important that people are satisfied with the process. To gain insight into experiences with the screening programme, *Bevolkingsonderzoek Nederland* has a client satisfaction survey (CTO) conducted every three years.

In the most recent CTO (2020), 1,853 respondents answered questions about their satisfaction with various components of the screening programme (8). These included 649 screening programme invitees (including 26 non-participants), 533 screening programme participants with negative stool test results and 671 with positive results.

7.1 Satisfaction results

Overall satisfaction with the programme was very high. Participants with a negative stool test result rated the programme a mean 9.1 on a scale of 1 to 10. For participants with positive results, the mean was 8.8; still high, but lower than for those with a negative result. The efficiency of the screening process was found to be an important determinant of overall satisfaction (see Figure 7.1). For participants with a negative result (533 respondents), the satisfaction was based on how soon the result follows upon return of the stool test; for participants with a positive result (671 respondents), this was also how soon the intake interview for the colonoscopy takes place. Other determinants of overall satisfaction were the conduct of the stool test, the test result letter, the fact that an appointment is automatically made for an intake interview (for positive results), and the information in the test result letter (for negative results).

Figure 7.1: Key determinants of overall satisfaction. *Percentage of respondents who mentioned the item as important for satisfaction, including rating of the item.*

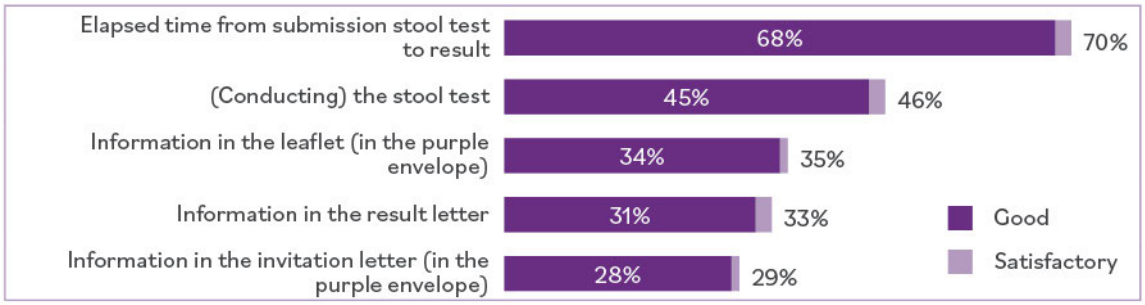

Figure 7.1a: *Participant satisfaction with negative outcome**

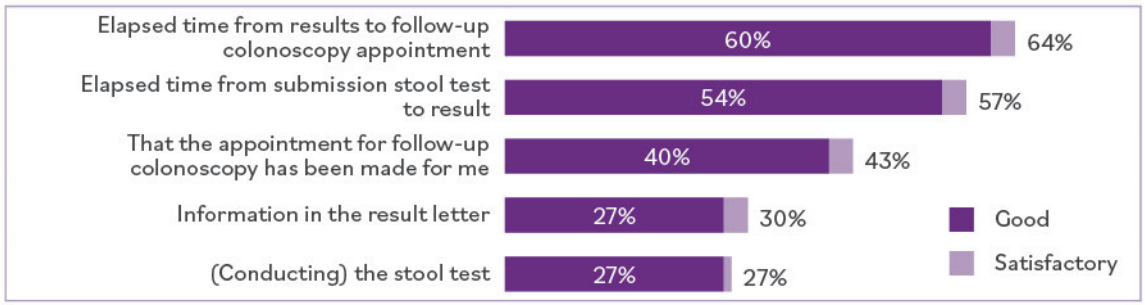

Figure 7.1b: *Satisfaction of participants with positive results**

**No unsatisfactory rating was scored.*

The letter, the information leaflet, the instructions for using and the stool test, the test result letter and the leaflet about the follow-up examination (intake interview and colonoscopy) were all rated 8.5 or higher. The information in the test result letter was rated better by people with negative results than by people with positive results: a 9.2 and 8.5, respectively.

7.2 Points for improvement

Although satisfaction was high, improvements appeared possible. The following points for improvement were mentioned:

1) a shorter invitation letter and instructions for use of the stool test;
2) less plastic and paper in the invitation (sustainability);
3) a broader age range;
4) a tool for collecting the stool;
5) clarification about the amount of stool to be collected;
6) receiving the results by phone from the general practitioner to be able to ask further questions.

