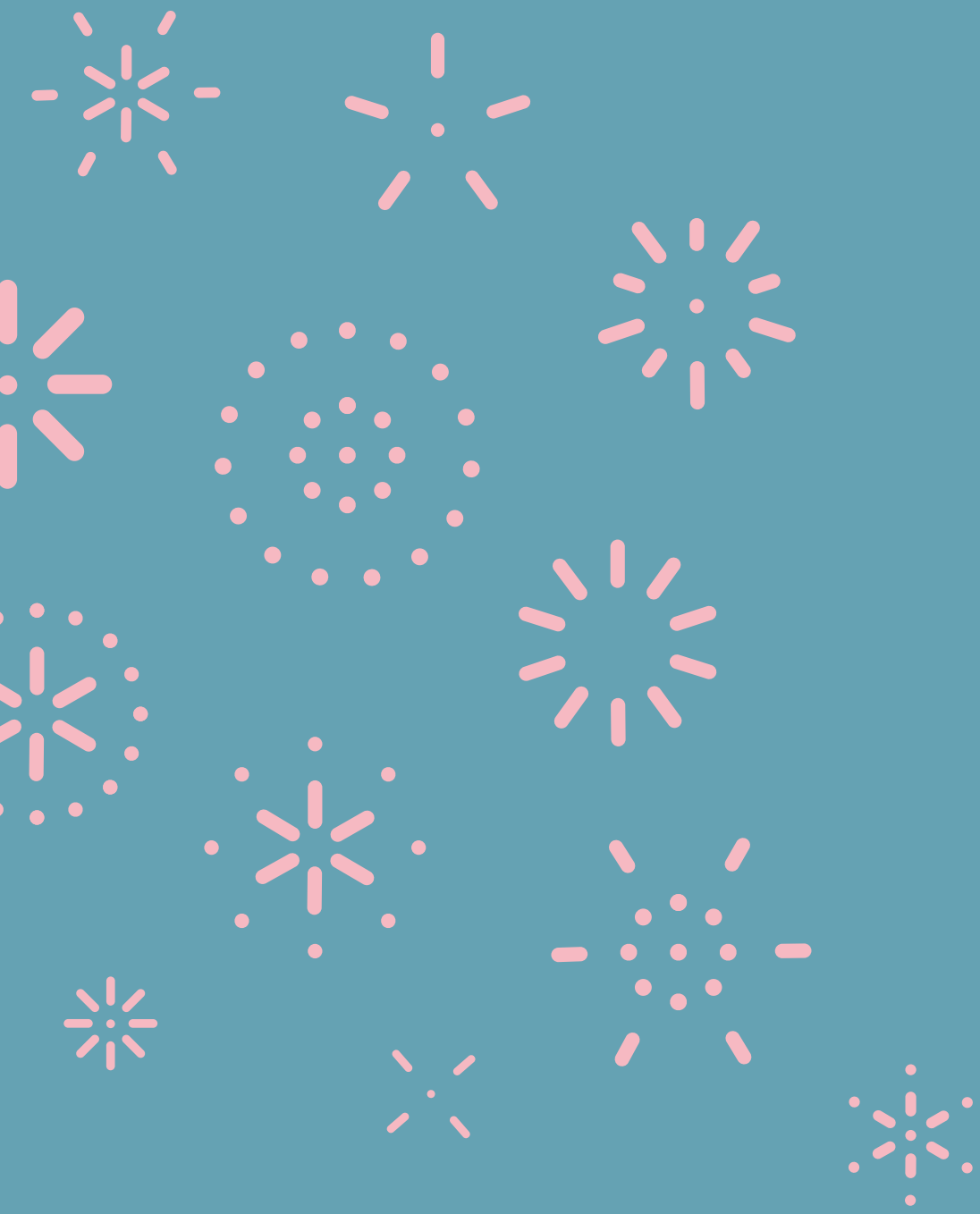
Cancer Registry of Norway 2022

BreastScreen Norway: 25 years of organized mammographic screening

Early performance measures, recent developments and the future



Cancer Registry of Norway

BreastScreen Norway

BreastScreen Norway: 25 years of organized screening

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Foreword

This report is part of our celebration of the 25th anniversary of BreastScreen Norway and is a continuation of the report published on our 20th anniversary, with a particular focus on the accomplishments and challenges over the last five years. Such anniversaries are excellent opportunities to reflect on the program's past achievements as well as its future challenges. Women targeted by the program are devoted: 94% of those who have received ten invitations to screening have attended at least once, and we are very proud to offer women a high-quality screening program. However, given the fact that the rates of recall and cancer detection have been stable for 25 years, and changes in the distribution of histopathological tumor characteristics are negligible, the time is ripe to look for further improvements.

We know that there are challenges related to the sensitivity of mammography for women with dense breasts and that women outside the current target group will benefit from organized screening. We are also aware of the benefits of personalization of health care, including screening for breast cancer. In the last chapter, we have described a possible future screening program for breast cancer, and we encourage the readers to reflect and discuss.

Screening activity has been registered in the Cancer Registry of Norway since the program's inception and the database is nearly 100% complete. In addition to being used for program administration, these data have been accessible and used extensively in quality assurance and research projects. The high number of scientific papers published using data from the program has improved the screening program's quality and visibility and has contributed to making the program and its employees attractive for national and international research collaboration. There is a substantial number of ongoing quality assurance and research projects, which can be considered a preparation for evidence-based changes. Any new developments that are incorporated into the program should be evidence-based and performed in such a way that their effects can be monitored.

This report aims to describe the program as it is today and present results from its 25 years of existence with particular focus on the last five years. Thank you to all who have contributed to this effort. In the previous report, we wrote that "A 20 year old woman is full of energy, willingness to change, and has a bright future". A 25 year old woman has matured and is ready for changes, and so is BreastScreen Norway.

Enjoy this report!

Oslo, May, 2022

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Contents

Definitions

Artificial intelligence (AI) Computer systems able to perform tasks normally requiring human intelligence.

Consensus If either of two radiologists determines that there is a slight chance that a woman has breast cancer, a consensus meeting is held to decide whether the woman needs to be recalled for further assessment.

Digital breast tomosynthesis (tomosynthesis) Pseudo three-dimensional imaging of the breast where the x-ray tube moves in an arch over the breast and multiple exposures make projection images.

Discordant interpretation A screening examination with an interpretation score of 2 or higher by one of the radiologists, and 1 by the other.

Ductal carcinoma in situ (DCIS) The presence of abnormal cells inside a milk duct in the breast. In some cases, DCIS may become invasive breast cancer and spread to other tissues.

Estrogen receptor (ER) status ER positive breast cancer cells have receptors that allow them to use estrogen to grow. Endocrine therapy with anti-estrogen hormone can block the growth of these cancer cells.

False positive screening result When a woman is recalled due to abnormal findings on the screening mammograms without being diagnosed with breast cancer.

Human epidermal growth factor receptor 2 (HER2) A protein which promotes cancer growth. Therapies targeting this protein are very effective.

Immunohistological subtype Classification of breast cancer based on ER status, PR status and Her2 status.

Interval cancer (IC) Breast cancer diagnosed after a negative screening result or more than 6 months after a false positive screening result and within 2 years after screening.

Invasive breast cancer Breast cancers that have spread into surrounding breast tissue.

Ki67 A protein associated with breast cancer cell proliferation.

Negative screening examination A screening examination which did not result in recall for further assessment.

Percentage Parts of one hundred, denoted by the symbol %.

Picture Archiving and Communication System (PACS) Medical image storage and communication technology.

Positive screening examination A screening examination resulting in a recall for further assessment.

Prevalent invitation/attendance A woman's first invitation/attendance in BreastScreen Norway.

Progesterone receptor (PR) status PR positive breast cancer cells have receptors that allow them to use progesterone to grow. As with ER-positive cancer, endocrine therapy can block the growth of these cancer cells.

Proportion The relation of one part to another or to the whole with respect to magnitude, quantity, or degree. Proportion can also be used for percentages, where the total is one hundred.

Quality adjusted life year (QALY) A measure of disease burden including both the duration of life and its quality.

Recall Women are recalled for further assessment due to abnormal findings on the mammogram, clinical symptoms or because of unsatisfactory image quality.

Screen-detected cancer (SDC) A ductal carcinoma in situ (DCIS) or invasive breast cancer diagnosed as a result of a recall assessment, and diagnosed within 182 days (6 months) following a screening examination.

Subsequent invitation/attendance A woman's invitation/attendance following a prevalent invitation/attendance.

Subsequent irregular attendance A woman who is not attending for the first time, but has skipped one or more previous screening examinations.

Subsequent regular attendance A woman attending all screening examinations.

1. BreastScreen Norway

BreastScreen Norway is part of the Norwegian public health care services and targets women aged 50-69 years for biennial mammographic screening. The program started as a pilot project in 1995 and became nationwide in 2005 following a staggered implementation. Organization, start-up, developments, and early performance measures of BreastScreen Norway's first twenty years were described in detail in the report "The Norwegian Breast Cancer Screening Program, 1996-2016: Celebrating 20 years of organised mammographic screening" (*1*).

1.1 Organization of the screening program

The Cancer Registry of Norway, which is a part of the Oslo University Hospital Trust and the South-Eastern Norway Regional Health Authority, is responsible for the administration of BreastScreen Norway. This includes planning and dispatch of invitations, design and dissemination of information, IT solutions, collection and registration of data, and coordination of technical quality control (for more details see chapter 1.2 and 1.3). These activities are performed in accordance with the provisions set out in the Regulations on the collection and processing of personal health data at the Cancer Registry of Norway (the Cancer Registry Regulations) (*2*).

The regional health authorities are responsible for offering specialized health services, and through the local health trusts they are performing screening and follow-up of the invited women. This includes performance of two-view mammographic screening, interpretation of the screening mammograms, and any further assessment, including diagnostic examinations, treatment and follow-up. The local breast centers are also responsible for ensuring that adequate facilities and capacity, including personnel, are available for screening and further assessment.

Breast centers

Women targeted by BreastScreen Norway are currently invited to screening at 30 screening units (26 stationary and 4 mobile units) associated with 17 screening areas and corresponding breast centers (Table 1.1). Screening areas are mainly defined by current and former county borders. Some women are invited to screening in a neighboring county due to shorter travel time. The program's four mobile screening units were acquired between 1995 and 1999. The mobile units usually service more rural areas where travel time to the stationary unit is long. The local health trusts independently decide whether to offer screening at mobile units. The Department for mobile electro-medical services, Vestre Viken Hospital Trust, owns and runs the mobile units, while the local health trusts rents the units, and are administratively and economically responsible for staffing and operating them.