In response to the improvement points mentioned, several improvement projects have been initiated. The result letter for people with positive results has been modified. Regarding sustainability, in a pilot study started in 2021, a small group of participants who have not participated twice receive only an invitation letter, instead of an invitation letter with information leaflet and stool test. People who want to participate can then contact the screening organization by phone or online to request the stool test. This trial will be evaluated in 2023. For people who have participated more often, it will be examined whether more concise information will suffice. The instructions for use of the stool test now show more clearly how much stool must be collected. Also, in the new information leaflets sent from 2023, more tips will be given on how best to collect stool in the toilet.

8. Cost-effectiveness of the colorectal cancer screening programme

It is important that the costs of the colorectal cancer screening programme are proportional to the benefits. This chapter discusses the costs of the colorectal cancer screening programme and then presents a trade-off between costs and benefits.

A distinction is made between the costs of the primary process and the costs of follow-up colonoscopy after a positive stool test. The primary process includes the organization, invitations, stool tests, laboratory analyses and sending out the results. This is funded by the Ministry of Health, Welfare and Sport. The follow-up examination involves the intake interview and the colonoscopy; this is covered by the basic health insurance package.

8.1 Costs of the colorectal cancer screening programme

8.1.1 Primary process costs

Total primary process costs increased from €12 million in 2014 to €28 million in 2019 (Figure 8.1). This is due to the phased rollout of the programme, with the total target population being invited since 2019. In 2020, costs were lower because temporarily fewer people were invited due to the COVID-19 pandemic.

The costs per participant decreased from about 23 euros in 2014 to about 14 euros in 2017, as the number of participants increased. The fixed costs were therefore spread over a larger group of participants. As of 2017, the costs per participant increased. This is largely due to the decrease in the participation rate. An increase in other variable costs, such as paper and postage costs, ICT developments and the like, may also play a role in the increase in total costs.

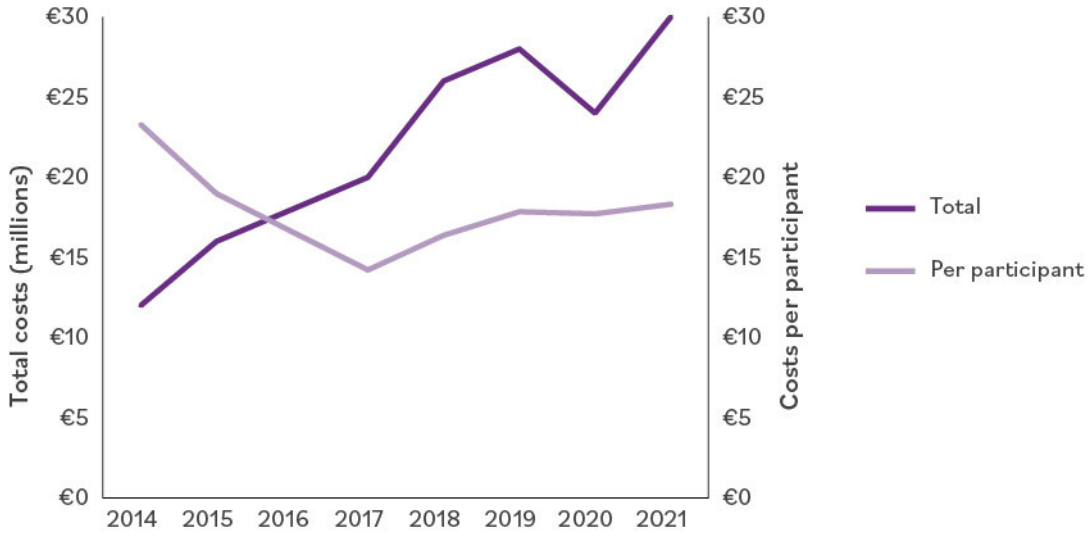

Figure 8.1: Costs of the primary process in the screening programme

8.1.2 Costs of follow-up examination

The total costs of follow-up examination after a positive stool test, intake interview and colonoscopy, exceeds the cost of the primary process. From 2014 to 2017, these costs increased from almost €28 million to over €51 million (Figure 8.2). This is because the number of people invited, and thus the number of follow-up colonoscopies, increased. In 2020, the costs were lower. Fewer follow-up colonoscopies were conducted at that time, because due to the COVID-19 pandemic temporarily fewer people were invited to participate in the screening programme. For every person who participated in the colonoscopy, one colonoscopy was included in the calculation (18). As a result, the costs of the colonoscopy slightly underestimate the true costs because some people underwent a second colonoscopy.

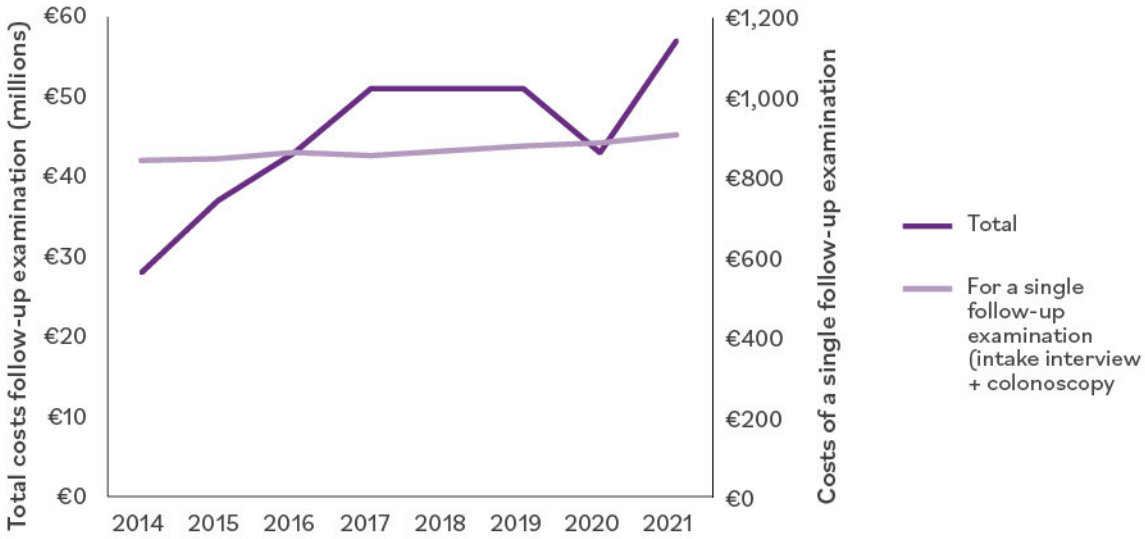

Figure 8.2: Cost of follow-up examination after positive stool test

8.2 Predicted costs and effects of the colorectal cancer screening programme

The effects (benefits) and costs of colorectal cancer screening should be carefully weighed against each other. Benefits of colorectal cancer screening are, for example, the number of prevented deaths or the number of prevented colorectal cancers. The benefits of colorectal cancer screening can be expressed in QALYs: Quality Adjusted Life Years. This is the number of life years gained, adjusted for quality of life. The costs are determined by adding up all costs surrounding colorectal cancer; these are the costs of the screening programme, but also, for example, the costs of medical examinations and treatment of colorectal cancer.

The aforementioned MISCAN-Colon model can be used to compare a situation without and with colorectal cancer screening and to make predictions about costs and benefits in the future. Figure 8.3 shows that the introduction of the colorectal cancer screening programme initially leads to an increase in costs related to colorectal cancer, as the screening costs are added. In the longer term, however, the costs associated with colorectal cancer will decrease, and from 2026 the situation with colorectal cancer