Current birth cohorts and screening rounds

Due to the stepwise start-up of the screening program, current birth cohorts invited and screening rounds vary between the screening areas (Table 1.1). The counties of Rogaland, Hordaland, Akershus, and Oslo were included in the pilot project in 1995/1996, covering roughly 40% of women in Norway aged 50 to 69. The first screening round in these counties took place during 1996-1997, and they are now in their 14th screening round. Expansion of the screening program continued gradually from 1999 until it became nationwide in 2005. The counties that joined last are now in their 10th screening round.

In 2020, the number of breast centers increased from 16 to 17 as the breast center Fonna was established. Women in the northern municipalities of Rogaland are invited to this new breast center, as will women from selected municipalities in the southern part of Hordaland.

Steering and advisory groups

A multidisciplinary Steering Group headed by the Norwegian Directorate of Health was established in 2015. The group's mandate is to provide advice and recommendations related to breast cancer screening to the Cancer Registry of Norway and the Norwegian Directorate of Health. To ensure the screening program maintains high quality, the Steering Group reviews aspects related to data sources, early performance measures, screening and diagnostic methods, information outreach, target groups, and ethics, among others. The Steering Group has an overall responsibility for ensuring that the program has a quality manual in line with international guidelines and that this manual is revised if necessary. Finally, the Steering Group can recommend the initiation of external evaluation of the program.

The national advisory group of BreastScreen Norway is appointed by the Cancer Registry. The group provides professional advice to the secretariat of the program, and should actively seek to improve and develop the screening program. There are also informal working groups within radiology, radiography, pathology and medical physics.

The right to refuse permanent data storage

Participants in BreastScreen Norway have the right to refuse permanent storage of their personal information (name, personal identification number and address) related to negative screening examinations. Information related to previous and future screening examinations of women who have refused data storage will be excluded from quality assurance and research activities. Information about this right is explicitly stated in the invitation letter.

The proportion of women who have ever refused permanent data storage of their negative screening examinations is 1.4% of invited and 1.6% of attending women (Table 1.2). Information about these women is not included in results presented in this report.

Table 1.1: Birth cohorts and the most recent screening rounds in BreastScreen Norway, June 2022

Screening area	Birth cohorts	Screening round	Start of round	End of round
Rogaland	1953-72	14	01.03.2022	08.03.2024
Hordaland	1953-72	14	16.05.2022	01.04.2024
Oslo	1953-72	14	24.02.2022	31.01.2024
Telemark	1953-72	12	30.08.2021	30.06.2023
Agder	1953-72	12	01.01.2022	31.12.2023
Troms og F	1951-70	11	21.09.2020	30.06.2022
Østfold	1953-72	11	06.09.2021	30.06.2023
Nordland	1953-72	12	01.08.2021	30.06.2023
Trøndelag	1953-72	11	15.11.2021	01.10.2023
Oppland	1953-73	11	28.03.2022	28.02.2024
Møre og R	1951-70	10	26.10.2020	15.09.2022
Sogn og F	1953-72	10	06.04.2021	01.03.2023
Vestfold	1953-73	10	01.01.2022	31.12.2023
Hedmark	1953-72	10	01.08.2021	30.06.2023
Akershus Øst	1953-72	14	01.03.2022	01.03.2024
Vestre Viken	1953-72	7	14.03.2022	01.03.2024
Fonna	1953-72	2	01.01.2022	31.12.2023

Table 1.2: Number (n) and proportions (%) of women who have ever refused permanent data storage of their negative screening examinations or have opted out from receiving future invitations, from start-up of the program until April 2022

	Invited	Attended	Refused permanent data storage			Opted out from the program	
Screening area	n	n	n	% of invited	% of attended	n	% of invited
Rogaland	73,584	65,141	986	1.3 %	1.5 %	2,751	3.7 %
Hordaland	96,134	84,503	1,874	1.9 %	2.2 %	1,532	1.6 %
Oslo	127,369	98,049	2,348	1.8 %	2.4 %	7,127	5.6 %
Telemark	44,315	37,924	548	1.2 %	1.4 %	1,501	3.4 %
Agder	67,050	58,483	835	1.2 %	1.4 %	2,340	3.5 %
Troms og F	58,935	51,858	1,009	1.7 %	1.9 %	1,642	2.8 %
Østfold	75,879	62,655	709	0.9 %	1.1 %	3,999	5.3 %
Nordland	50,243	44,912	518	1.0 %	1.2 %	1,644	3.3 %
Trøndelag	95,550	83,496	1,007	1.1 %	1.2 %	3,323	3.5 %
Oppland	47,357	39,674	572	1.2 %	1.4 %	1,675	3.5 %
Møre og R	55,570	45,977	690	1.2 %	1.5 %	3,638	6.5 %
Sogn og F	22,895	20,424	215	0.9 %	1.1 %	558	2.4 %
Vestfold	56,150	46,651	497	0.9 %	1.1 %	2,758	4.9 %
Hedmark	38,865	31,914	472	1.2 %	1.5 %	1,572	4.0 %
Akershus Øst	103,492	88,015	1,643	1.6 %	1.9 %	4,232	4.1 %
Vestre Viken	109,017	92,703	1,347	1.2 %	1.5 %	4,746	4.4 %
Fonna	40,890	36,301	681	1.7 %	1.9 %	1,348	3.3 %
Total	1,163,295	988,680	15,951	1.4 %	1.6 %	46,386	4.0 %

Opting out

Women can opt out from receiving invitations to BreastScreen Norway, either for a fixed period or permanently. Although it is voluntary to cite a reason for opting out, about 50% of women cites a diagnosis of breast cancer as the reason for their request. These women are typically followed up outside of the screening program. It is reasonable to expect that some women opt out due to attend screening at private clinics, or because they consider the potential harms of mammographic screening to outweigh the benefits. The proportion of women who have ever requested to opt out of the program is 4.0%, varying from 1.6 to 6.5% between screening areas (Table 1.2). Information about data processing, confidentiality, and privacy, including the right to opt out, is available on the Cancer Registry's website (*3*).

Screening intervals

BreastScreen Norway invites women with a two-year screening interval. Screening appointments are scheduled every 2 years ± 6 months (730 days ± 180 days). In practice, individual screening intervals are determined based on the date of a woman's last screening examination. In the period 2015-2019, the median time between dispatch of two screening invitations was 728 days (Table 1.3). The median number of days between two consecutive screening examinations following ordinary invitations was 731 days.

Women who do not respond to their ordinary invitation, receive a reminder, usually 5-6 weeks after the date of their ordinary invitation. The median number of days between dispatch of an ordinary invitation and a reminder was 70

days in the period 2015-2019 (Table 1.3). The median number of days between dispatch of an ordinary invitation and attendance on a reminder in the next screening round was 832 days. Women who attend screening after a reminder are invited to screening two years after the date of their screening examination. This increases the average screening interval for these women and the program. Those who do not attend screening following the reminder, receive a new invitation two years after the original appointment.

The use of mobile screening units can affect screening intervals. These units are stationed at a specific site for up to 23 weeks. Thus, women's opportunity to attend screening at a mobile unit in response to a reminder, depends on the length of the mobile unit's stay at a given site. Once a mobile unit has moved, women must travel to their local stationary screening unit to attend screening.

Table 1.3: Median number of calendar days between invitations and screening examinations for women invited in 2015-2019

Time between	Median	Interquartile range
Dispatch of two ordinary invitations	728	721-742
Dispatch of an ordinary invitations and the reminder	70	63-87
Dispatch of ordinary invitation and attendance on a reminder next screening round	832	799-880
Two consecutive screening examinations following ordinary invitations	731	722-744
Two consecutive screening examinations following an ordinary invitation and a reminder	827	797-873
Two consecutive screening examinations regardless of invitation pattern	734	722-750

Table 1.4: Number of screening examinations performed using screen-film mammography (SFM) and digital mammography (DM) in the screening program by invitation year, 1996-2021

Invitation year	SFM	DM	Total
1996	48,836		48,836
1997	64,084		64,084
1998	64,596		64,596
1999	69,021		69,021
2000	89,585	713	90,298
2001	107,103	3,379	110,482
2002	147,317	1,895	149,212
2003	156,254	5,679	161,933
2004	165,432	12,294	177,726
2005	149,855	27,253	177,108
2006	154,997	31,304	186,301
2007	121,604	61,763	183,367
2008	96,101	93,732	189,833
2009	51,246	142,137	193,383
2010	22,502	176,188	198,690
2011	8,007	188,989	196,996
2012		205,106	205,106
2013		199,931	199,931
2014		213,909	213,909
2015		214,776	214,776
2016		221,066	221,066
2017		212,926	212,926
2018		221,397	221,397
2019		222,106	222,106
2020		175,394	175,394
2021		243,717	243,717
Total	1,516,540	2,875,654	4,392,194

Transition to digital mammography

At the start-up of BreastScreen Norway, mammography systems were still analogue. The advent of full-field digital mammography systems on the market coincided with the gradual implementation of the screening program. From 2009, digital mammography was used for the majority of screening examinations, and digital mammography has been used exclusively since 2012 (Table 1.4).

The transition from screen-film to full-field digital mammography was described in detail in the report "The Norwegian Breast Cancer Screening Program, 1996-2016: Celebrating 20 years of organised mammographic screening" (*1*). In this report, the period for the main transition from screen-film to digital mammography is marked from 2004 to 2011 in figures on early performance measures which include this period.

1.2 Information

The Cancer Registry is responsible for providing information to women targeted by BreastScreen Norway, as well as health professionals, other program stakeholders, and the general population about the program, using various channels.

The main purpose of information shared with women in the target group is to provide them with balanced, high-quality information about mammographic screening to enable them to make an informed choice regarding their participation. This information should also ensure that women have the practical information they need to make use of their screening invitation.

The screening program conveys information to women through personally addressed invitations and response letters. The Cancer Registry is responsible for developing and dispatching this information. In some screening areas, an information letter is sent to women prior to their first screening invitation to increase awareness about the program. The Cancer Registry has also established routines to provide municipalities where women are screened on mobile screening units with a standardised information package when mammographic screening takes place.

The Cancer Registry also aims to provide health professionals and other program stakeholders with relevant, updated information on important developments, news and events in BreastScreen Norway, and to support the breast center's opportunities for joint academic and professional updates related to the screening program.

The screening program also aims at facilitating discussions about screening results and other topics, both within and between breast centers. To achieve this, the Cancer Registry hosts regular digital administrative meetings with representatives from all breast centers, invite all health care professionals in BreastScreen Norway to monthly digital presentations about selected topics, provide regular reports on early performance measures or other topics to the breast centers, and distribute regular newsletters. Information targeting the general population is mainly presented through the Cancer Registry's website, social media and in press releases when relevant.

The program's website is central in all BreastScreen Norway's outreach activities and is continuously updated. Information about research activities and scientific results in BreastScreen Norway has been a particular focus over the last few years, as well as keeping information updated about the COVID-19 pandemic in relation to BreastScreen Norway. Also, information about benefits and harms of mammographic screening have been further developed. A Facebook page – Kreftsjekken - is used for sharing news about BreastScreen Norway, and for communicating with the target group.

Current information material

The information material sent to women along with their invitation to screening, is based on the principle of levelled information. In this way, the most important information is presented to all women in the invitation letter and an attached fact sheet, while more detailed information can be obtained from the Cancer Registry's website.

The current version of the information material was launched in 2021. More simplified language and clearer messages, especially in the invitation letter and the fact sheet, were the main changes since the last major revision in 2017 (Figure 1.1). New illustrations of the effects of mammographic screening and an explicit statement that Norwegian and international health authorities recommend participation in mammographic screening for the target group, was also included. The design, including the updated program logo, was new.

In 2016, BreastScreen Norway implemented digital invitations and response letters. The number of women who have signed up for digital letters have steadily increased since digital mailboxes became available, and in 2021, 57% of the invitations were sent digitally. When updated information material was launched in 2021, the Cancer Registry also released new versions of the digital letters more adapted for digital display.

In 2021, the Cancer Registry launched translated versions of the program's information material in selected languages. The invitation letter, reminder, standard response letter, fact sheet, and a short hand-out, are now available on the website in Northern Sami, English, Arabic, Polish, Somali and Urdu.

To support the written information material, a five-minute information video demonstrating the screening examination will be released in 2022. The video aims to inform women about what happens when they attend a screening appointment and how a screening mammogram is taken. This video will be made available in several languages.

BreastScreen Norway has developed informative posters targeting women and health care professionals, i.e. about symptoms of breast cancer and that all women, regardless of breast size and shape, are welcome to participate in BreastScreen Norway.

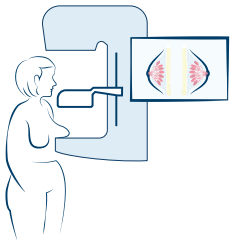
Information about BreastScreen Norway

Breast cancer is the most common type of cancer among women in Norway. One in nine women will be diagnosed with breast cancer in their lifetime. A mammogram is an X-ray picture of the breasts that can detect breast cancer before it causes symptoms, such as a lump you can feel.

What happens during a mammogram?

The entire appointment takes 10-20 minutes. First, a radiographer will ask you a few questions and look for any changes on your breasts. The doctors use this information when they read your images.

A mammogram can be done regardless of the size of your breasts. The mammography machine compresses or flattens the breasts for a few seconds while the images are taken. Some women find this uncomfortable, but we do this to obtain the highest-quality images.



What happens afterwards?

Two doctors independently check your images for any abnormalities. You will receive a written response, regardless of the result. This usually takes 2-4 weeks. Doctors do not find anything wrong in most of the women who are examined.

You may need additional follow-up

Some women are called back for additional tests at a breast centre. This is more common for women having their first mammogram and those with breast implants. For most women, the additional examination involves new mammograms and an ultrasound. In some cases, it is also necessary to take a tissue sample from the breast (biopsy). Being recalled for additional tests does not necessarily mean that you have breast cancer.

Have you had surgery for breast cancer?

If you are still attending regular check-ups, do not stop going to your appointments. Some of your check-ups can take place through BreastScreen Norway if this has been agreed with your doctor. When your control period is over (up to ten years), you may attend regular screening through BreastScreen Norway. Let us know if we should stop the invitations during the control period.

Are you worried about hereditary breast cancer?

Consult your doctor (fastlege) about counselling from the department of medical genetics in your health region.

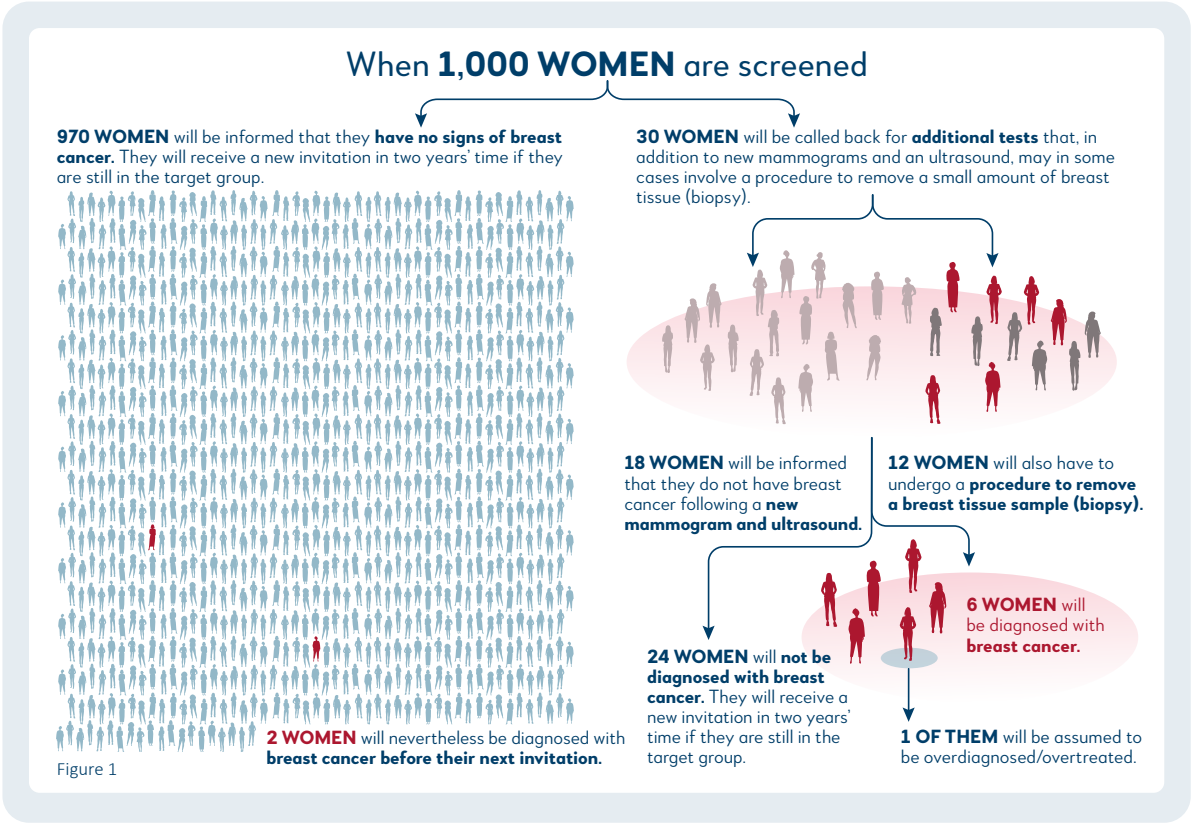


Figure 1

Information in other languages: kreftregisteret.no/mammografi

Is this something for me?

Norwegian health authorities recommend breast cancer screening every other year for all women between the ages of 50 and 69. This is in line with recommendations from the World Health Organization and the EU. The benefit is best documented in the 50 to 69 age group.

Routine examinations such as breast cancer screening has both advantages and disadvantages. You can read more about this below to decide whether you will accept this offer.

Advantages

Fewer deaths from breast cancer: The most important benefit of breast cancer screening is fewer deaths from the disease. This has been shown in a number of studies. A conservative estimate of the effect is shown in *Figure 2* to the right.

More gentle treatment: Screening allows breast cancer to be detected at an earlier stage. This increases the possibility of keeping your breast after an operation, and for more gentle treatment.

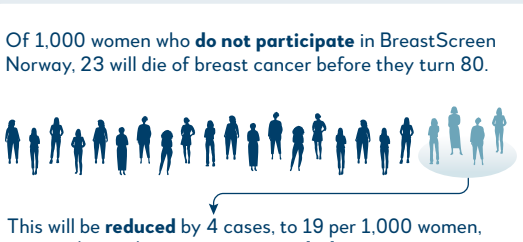


Figure 2

Disadvantages

False alarm: If the mammograms show changes in your breast, you will be called back for additional tests. For most women, these tests show that the changes are harmless, and that it was a "false alarm".

Stress and anxiety: Some may feel anxiety and stress while waiting for their results and if they are called back for additional tests.

Overdiagnosis and overtreatment: We find more breast cancer among women who go to screening than among those who do not go to screening. One reason is that some breast cancer tumours grow so slowly that they would not have been detected if the women had not been screened. It is possible to tell the difference between breast cancers that have the ability to grow slowly and those that have the ability to grow quickly, and adjust the treatment accordingly. However, it is impossible to tell which breast cancers grow so slowly that it is not necessary to provide treatment. This means that some women receive too much treatment. We do not know which women this applies to, but we know that they are mainly in the group that receives the gentlest treatment.

Since we can't tell which breast cancers do not need treatment, we can't count them either. Based on our current knowledge, our best estimate of the extent of overdiagnosis is as you see in *Figure 1* on the reverse side of this sheet.

If breast cancer is detected, you will receive follow-up at the breast centre. Screening, diagnostics and treatment are based on national guidelines and interdisciplinary collaboration.

Mammograms do not find all breast cancers. Breast cancer can also be discovered between two screenings. **For this reason, you should always consult a doctor if you notice a new lump or changes in your breast, even if you recently had a mammogram.**

Mammography uses X-rays, which in theory can increase the risk of developing breast cancer. The risk is very low, even with regular participation in BreastScreen Norway.

Please visit our website for more information, statistics, references and information on discussions about the effect of breast cancer screening. You can also talk to your doctor about breast cancer screening.

Read more at **kreftregisteret.no/mammografi**

Kreftregisteret

Faktaark Mammografiprogrammet – engelsk. Versjon november 2020

Figure 1.1: Fact sheet from BreastScreen Norway - english version from November 2020

1.3 The Cancer Registry of Norway

The Cancer Registry Regulations §1-9 give the Cancer Registry legal basis to collect and process personal health data about individuals who participate in BreastScreen Norway (*2*). This includes all invitees to the program as long as they have not made a reservation against storage of negative screening examinations (for details see chapter 1.1). The local health trusts and health care personnel have a statutory duty to report cancer related health data to the Cancer Registry (*2*, *4*). According to the Cancer Registry Regulation §1-3, information stored in the Cancer Registry can be processed for management, planning and quality assurance of the health and care service and the health and care administration, preparation of statistics and for research (*2*).

A quality assurance manual published by the Cancer Registry provides a foundation for the screening program (*5*). The manual is based on European Guidelines (*6*, *7*). For more details see section 1.4.

Invitation planning

The Cancer Registry ensures that invitations, reminders and response letters are sent to women targeted by the program. The Cancer Registry also provides information about the program and the screening examination together with the invitation letter (see chapter 1.2 for more information).

The planning of invitations for each screening round is performed in close cooperation with each breast center. Plans are made for each municipality covered by the respective breast centers, to specify which women should be invited to each screening unit at what time, to maintain the intended screening intervals. These plans are updated regularly to ensure a sufficient number of examinations is being performed.