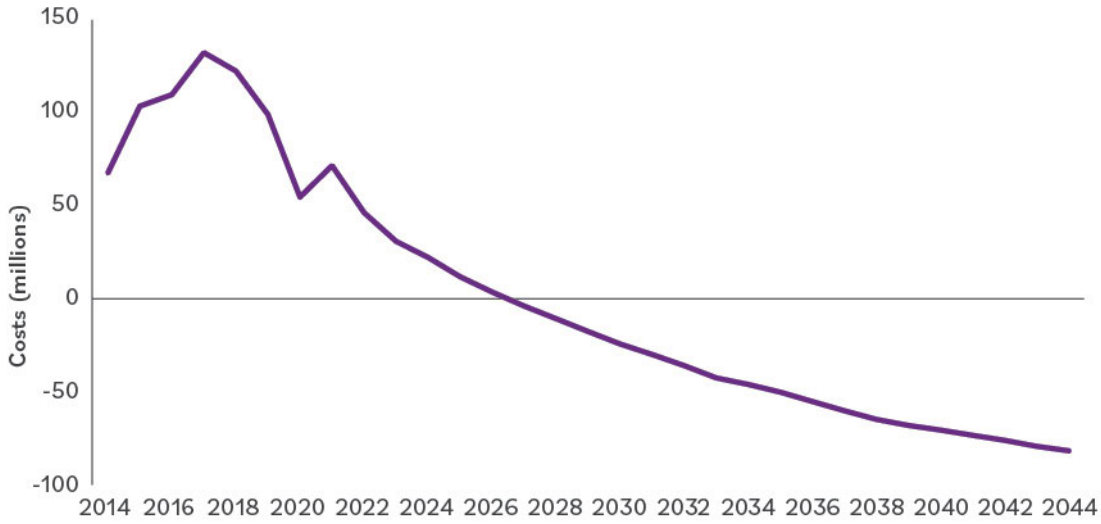

Figure 8.3: Predicted cost of colorectal cancer care. *Annual costs relative to a situation without colorectal cancer screening.*

screening will even lead to lower costs than the situation without screening. This is related to savings in colorectal cancer treatment. By detecting precursors (advanced adenomas) or early-stage colorectal cancers, late-stage colorectal cancers will be prevented in the future. The treatment of late-stage colorectal cancers is much more expensive than that of early-stage colorectal cancers, and for the treatment of precursors, only a colonoscopy is sufficient. These cost savings are that high that they even exceed the additional costs of the colorectal cancer screening programme.

The model predicts that with colorectal cancer screening, 183 QALYs per 1,000 people will be gained compared to a situation without screening. In addition to these health gains, the model predicts that the colorectal cancer screening programme is cost-effective. It was previously predicted that the programme would cost about €2,200 per QALY (19). That it now appears to be cost-saving is because late-stage colorectal cancer treatment has become more expensive in recent years due to the emergence of more expensive treatments.

9. New developments

This chapter describes developments that have been or are being investigated in the Dutch colorectal cancer screening programme and that are considered to be potential improvements for the future. A distinction is made between improving the processes of the programme and improving the outcomes of the programme.

9.1 Optimizing the outcomes of the colorectal cancer screening programme

Optimization of the outcomes of the colorectal cancer screening programme is achieved when the balance between all the benefits and harms of the population screening programme improves. This can happen, for example, if more colorectal cancers and advanced adenomas are detected while the number of people screened remains the same. It can also happen if the same number of colorectal cancers and advanced adenomas are detected while the number of people screened becomes smaller. These optimizations must be cost-effective and the adjustments must be practicable.

9.1.1 Adjustments of target population, invitation interval and stool test cut-off value

On the advice of the Health Council, it was decided at the start of the programme in the Netherlands to offer screening every two years to people aged 55 to 75 years, as explained in **Chapter 2**. Because the number of colorectal cancer cases in persons under 55 years of age is expected to increase (20), it may be beneficial to also invite the group 50 to 55 years of age. In most countries around us, this group is already being invited for colorectal cancer screening – and this is also in line with the advice of the European guideline (6,21). Because life expectancy is increasing, screening at a later age may also be useful. To investigate the effects of adjustments in the start and stop ages for the screening programme, a cost-effectiveness analysis was performed using the aforementioned MISCAN-Colon model (see **Chapters 6** and **8**). In addition to adjustment of the start and stop ages, adjustments of the invitation interval and the cut-off value of the stool test were also included in the analysis. The costs and QALYs gained from more than 1,000 different screening scenarios were calculated and compared with a situation without colorectal cancer screening. Limitations in colonoscopy capacity were also taken into account. These scenario analyses formed the basis for the Health Council's advisory report of December 14, 2022 (see advisory report in box).