A custom IT program, the "Invitation Program", automatically assigns all eligible women to a specific time and place for screening. Invitations are automatically generated and sent three weeks before scheduled appointments. Women who have a secure digital mailbox receive their invitations digitally, while all others receive their invitations by regular mail. If a woman does not attend her appointment, she will receive a reminder. She must then contact her breast center if she wishes to reschedule.

All participants are notified of their screening result via a letter or a call. Letters with information about negative screening examinations are sent by the Cancer Registry, while dispatch of letters or calls about positive screening examinations is performed by the breast centers. Women with a positive screening examination are offered a recall for further assessment.

Women who do not wish to participate in the screening program, whether permanently or for a specified time, can contact the Cancer Registry or their breast center to opt out of the screening program (for details see chapter 1.1).

Data registration

The Cancer Registry of Norway collects, registers and stores data from BreastScreen Norway in a national screening database, and ensures the quality of these data.

Data is registered on an individual level, making it possible to follow each woman through an entire screening episode, including further assessment and diagnosis. Data is also captured for women who are diagnosed outside the screening program, enabling detection of interval cancers.

The Norwegian Breast Cancer Registry has since 2010 collected information about all breast cancers, including DCIS, before being mapped to the screening database.

Data collected by the screening program currently consists of over 200 unique variables about women's screening history (including information about invitations, attendance, interpretations of the screening mammograms, recalls, associated outcomes, and pathology results), and about premalignant breast lesions, breast cancers, and treatment.

IT systems

The Cancer Registry is responsible for the management and development of software and database solutions for the screening program. The program developed its own IT solutions between 1994 and 1996 to securely share personal information about women between the Cancer Registry, the breast centers, and the screening units. These solutions are also used to send invitations and response letters to women.

The screening program's IT systems are based on distributed, replicated databases. Each breast center has a database server containing all data registered by the breast center and its associated screening units. MedOutlook, a radiology information system (RIS) application, is used to connect to this database server.

All screening mammograms are stored in the local health trusts' Picture Archiving and Communication System (PACS) where images from each screening examination are tagged with a unique number. This number is identical to the number generated for each invitation and makes it possible to link mammograms to the MedOutlook RIS for screen-reading and consensus meetings.

The platforms used in the 1990s to support the screening program's IT systems are now outdated. This presents a significant challenge with respect to making changes and upgrades to meet current privacy and technology standards.

Indeed, many temporary changes made during the transition from screen-film to digital mammography (2000-2011) are still in use today. Modernization and updates to the screening program's IT systems are urgently needed.

Quality assurance and improvement

According to the quality assurance manual, the Cancer Registry is responsible for the quality assurance of screening activities and for reporting results of early performance measures, including target values, in addition to providing regular feedback to health care personnel at the breast centers (*5*). Currently, this is primarily done through three to six annual reports ("Minirapporter"), presenting results of early performance measures on e.g. recalls, screen-detected cancer, and time from examination to dispatch of response letters, for each breast center. Additionally, each breast center is equipped with a quality assurance software, "MedStat", to monitor their own performance by running analyses for selected early performance measures. Target values from the European guidelines (*6*, *7*) are the basis for the majority of target values set in the quality assurance manual (*5*), but in some cases BreastScreen Norway has established their own reference values based on quality improvement studies, research and expert opinions (see chapter 1.4 for more details).

If the Cancer Registry identifies deviations from the set target values for early performance measures, such as a too long period between examination and screen-reading or too high or low recall rate, a notification is sent to the leader and/or the medical director at the breast center. If deviations are not followed up, this is reported to the Steering Group of BreastScreen Norway.

From 2022, the Cancer Registry has a goal of attending meetings and symposiums at all breast centers, at least every three years. It is desirable that the visits are initiated by the breast centers and that the senior radiological adviser, professionals in the program, and others with an interest in screening, are present.

Quality assurance and quality improvement studies can be performed according to the Cancer Registry Regulations (*2*). However, all projects involving data from medical records, such as mammographic images, requires a waiver from the duty of confidentiality and thus an additional approval from the Directorate of Health.

Technical quality assurance and quality control

The Cancer Registry and the regional health authorities have joint responsibility for technical quality assurance and quality control of mammography equipment used in BreastScreen Norway, with the Cancer Registry in a coordinating role. Practical performance and evaluation of technical quality control procedures are done by medical physicists at a local, regional or national level, and by local radiographers. If follow-up is required, this is the responsibility of the health trust as owners of the mammography equipment in question.

Research activities

BreastScreen Norway constantly performs research on breast cancer screening through several research projects (see Chapter 10 for details). All processing of personal and health data, including research projects using data from BreastScreen Norway must be carried out in accordance with the General Data Protection Regulation (EU) 2016/679 (GDPR), enforced from May 25, 2018 (*8*).

All research projects covered by the Health Research Act (*9*) must obtain an approval from the Regional Committees for Medical and Health Research Ethics (REK). In addition, all projects must have an explicitly stated basis for data processing in accordance with GDPR article 6 and article 9. After REK approval, and before processing of personal and health data begins, an assessment of privacy implications needs to be made to determine whether data processing will entail a high risk for individuals' rights and freedoms, and thus whether a Data Protection Impact Assessments (DPIA) should be performed. Information on when a DPIA should be performed is given in GDPR article 35 (*8*).

All research in BreastScreen Norway that involves collaboration between legal entities must be formalized in separate agreements. Institutions processing data on behalf of the Cancer Registry must sign a data processing agreement, while a collaboration agreement is recommended for regulating rights and matters of finance. In projects where two or more legal entities determine the purposes and means of a data processing operation together, they are considered joint controllers. In such projects, the parties have the same data responsibilities. Before data sharing and processing can start, a data sharing agreement and a joint controller agreement must be signed. All parties in such projects are responsible for ensuring that they have obtained the necessary approvals and legal basis for processing the data.

All research projects at the Cancer Registry are registered in a separate research registry ("Forskningsregister") to keep record of all projects, including REK approvals, legal basis for data processing, agreements, start and end date, and date of data deletion. Keeping record of all research activity is also important in the case of audits from the Norwegian Data Protection Authority.

Collaborators from hospitals who participate in projects at the Cancer Registry are responsible for reporting and registering the project according to their internal procedures. Often this means reporting the project to their local data protection officer and/or keep record of all data processing.

Current research initiatives carried out by the Cancer Registry focuses on artificial intelligence, screening with digital breast tomosynthesis, quality of life, radiographic quality improvement, and immigrants. During the last five years, five PhD projects using data from BreastScreen Norway have been conducted, and six PhD, postdoctoral and master's projects are ongoing (See section 10.6 and 10.7).

1.4 New European guidelines for breast cancer screening and diagnosis

The first version of the "European guidelines for quality assurance in breast cancer screening", later called "European guidelines for quality assurance in breast cancer screening and diagnosis" and hereafter referred to as the EU guidelines, was published in 1993 (*10*), and has been revised several times. The fourth and latest version was published in 2006 and was substantially extended compared with the first (*6*). Version four included associated aspects of screening and diagnostics of breast cancer, such as epidemiology, physical and technical parameters, radiography and radiology, multidisciplinary aspects, pathology, surgery, communication, in addition to data collection and monitoring of breast cancer screening, requirements for breast centers, training and certification. These aspects were described and the quality assurance parameters included acceptable and desirable target values. Descriptions and targets were mainly based on best practice and expert opinions.

BreastScreen Norway established their own guidelines during the start-up of the screening program. The first version was launched in 1996, and was based on the edition of the EU guidelines available at the time. The Norwegian guidelines were first revised in 2003 (*5*). Further revisions of particular sections have been published for medical physicists in 2009 and 2010 (*11*, *12*), for pathologists in 2018 (*13*), for radiologists in 2019 (*14*), and for radiographers in 2011 and 2021 (*15*, *16*). The sections describing guidelines for the administration of the program, for the Cancer Registry of Norway and for the mobile units are in progress, as is an update of one of the sections for technical quality control.

In 2015, the European Commission Initiative on Breast Cancer (ECIBC) started their work. Recommendations were published continously as they were finalized. In 2021, the New European guidelines on breast cancer screening and diagnosis (*7*) and the European quality assurance (QA) scheme for breast cancer services (*17*) were launched. The revised Norwegian guidelines are based on the ECIBC guidelines and QA scheme.

ECIBC guidelines and QA scheme

The ECIBC guidelines represent up-to-date, evidence-based requirements on breast cancer screening and diagnosis. The procedures used for developing the guidelines aim to be transparent, and result in clear, objective and independent guidelines on breast cancer screening and diagnosis to health care providers and women. They also provide health care managers and policymakers with guidance regarding planning, organizing and monitoring the effectiveness of screening programs.

The ECIBC QA scheme defines a set of 86 requirements, ranging from screening to follow-up, to support breast cancer screening and services in improving their quality. The scheme is divided into 7 sections where most of the requirements include several measures of compliance: Section 1: General aspects (20 requirements); Section 2: Screening (10 requirements); Section 3: Diagnosis, Pathology and Imaging (25 requirements); Section 4: Treatment (25 requirements); Section 5: Rehabilitation (2 requirements); Section 6): Follow-up (3 requirements); and Section 7: Palliative care (1 requirement).

Section 2: Screening, includes 4 requirements from Section 1: General aspects and 6 requirements from Section 3: Diagnosis, Pathology and Imaging, in addition to the 10 requirements mentioned above. The requirements will be further described and discussed in the revised version of the quality assurance manual of BreastScreen Norway. The 10 screening requirements of Section 2 are:

1) The organized screening program must comply with the European guidelines for breast cancer screening and diagnosis. 9 indicators.

2) The population screening program should collect and periodically report data to monitor the results of the screening process. 20 indicators.

3) The center performing mammographic screening must collect and periodically report data to monitor the results of the screening process. 3 indicators.

4) Women aged 50–69 must be invited for mammographic screening as part of a screening program. 1 indicator.

5) The center providing breast screening must have a written policy for informing women about a healthy lifestyle (including nutrition and physical activity). 2 indicators.

6) The screening program must have a policy for routine measurement of women-reported outcomes (satisfaction with screening) to monitor the well-being of women attending breast cancer screening. 1 indicator.

7) The screening program must have implemented a policy to ensure relevant women-centered care. 7 indicators.

8) The screening program must have a written policy on how to keep women participating in the screening process informed. Five indicators.

9) The screening program must participate in and have a written policy for participation in research activities. Five indicators.

10) The screening program must hold multidisciplinary meetings at least once a week to analyse the screening activity. One indicator.

Screening requirement 2) *The population screening program should collect and periodically report data to monitor the results of the screening process*, includes 20 indicators of compliance. Results from BreastScreen Norway for the 20 indicators are given in Table 1.5. By May 2022, BreastScreen Norway was able to provide results for 18 out of the 20 indicators. The two indicators that were not available are related to retrospective reviews of screening mammograms. Efforts to be able to report on all of the indicators are ongoing by the Cancer Registry, and planned to be completed by the end of 2022. In the screening round 2020-2021, indicator 3: Screening coverage, was expected to be close to the attendance rate given in indicator 1: Participation rate. However, the screening coverage was calculated to 62.6%, which is much lower than expected (Table 1.5). Stops and delays in the invitations to screening due to the COVID-19 pandemic is the reason for the low coverage.

Ongoing work on cancer prevention in the EU

In 2022, there are several European groups and institutions working on screening recommendations, cancer prevention, breast cancer care, research and guidelines to ensure the best screening, diagnostics, treatment and follow-up for breast cancer. The following is stated by the initiatives.

The Europe's Beating Cancer Plan is a founding pillar of a strong European Health Union and the EU's commitment to improve cancer prevention, treatment and care (*18*). The Cancer Plan is an approach to reduce the burden of cancer in the EU, tackling the entire disease pathway, from prevention to quality of life of cancer patients and survivors. *Horizon Europe Mission on Cancer* is the EU's response to the increasing number of cancer cases and deaths across the EU population (*19*). In March 2022, the *Group of Chief Scientific Advisors (GCSA)* published a scientific opinion, "Cancer Screening in the European Union", providing recommendations on how to improve cancer screening across Europe (*20*), while *DG SANTE - European Beating Cancer Task Force*, has proposed a call for evidence to update the cancer screening recommendations in 2022 (*21*).

EU Missions aims to bring concrete solutions to some of our greatest challenges in cancer and will deliver tangible results by 2030 (*22*). They aim to provide impact by putting research and innovation into a new role, combined with new forms of governance and collaboration, as well as by engaging citizens. EU Missions are a novelty of the Horizon Europe research and innovation program for the years 2021-2027.

The Innovative Partnership for Action Against Cancer (iPAAC) Joint Action brings together 24 associated partners across Europe whose main objectives are to build upon deliverables of the *Cancer Control (CanCon) Joint Action* and to implement innovative approaches to cancer control. A "Roadmap on the Implementation and Sustainability of Cancer Control Actions" is the main deliverable of this Joint Action (*23*).

The overall aim of *EU-TOPIA - TOwards imProved cancer screening*, is to improve health outcomes and equity of breast, cervical and colorectal cancer screening programs in ways that take full account of the different demographical, medical, political, economic and cultural contexts across Europe. The group will provide national, regional, and local policymakers with tools to evaluate and quantify their cancer screening programs (*24*).

Table 1.5: Screening program indicators from the ECIBC manual for breast cancer services (*7*)

Indicator	Definition	Year measured	Result
1. Participation rate	Numerator: No. women screened. Denominator: Total no. women invited	Invited in 2021	75.9%
2. Invasive breast cancer detection rate	Numerator: No. invasive SDC. Denominator: Total no. women screened	Screened in 2021	0.52%
3. Screening coverage	Numerator: No. women screened. Denominator: Total no. eligible women.	Screened in 2020-2021	62.6%
4. Interval cancer rate	Numerator: No. IC. Denominator: Total no. screened negative woman	Screened in 2019	0.19%
5. Episode sensitivity	Numerator: No. SDC. Denominator: Total no. SDC and IC	Screened in 2019	78.3%
6. Recall rate	Numerator: No. Recalls due to abnormal findings. Denominator: Total no. women screened	Screened in 2021	3.23%
7. Breast cancer detection rate	Numerator: No. SDC. Denominator: Total no. women screened	Screened in 2021	0.61%
8. Invasive cancers $\leq$10 mm rate	Numerator: No. Invasive SDC cancers $\leq$10 mm. Denominator: Total no. Invasive SDC	Screened in 2021	33.4%
9. Invasive cancers > 20 mm rate	Numerator: No. invasive SDC > 20 mm Denominator: Total no. invasive SDC	Screened in 2021	18.2%
10. Lymph node negative rate	Numerator: No. node-negative SDC. Denominator: Total no. invasive SDC	Screened in 2021	78.7%
11. Time interval between screening and treatment	Time interval between screening mammogram and treatment: median number of days	Screened in 2019-2020	42
12. Benign open surgery biopsy rate	Numerator: No. women found not to have cancer after open surgical biopsy. Denominator: Total no. women screened	Screened in 2021	0.01%
13. Advanced cancer (T2+), review errors	Numerator: No. T2+ SDC with previous mammogram reviewed and defined as incorrect reading. Denominator: Total no. T2 cancers detected		N/A[1]
14. Interval cancer, review errors	Numerator: No. interval cancers with previous mammogram reviewed and defined as an incorrect reading. Denominator: Total no. interval cancers		N/A[1]
15. Technical repeat examination	Numerator: No. women with a repeat examination for technical reasons. Denominator:Total no. women screened	Screened in 2021	0.07%
16. Time between screening mammogram and issuing of results	Time interval between screening mammogram and issuing of results: median number of days	Screened in 2021	6
17. Proportion of screened women subject to early recall following diagnostic assessment	Numerator: No. Women subjected to early recall following diagnostic assessment. Denominator: Total no. women with negative diagnostic assessment		0[2]
18. Time between result of screening mammography and assessment offered	Time between the screening mammography and the first step of diagnostic assessment: median number of days	Screened in 2021	26
19. Time between the assessment and issuing the result of the assessment when needle biopsy is not performed	Time between date of diagnostic imaging and the date of the first step of further assessment: median number of days		0[3]
20. Time between the assessment and issuing the result of the assessment when needle biopsy is performed	Time between the first step of the diagnostic assessment and issuing the final result (cytological or histological) of the needle biopsy, when performed: median number of days	Screened in 2021	4
	Cytological	Screened in 2021	3
	Histological	Screened in 2021	5

[1] Review procedures are not yet implemented
[2] Early recall following diagnostic assessment is not part of BreastScreen Norway
[3] Diagnostic imaging as a result of a positive screening examination and the first step of further assessment are performed at the same visit at the breast center in Norway

1.5 COVID-19

On March 12, 2020, to prevent and control the spread of COVID-19, the Norwegian government announced a lock-down with the strongest and most far-reaching measures initiated in Norway during peacetime (*25*). This initial lock-down period was extended by almost a month before the first restrictions were lifted on April 20, 2020 (*26*). On September 25, 2021, the Norwegian government began to lift social distancing restrictions and return to "a normal everyday life with increased emergency preparedness" (*27*).

The Cancer Registry of Norway contacted the Norwegian Institute of Public Health and the Norwegian Directorate of Health regarding the COVID-19 outbreak in early March 2020. Following these discussions, the Cancer Registry suggested to the 17 breast centers that they should consider suspending screening due to uncertainties associated with the pandemic. When all screening units closed from March 12, 2020 this was based on decisions made locally. Screening resumed gradually from May, and after a regular summer break, all centers had started screening in August 2020 (*28*).

The invitation letter sent to women after the temporary suspension included information on how to prevent the spread of COVID-19 and encouraged the women to act in accordance with local infection prevention measures when attending screening.

Screening volume and delays

In a typical year, BreastScreen Norway performs fewer screening examinations during Easter, summer vacation, and Christmas Holidays (Figure 1.2). The pandemic was managed locally in the screening program due to large differences in infection burden across the country. Infection control measures also differed across the breast centers, and more stringent measures affected screening volumes at some of the larger centers. Overall, screening levels were slightly lower than in previous years.

By November 2020, some of the screening centers experienced no delay, while others had a 3-month delay due to the earlier suspension of screening (*28*). In September 2021, some centers had a 5-7 month delay, and an estimated 90% of women targeted by BreastScreen Norway had or would experience a delayed invitation to screening. Screening attendance during 2020 is further described in Chapter 2.

Diagnosing breast cancer during the pandemic

In Norway, about 70% of breast cancers among women of all ages are detected outside of organized screening (*29*). Diagnostic mammography was prioritized during the pandemic, but there was a concern that women experiencing breast cancer symptoms would not contact their doctor and thus would experience a delayed cancer diagnosis that would negatively affect their prognosis.

In parallell with a decreased screening volume, fewer breast cancer cases were diagnosed during Easter, the Norwegian summer vacation, and Christmas Holidays in 2020, compared to 2017-2019 (Figure 1.3). During 2020, an expected number of breast cancers were detected at the start of the year, but the number of weekly diagnoses decreased greatly after the first social lock-down was announced and screening temporarily stopped. The number of weekly breast cancer diagnoses was lowest during Easter 2020. The number of weekly diagnoses started to increase after some centers started screening again, and was generally similar or higher than that observed in previous years after all screening centers reopened after summer vacation in 2020.

During 2020, there were 316 fewer breast cancers diagnosed in BreastScreen Norway than the average of 2017–2019 (*29*). There was a small reduction in small cancers (cT1 and cT2), but no clear increase in the number of larger (cT3 and cT4) cancers, or cancers with unknown size. Longer follow-up is required to determine what effect the temporary suspension of screening had on breast cancer incidence and tumor characteristics among women invited to screening. However, resources for diagnosis and treatment should be allocated based on the assumption that, on average, larger cancers will be diagnosed in the years to come due to the suspension in screening.

COVID-19 vaccines

The first COVID-19 vaccines arrived in Norway in December 2020 (*30*). One of the potential side effects of COVID-19 vaccines is swollen lymph nodes in the axilla near the injection site. This risk was reported as roughly 0.3–16% in trial participants for the Moderna and Pfizer BioNTech COVID-19 vaccines, but these are likely underestimates of the true risk (*31*–*33*).

The Cancer Registry informed screening centers, clinicians, and women of the risk of swollen lymph nodes after receiving a COVID-19 vaccine. Written information for women was provided with the invitation letter. Information in English was provided online. Women were asked about the date of their last COVID vaccination, and in which arm the vaccine was administered, when they attended screening. This information was intended for the radiologist screen-reading their mammograms. Invitation letters dispatched after April 15, 2022, no longer include this information.

Long-term effects

The COVID-19 pandemic caused an unprecedented disruption to BreastScreen Norway and it could take years to fully understand the consequences of temporarily halting

population-based screening. BreastScreen Norway continuously monitors early performance measures to evaluate the screening program and this surveillance will help elucidate the long-term effects of suspending screening. In the shorter term, some breast centers have experienced difficulties in catching up with delayed invitations to screening. BreastScreen Norway continues to collaborate closely with all breast centers to aid in catching up with these delays and it is expected that all centers have caught up by the end of 2022. Long-term effects of screening during the pandemic is the focus of several planned research projects. Results from these projects will provide important knowledge for any future temporary suspension of screening.