Health Council advisory report

On 14 December 2002, the Health Council of the Netherlands published an advisory report concluding that the benefits of the current colorectal cancer screening programme (prevention of colorectal cancer and mortality from colorectal cancer) outweigh the risks associated with the programme (colonoscopies in which nothing is found, which are stressful and cause anxiety, and cancers that are missed). Therefore, the Health Council does not recommend any changes to the regular colorectal cancer screening programme at this time. However, the Health Council recommends that a pilot study should be carried out offering colorectal cancer screening to people aged 50-55. This can be used to assess the extent to which there are health benefits and whether the benefits outweigh the risks. Based on the results, a decision can be made to lower the age limit for colorectal cancer screening. A promising development that could improve the programme is personalised screening. The Health Council recommends that this option be investigated. The Health Council also recommends that further efforts be made to increase participation.

Participants with no polyps or only one small polyp at colonoscopy (a negative colonoscopy) are re-invited after 10 years by protocol, but may develop colorectal cancer during these 10 years (see section 4.5). The 10-year invitation interval is not based on scientific research, so it is not known whether this 10-year invitation interval is optimal. A new study is planned to investigate whether participants with a negative colonoscopy should be invited back sooner than 10 years. This study will evaluate the yield (number of colorectal cancers and advanced adenomas) of colorectal cancer screening cancer when people are sent another stool test after two, after five or after 10 years following a negative colonoscopy. The study is expected to start in late 2023.

9.1.2 Risk-based screening.

Because they do not have (precursors of) colorectal cancer, a large group of people participating in the colorectal cancer screening programme will never have a positive stool test result or a relevant finding at colonoscopy. Therefore, they do not benefit from population screening. By inviting people based on their personal risk of colorectal cancer, the benefits and harms of population screening can be better distributed. One way of risk-based screening is screening based on people's screening history. By screening history is meant the Hb concentration in the previous screening round. Faecal Hb concentration is a good predictor of a future diagnosis of colorectal cancer or a precursor of colorectal cancer (22). The risk of interval cancer in participants with a faecal Hb concentration just below the cut-off (40-47 µg Hb/g stool) in the first round was found to be 17 times higher than in participants with undetectable faecal Hb (0-2.6 µg Hb/g stool) (9). These participants may benefit from more intensive screening. On the other hand, after, for example, two or three stool tests with an undetectable Hb concentration, participants could potentially benefit from less intensive screening. A nationwide scientific study (PERFECT-FIT) has therefore been launched in October 2022, in which participants with a negative stool test will be invited to the colorectal cancer screening programme after one (>15-47 µg Hb/g stool), two (>0-15 µg Hb/g stool) or three years (0 µg Hb/g stool), depending on the level of Hb in the stool in the

previous screening round (23). This personalised approach is expected to increase the detection rate of colorectal cancer and advanced adenomas. This personalised approach aims to improve the balance of benefits and harms of colorectal cancer screening in the population.

Another way to potentially improve the detection of colorectal cancer and advanced adenomas is to use colorectal cancer risk factors as selection criteria for colonoscopy referral. A study conducted in 2020, which was embedded in the Dutch colorectal cancer screening programme, has not yet found any good predictive risk factors for colorectal cancer that could be used to select people at higher risk of colorectal cancer (24). In this study, over 3,000 participants completed a questionnaire prior to the stool test that included questions about smoking and colorectal cancer in the family. A risk score for colorectal cancer or advanced adenoma was then calculated based on Hb concentration, sex, age, yes/no current smoker and yes/no colorectal cancer in the family. The study compared two groups: participants who were referred based on a positive stool test or a high-risk score based on the completed questionnaire (intervention group) and participants who were referred based on only a positive stool test (control group). No significantly more advanced adenomas and colorectal cancers were found in the intervention group than in the control group.

9.1.3 New detection methods.

A new or improved test to detect bowel cancer may also help to improve the colorectal cancer screening programme. The most promising development in this area is a stool test developed in the Netherlands (the multitarget FIT), which measures two other proteins in the stool in addition to Hb. In a study of a number of existing stool samples, this new test proved to be better at detecting advanced adenomas and just as good at detecting colorectal cancer than the test that measured Hb alone. The number of people who received a false-positive test result was similar for both methods (25). Research is underway to see if this test will show similar results in the colorectal cancer screening programme in the Netherlands.