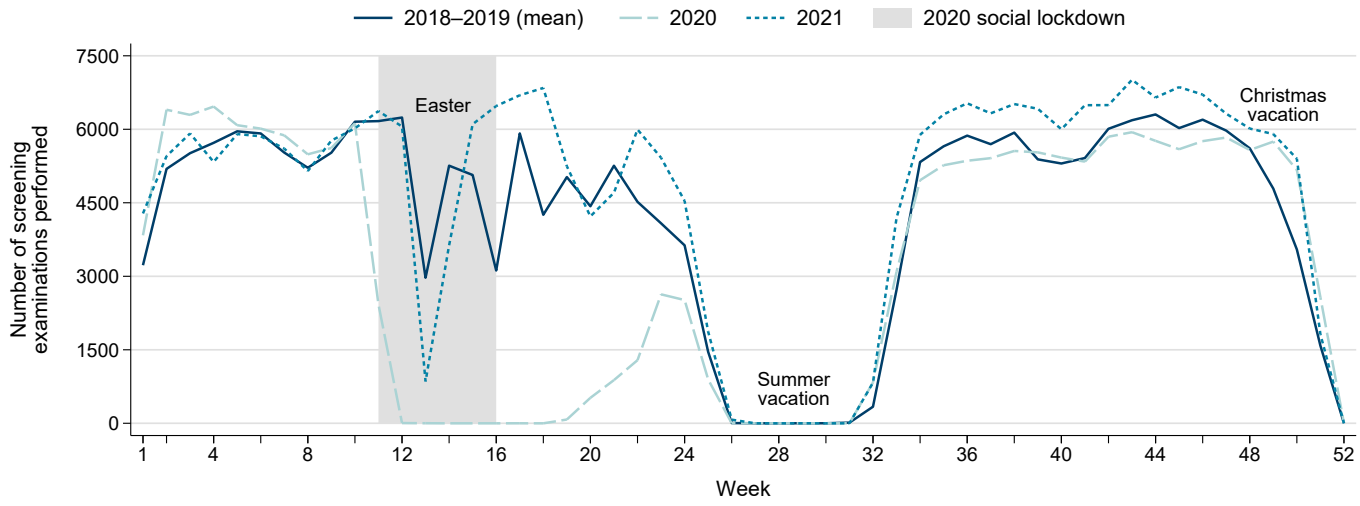


Figure 1.2: Weekly number of screening examinations performed in BreastScreen Norway for 2018–2019 (mean), 2020 and 2021

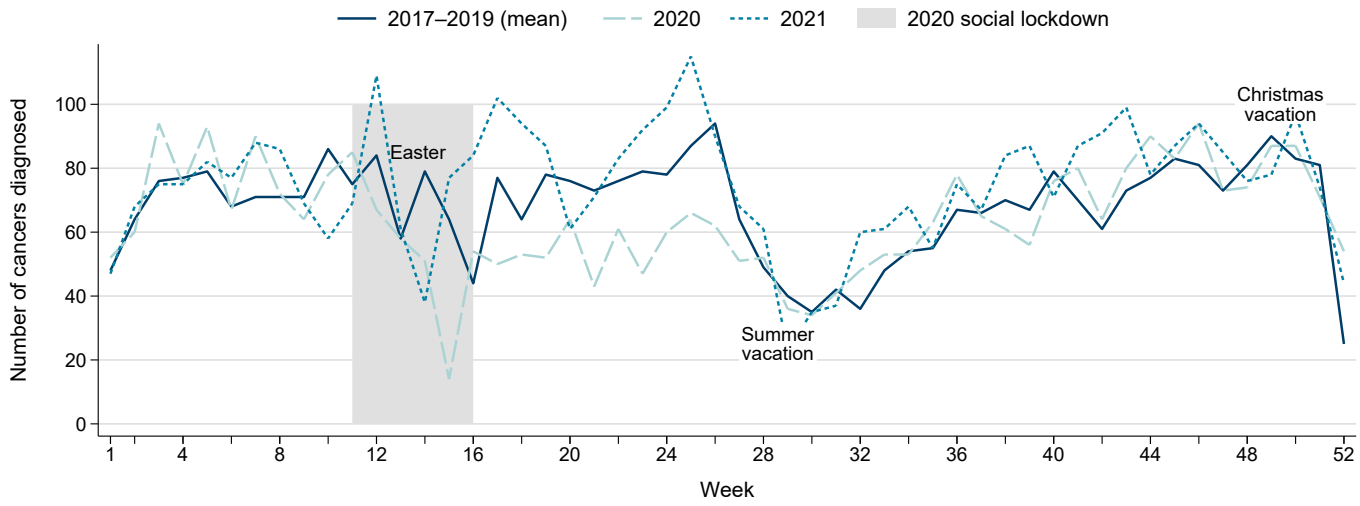


Figure 1.3: Weekly number of breast cancers diagnosed in BreastScreen Norway for 2017-2019 (mean), 2020 and 2021

2. Invitations and attendance

The aim of BreastScreen Norway is to reduce the mortality from breast cancer among the women who are invited, and to detect tumors at an early stage. Chapter 2-9 presents results for early performance measures, including attendance, consensus, recall and cancer detection rates, positive predictive values, tumor characteristics, mammographic features and breast cancer treatment. These measures are considered important for program surveillance, quality assurance and research in order to reach the aim of BreastScreen Norway.

In this chapter, number of invitations and attendances are presented, in addition to overall attendance rate and attendance rate among prevalently and subsequently invited women. Number of attendances among women invited ten times and attendance among immigrant-women are also presented.

2.1 Invitations

From the initiation of BreastScreen Norway in 1996 through the end of 2021, over 5,900,000 invitations have been sent to more than 1,100,000 women across the country. The number of women invited annually increased from 228,546 in 2005 when BreastScreen Norway became nationwide, to 321,313 in 2021 (Figure 2.1, Table 2.1). A total of 180,466 women attended in 2005, and 245,071 attended in 2021. The drop in the number of invited and attended women in 2020 was related to the COVID-19 pandemic as described in Chapter 1.5.

2.2 Attendance rates

After becoming a nationwide screening program in 2005, the attendance rate in BreastScreen Norway declined from about 77% in 2006 to 73% in 2012 (Figure 2.2). Over the past 25 years, the average attendance rate following an ordinary invitation was 71%. The average attendance rate among women who received a reminder following an ordinary invitation was 17%, which corresponds to a nearly five percentage-point increase in overall attendance and is an important factor in increasing the attendance rate towards the target of at least 75%. In 2021, the average attendance rate in the program was 75.9% (Table 2.1).

Prevalent invitations are the first invitations sent to women in the target group, and subsequent invitations are all invitations following a prevalent invitation. All women following a regular screening scheme will receive ten invitations to screening. Attendance after prevalent invitations was lower than after subsequent invitations during the period from 1996 to 2021 (Figure 2.3).

In 2017, 2018, and 2019, about 300,000 women were invited to BreastScreen Norway annually (Table 2.1). In 2020, the suspension of the screening program due to the COVID-19 pandemic affected the number of invitations and about 240,000 were invited. As a result, a higher number of women were invited in 2021. The average attendance rate in BreastScreen Norway during the last five years was 75.5%. The rate was highest in 2017, where 76.2% of the invited women attended. In 2020, 74.1% of the invited women attended, the lowest rate observed in the period 2017-2021.

The highest overall attendance rates, above 79%, were observed in Rogaland, Nordland, and Sogn og Fjordane (Table 2.1). High attendance rates have been observed in these screening areas from the start-up of the program. Oslo, Telemark, Østfold, Vestfold and Vestre Viken had overall attendance rates below 75% when looking at the last five years. For prevalently screened women, Rogaland, Nordland and Sogn og Fjordane had the highest attendance rates. For subsequently screened women, Rogaland, Nordland and Sogn og Fjordane had an attendance rate above 80%.

Numerous factors affect a woman's decision of whether to attend breast cancer screening or not. A recently published systematic review and meta-analysis with data from several countries, reported lower attendance among immigrants, women with lower socioeconomic status, and women with a prior false-positive screening result (*34*). A large immigrant population and easy access to mammography at private clinics could partially explain the low attendance rate in Oslo (*35*). Whether attendance increases during Breast Cancer Awareness Month (BCAM) has been studied in BreastScreen Norway (*36*). However, results did not support this hypothesis, and it is possible that organized screening with predetermined appointments evens out the effect BCAM has on screening attendance. More research is needed to explore reasons for high rates in some counties.

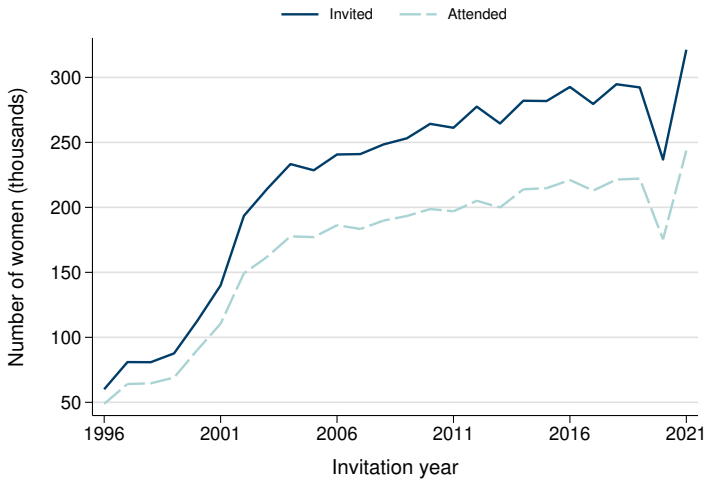


Figure 2.1: Annual number of women invited and attended by invitation year, 1996-2021

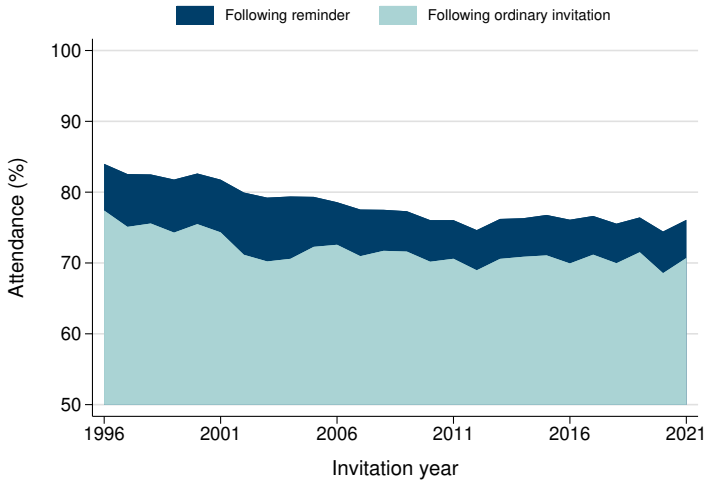


Figure 2.2: Attendance rate (%) following an ordinary invitation and a reminder by invitation year, 1996-2021