Other detection methods under development are tests that measure other proteins or DNA in stool, blood or exhaled air (26-28). These methods have some significant drawbacks. Measuring DNA in stool currently requires more stool than the amount currently collected, so the costs for application in population-based screening will be higher than that for the current stool test. In addition, the cost of DNA analysis is many times (€500) higher than current analysis (less than €10). DNA measurements in blood do have higher sensitivity but lower specificity. Measurements in exhaled air do not yet yield better results than the current stool test (29).

9.2 Process innovations in the screening programme.

This section discusses process innovations that have been or are being investigated in the colorectal cancer screening programme. A number of process innovations in the areas of invitation and referral have already been discussed in **Chapter 7** on satisfaction.

9.2.1 Digital intake

All participants with a positive stool test will be invited to a pre-colonoscopy intake interview at a hospital or independent treatment centre. During the intake interview, the risks and benefits of colonoscopy are discussed and any reasons for not having a colonoscopy are considered. Information is given on how to prepare for the colonoscopy and on the colonoscopy itself. A scientific study with 1,000 participants is investigating whether the intake interview can be done digitally from home. Participants in this study will receive a digital module to complete at home. The module includes a medical questionnaire and spoken animation videos explaining the positive stool test, colonoscopy, bowel preparation and follow-up. The answers are used to assess whether the colonoscopy can be done safely or if there are reasons not to have the procedure. Only people who have doubts about the safety of the colonoscopy will be invited for a physical examination. In addition to knowledge transfer and satisfaction, the study will also evaluate whether the digital tool can reduce the anxiety people feel after a positive result. The first results of this study are expected in early 2024.

9.2.2 Video capsule

A video capsule is a pill with two cameras, which is swallowed and takes pictures of the entire gastro-intestinal tract. Examinations with the video capsule can be performed at home. The video capsule could potentially be used as a primary screening test or as a follow-up after a positive stool test. For now, it seems especially suitable as a follow-up test. Undergoing a colonoscopy is then not necessary and there is little risk of complications when using the video capsule. The sensitivity of the video capsule for detecting colorectal cancer and advanced adenomas appears to be about as high as that of the colonoscopy. Despite its advantages, there are also limitations at present: in 8 to 43% of cases, it fails to image the entire intestine (30). In addition, people in whom polyps are found must still undergo a colonoscopy to remove the polyps.

10. Conclusion

After five years of phased implementation, the national colorectal cancer screening programme was fully implemented in 2019. The entire target population, people aged 55 to 75, are invited to participate every two years. The findings in this report show good results from the programme. Participation rates are high and the stool test appears to be a sensitive test for detecting colorectal cancer. Colorectal cancers detected in the screening programme are more likely to be at an early stage than cancers detected outside the screening programme. They are also less likely to require invasive treatment. This reduces the burden of disease for people with colorectal cancer.

The annual number of cases of colorectal cancer (the incidence) is decreasing and is now lower than before the screening programme was introduced. This suggests that population screening can prevent colorectal cancer. If the performance of the programme remains stable over the next few years, it is expected that in the long term (2034-2044) the colorectal cancer screening programme will prevent an average of more than 4,300 colorectal cancer cases and nearly 2,900 colorectal cancer deaths per year. The programme is also expected to become cost-saving over time by reducing the need for (expensive) treatment.

Due to the COVID-19 pandemic, no (new) invitations were sent out for the colorectal cancer screening programme for 2.5 months in 2020. The impact of this on the results of the colorectal cancer screening programme was found to be small.

The declining willingness to participate, especially among men under the age of 60, is an issue for the future. Now that the colorectal cancer screening programme is fully implemented and the programme is stable, there are opportunities for research to optimise the current colorectal cancer screening programme. This research will show in the coming years what, if any, changes to the national colorectal cancer screening programme are desirable. On 14 December 2002, the Health Council's advisory report was published, concluding that the benefits of the current screening programme outweigh the harms. Therefore, the Health Council recommends that no changes be made to the regular colorectal cancer screening programme at this time. However, it recommends research into the benefits of one-time screening at age 50.

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