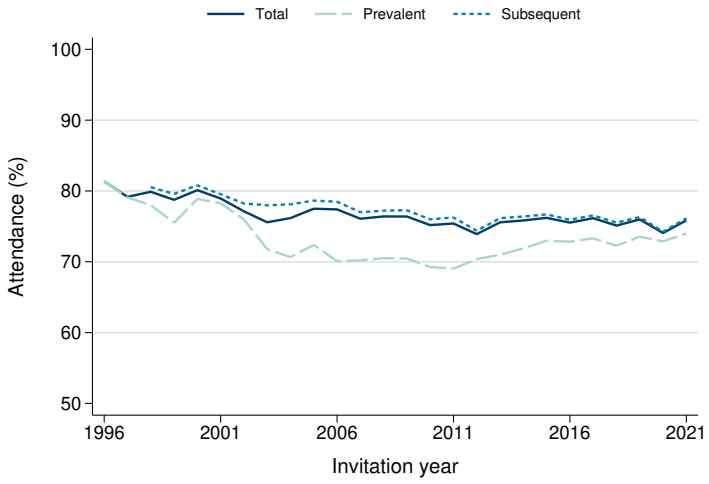


Figure 2.3: Attendance rate (%) for prevalent and subsequent invitations by invitation year, 1996-2021

Table 2.1: Invitations (n) and attendance rate (%) in the screening program by screening area and invitation year, for all invitations (upper table), prevalently invited (middle table) and subsequently invited (lower table), 2017-2021

Total	Invitation year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	22,068	80.7%	26,578	79.0%	24,255	80.5%	15,123	78.9%	19,757	80.2%	107,781	79.9%
Hordaland	25,077	78.1%	24,233	75.9%	29,434	77.4%	19,443	71.3%	25,884	75.9%	124,071	76.0%
Oslo	28,640	67.4%	30,383	66.8%	29,917	68.0%	23,082	65.8%	32,265	67.4%	144,287	67.1%
Telemark	10,950	75.3%	10,991	73.7%	10,384	74.5%	9,450	72.7%	12,822	74.5%	54,597	74.2%
Agder	15,851	78.8%	17,565	77.9%	16,148	78.2%	15,871	76.9%	19,505	78.5%	84,940	78.1%
Troms og F	15,175	76.6%	14,654	76.0%	16,165	76.8%	13,822	75.7%	15,832	77.5%	75,648	76.6%
Østfold	16,884	74.7%	18,931	72.4%	17,643	73.5%	16,516	73.3%	22,211	73.5%	92,185	73.5%
Nordland	12,956	81.1%	12,838	80.3%	12,925	81.2%	12,364	79.3%	15,174	81.7%	66,257	80.8%
Trøndelag	23,262	78.8%	25,917	78.6%	25,291	78.2%	17,543	77.2%	28,472	77.7%	120,485	78.1%
Oppland	12,062	77.3%	12,728	77.2%	12,041	77.9%	9,353	76.4%	13,007	77.4%	59,191	77.3%
Møre og R	14,058	76.9%	14,641	75.1%	14,765	77.2%	11,513	75.8%	15,971	77.3%	70,948	76.5%
Sogn og F	6,385	82.0%	6,044	80.7%	6,303	82.3%	4,418	78.7%	6,627	81.6%	29,777	81.2%
Vestfold	14,502	73.6%	15,348	73.1%	14,739	73.2%	14,105	71.8%	17,209	73.0%	75,903	73.0%
Hedmark	13,100	75.6%	12,690	75.4%	12,009	75.2%	8,757	76.2%	10,414	76.6%	56,970	75.7%
Akershus Øst	22,115	74.9%	23,096	73.6%	22,944	75.6%	18,137	72.7%	30,259	76.9%	116,551	75.0%
Vestre Viken	26,505	75.0%	28,125	74.4%	27,338	74.3%	21,037	72.4%	29,253	73.5%	132,258	74.0%
Fonna							6,268	77.5%	6,651	80.3%	12,919	78.9%
Total	279,590	76.2%	294,762	75.1%	292,301	76.0%	236,802	74.1%	321,313	75.9%	1,424,768	75.5%

Prevalent												
Rogaland	2,583	79.3%	3,850	77.8%	2,642	78.7%	2,483	78.8%	2,549	79.5%	14,107	78.7%
Hordaland	2,532	74.0%	3,680	72.7%	3,196	74.7%	2,242	72.1%	4,475	74.5%	16,125	73.7%
Oslo	4,044	65.3%	4,488	64.7%	3,706	66.6%	3,643	63.8%	4,573	65.3%	20,454	65.1%
Telemark	1,410	73.5%	1,184	70.4%	1,326	73.1%	996	71.4%	1,749	74.3%	6,665	72.8%
Agder	1,734	76.5%	2,472	76.5%	1,415	75.7%	1,891	75.1%	2,597	78.5%	10,109	76.7%
Troms og F	1,576	74.3%	1,889	70.8%	2,242	73.7%	1,539	73.2%	1,861	74.4%	9,107	73.2%
Østfold	1,998	69.8%	2,618	69.9%	2,558	68.8%	816	68.8%	4,143	70.5%	12,133	69.8%
Nordland	1,540	76.5%	1,475	75.4%	1,552	79.3%	1,514	76.0%	1,457	77.3%	7,538	76.9%
Trøndelag	2,850	75.2%	2,961	77.9%	2,997	75.6%	2,893	77.1%	2,015	76.7%	13,716	76.5%
Oppland	1,879	76.2%	1,720	74.6%	1,162	74.5%	881	76.4%	1,780	74.6%	7,422	75.2%
Møre og R	1,667	75.0%	1,554	70.8%	1,961	76.5%	1,255	74.3%	2,109	77.8%	8,546	75.2%
Sogn og F	808	79.8%	592	77.0%	726	76.3%	551	74.6%	770	77.4%	3,447	77.2%
Vestfold	1,605	71.3%	2,014	68.3%	1,454	71.9%	1,610	69.2%	2,058	69.9%	8,741	70.0%
Hedmark	1,434	72.2%	1,511	72.2%	1,265	71.8%	1,414	76.2%	837	73.8%	6,461	73.2%
Akershus Øst	3,131	74.1%	3,191	71.7%	3,319	74.3%	2,612	72.8%	4,291	75.8%	16,544	73.9%
Vestre Viken	3,082	71.2%	3,580	71.1%	3,468	72.4%	2,926	71.8%	3,949	74.1%	17,005	72.2%
Fonna							815	75.1%	883	77.8%	1,698	76.5%
Total	33,873	73.3%	38,779	72.3%	34,989	73.6%	30,081	72.9%	42,096	74.0%	179,818	73.2%

Subsequent												
Rogaland	19,485	80.9%	22,728	79.2%	21,613	80.7%	12,640	79.0%	17,208	80.3%	93,674	80.1%
Hordaland	22,545	78.6%	20,553	76.4%	26,238	77.7%	17,201	71.2%	21,409	76.2%	107,946	76.3%
Oslo	24,596	67.7%	25,895	67.1%	26,211	68.2%	19,439	66.2%	27,692	67.8%	123,833	67.5%
Telemark	9,540	75.6%	9,807	74.1%	9,058	74.7%	8,454	72.9%	11,073	74.6%	47,932	74.4%
Agder	14,117	79.1%	15,093	78.1%	14,733	78.4%	13,980	77.1%	16,908	78.5%	74,831	78.2%
Troms og F	13,599	76.9%	12,765	76.7%	13,923	77.3%	12,283	76.0%	13,971	77.9%	66,541	77.0%
Østfold	14,886	75.4%	16,313	72.8%	15,085	74.2%	15,700	73.5%	18,068	74.2%	80,052	74.0%
Nordland	11,416	81.8%	11,363	80.9%	11,373	81.5%	10,850	79.7%	13,717	82.1%	58,719	81.3%
Trøndelag	20,412	79.3%	22,956	78.7%	22,294	78.6%	14,650	77.2%	26,457	77.8%	106,769	78.4%
Oppland	10,183	77.5%	11,008	77.6%	10,879	78.2%	8,472	76.5%	11,227	77.8%	51,769	77.6%
Møre og R	12,391	77.1%	13,087	75.6%	12,804	77.3%	10,258	76.0%	13,862	77.3%	62,402	76.7%
Sogn og F	5,577	82.3%	5,452	81.1%	5,577	83.1%	3,867	79.2%	5,857	82.2%	26,330	81.7%
Vestfold	12,897	73.9%	13,334	73.8%	13,285	73.4%	12,495	72.2%	15,151	73.4%	67,162	73.3%
Hedmark	11,666	76.0%	11,179	75.9%	10,744	75.6%	7,343	76.2%	9,577	76.8%	50,509	76.1%
Akershus Øst	18,984	75.1%	19,905	73.9%	19,625	75.8%	15,525	72.6%	25,968	77.1%	100,007	75.1%
Vestre Viken	23,423	75.5%	24,545	74.9%	23,870	74.6%	18,111	72.4%	25,304	73.4%	115,253	74.3%
Fonna							5,453	77.8%	5,768	80.7%	11,221	79.3%
Total	245,717	76.5%	255,983	75.5%	257,312	76.3%	206,721	74.2%	279,217	76.1%	1,244,950	75.8%

2.3 Attendance after ten screening rounds

Since the start of the program, about 90,000 women have received ten invitations to screening. Among these women, over 50% have attended all ten screening examinations (Figure 2.4). A total of 16% have attended nine times and 6% have never attended organized mammography screening. It has previously been reported that physical activity and smoking were associated with the total number of attendances for women who have received ten invitations to BreastScreen Norway (*37*), but more research is needed to understand why women have a regular or irregular attendance pattern.

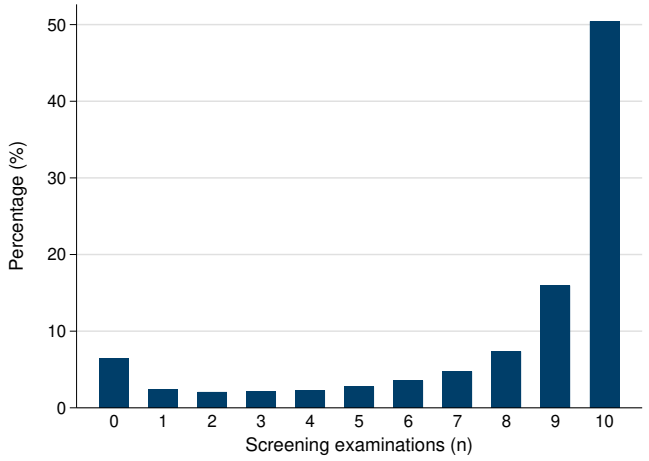


Figure 2.4: Percentage (%) of total number of attendances among women who have received ten invitations to screening

2.4 Attendance among immigrants

Attendance among immigrant women has been reported to be lower compared to non-immigrant women in BreastScreen Norway (*38*). During the last five years, the attendance rate among immigrants has been stable, with an overall rate of 58.0% for immigrants and 77.1% for non-immigrants (Table 2.2). Urban areas, such as Oslo, tend to have lower attendance rates compared to rural areas, and this has also been observed in the last five years in BreastScreen Norway (Table 2.1). A larger immigrant population in urban versus rural areas has been stated as an important reason for this difference, and immigrant women in Oslo have a lower attendance compared to immigrant women invited to other breast centers in BreastScreen Norway (*35*).

Information about country of birth was included in the Cancer Registry's databases in 2018, facilitating more quality assurance and research concerning this issue. To explore possible efforts to increase screening attendance among immigrants, qualitative studies have been performed (*39*) and are in progress. In addition, a randomized controlled trial (ImmigrantScreen) aimed at exploring the effect of sending the screening invitation in the women's presumed mother tongue based on country of birth on the attendance is ongoing (*40*). The trial is presented in short in Chapter 10.5.

Table 2.2: Invitations (n) and attendance rate (%) for non-immigrants and immigrants by invitation year, 2017-2021

	Invitation year											
	2017		2018		2019		2020		2021		Total	
	n	%	n	%	n	%	n	%	n	%	n	%
Non-immigrants	257,105	77.8%	269,386	76.8%	267,258	77.7%	216,139	75.6%	291,751	77.6%	1,301,639	77.1%
Immigrants	22,485	57.8%	25,376	57.1%	25,043	58.1%	20,663	58.2%	29,562	58.7%	123,129	58.0%
Total	279,590	76.2%	294,762	75.1%	292,301	76.0%	236,802	74.1%	321,313	75.9%	1,424,768	75.5%

3. Interpretation of screening mammograms

All screening mammograms in BreastScreen Norway are independently interpreted by two radiologists. Radiologists' performance has been shown to be related to reading volume, and it is recommended that radiologists read 4,000-10,000 screening examinations annually (*7*, *14*, *41*). Further, in a recent study including about 3 million screen-readings from BreastScreen Norway, image position in the reading batch was found to be associated with radiologists' performance (*42*). There was a decrease in the radiologists' sensitivity throughout the batch, and although this effect was small, the results may be clinically relevant at a population level or when multiplying the differences with the number of screen-readings for the individual radiologist.

In this chapter, number of radiologists, number of screen-readings, individual interpretation scores, consensus rates, and discordant interpretations are presented.

3.1 Radiologists and interpretation scores

During screen-reading, the radiologists give each breast an interpretation score between 1 and 5, where 1 indicates negative for abnormality; 2, probably negative or benign; 3, intermediate suspicion; 4, probably malignant; and 5, high suspicion of malignancy. Average reading time of one examination is reported to be about 40 seconds (*43*). If both breasts are scored 1 by both radiologists, the screening examination is considered negative. If either radiologist gives a score of 2 or higher, the examination is discussed in a consensus meeting to determine whether to recall the woman for further assessment. Usually, two radiologists attend the consensus meeting, and the average time spent on each examination at the consensus meeting is 2 to 3 minutes (*43*). If the two radiologists do not agree, a third radiologist is consulted. All cases with a score of 2 by both radiologists could be dismissed at consensus without any discussions, but all cases with a score of 3 or higher are expected to be recalled. If these cases are dismissed, the radiologist who gave a score of 3 or higher should be informed about the final decision.

The number of radiologists involved in the interpretation of mammograms have increased since the program became nationwide in 2005. During the last five years roughly 95 radiologists have interpreted screening mammograms in BreastScreen Norway (Table 3.1). The highest number during 25 years of screening was seen in 2018, when 99 radiologists were involved in screen-reading.

A total of 95% of the readings performed between 1996 and 2021 had an interpretation score of 1. Among readings with a score between 2 and 5, 83% had a score of 2 (Figure 3.1). Only 2% of readings with a positive score had a score of 5, which corresponds to 0.1% of all screen-readings.

Table 3.1: Number of radiologists interpreting mammograms and median number of mammograms interpreted by a radiologist per year with the corresponding interquartile range (P25: 25th percentile, P75: 75th percentile). Radiologists with less than 300 annual screen-readings were excluded

Year	Radiologists (n)	Median no. readings	P25	P75
1996	18	6,701	4,093	8,447
1997	22	7,388	5,414	10,406
1998	22	8,630	5,250	11,803
1999	25	7,091	5,617	11,435
2000	35	6,623	4,746	10,165
2001	47	8,322	4,214	10,204
2002	58	8,307	4,565	11,974
2003	69	6,558	4,419	10,200
2004	73	7,274	4,750	9,574
2005	80	6,554	4,760	9,843
2006	81	6,397	4,247	9,131
2007	81	6,758	4,380	9,400
2008	80	7,032	4,081	9,234
2009	82	6,977	4,568	9,621
2010	79	7,448	4,502	8,965
2011	81	6,686	4,691	9,692
2012	77	7,550	5,143	9,435
2013	84	7,098	4,226	9,970
2014	86	6,266	4,493	11,321
2015	91	6,735	4,528	10,500
2016	94	6,197	4,449	9,351
2017	94	5,827	4,534	9,468
2018	94	6,447	4,696	9,179
2019	99	6,082	4,150	8,313
2020	94	5,032	3,536	6,284
2021	96	6,630	4,629	9,373

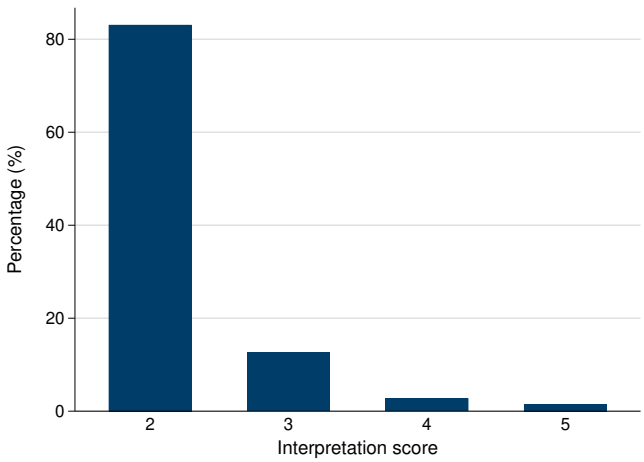


Figure 3.1: Distribution (%) of screen-readings with an interpretation score between 2 and 5, 1996-2021

3.2 Consensus rates

The overall consensus rate, examinations discussed at consensus divided by the total number of examinations, has been stable at about 7% during 25 years of screening (Figure 3.2). The lowest rate was observed in 1998 and the highest in 2007. Women attending each screening round are defined as regularly screened, while women skipping a round are defined as irregularly screened in the consecutive screening round. Prevalent screening examinations had higher consensus rates compared with subsequent regular and irregular examinations. Subsequent regular examinations had the lowest consensus rate. Higher consensus rates for prevalently screened women might be explained by the lack of prior mammograms for comparison. The consensus rate for prevalently screened women increased during the transition from screen-film to digital mammography, but has been stable in the last years.

The overall consensus rate between 2017 and 2021 was 7.8% (Table 3.2), ranging from 3.4% in Telemark to 12.5% in Sogn og Fjordane. The lowest consensus rate during the five year period was observed in Telemark (2.8%) in 2020, and the highest rate was 16.9% in Sogn og Fjordane in 2017.

The consensus rate was 16.6% for prevalently screened and 6.3% for subsequently screened women (Table 3.2) between 2017 and 2021. The lowest rate for prevalently screened during this period was 5.5% in Telemark in 2020, and the highest was 34.9% in Sogn og Fjordane in 2017. For subsequently screened women, the lowest rate was 2.4% in Telemark in 2020, and the highest was 13.6% in Sogn og Fjordane in 2017.

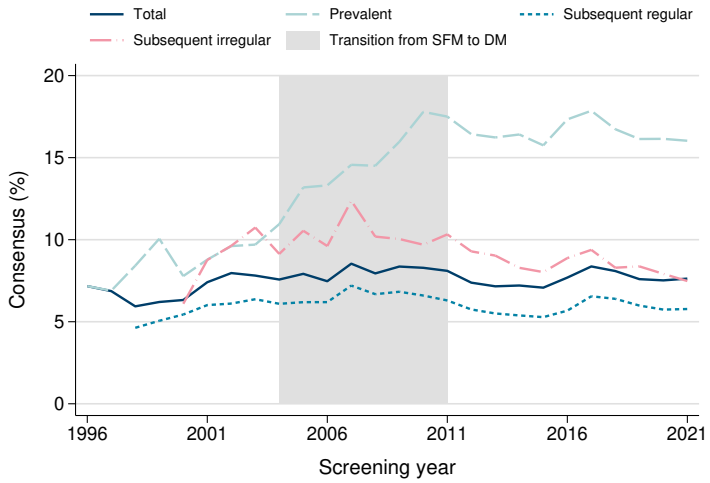


Figure 3.2: Consensus rate (%) among prevalently, subsequently regularly and irregularly screened by screening year, 1996-2021. SFM: Screen-film mammography, DM: digital mammography

Table 3.2: Number of consensus meetings (n) and consensus rate (%) by screening area and screening year, for all screening examinations (upper table), prevalently screened (middle table) and subsequently screened (lower table), 2017-2021

Total	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	727	3.8%	937	4.7%	1,164	5.9%	787	6.7%	1,127	7.1%	4,742	5.5%
Hordaland	1,519	7.1%	1,701	9.7%	1,738	7.8%	977	7.4%	1,912	9.4%	7,847	8.3%
Oslo	1,765	9.2%	1,747	8.5%	1,953	9.9%	1,604	10.4%	1,971	9.0%	9,040	9.3%
Telemark	314	3.8%	297	3.6%	262	3.3%	189	2.8%	302	3.2%	1,364	3.4%
Agder	780	6.1%	916	6.7%	566	4.4%	606	5.2%	1,014	6.5%	3,882	5.8%
Troms og F	696	5.8%	583	5.3%	679	5.3%	625	6.5%	1,044	8.1%	3,627	6.2%
Østfold	1,064	8.4%	964	7.0%	1,077	8.2%	812	7.0%	1,361	8.3%	5,278	7.8%
Nordland	656	6.2%	677	6.5%	617	5.8%	397	4.2%	630	5.0%	2,977	5.6%
Trøndelag	2,428	12.4%	1,738	9.0%	1,517	7.6%	1,073	8.0%	1,294	6.0%	8,050	8.6%
Oppland	652	6.9%	587	6.0%	516	5.4%	454	6.8%	664	6.4%	2,873	6.3%
Møre og R	971	8.9%	1,031	9.3%	893	7.8%	581	6.8%	835	6.8%	4,311	7.9%
Sogn og F	893	16.9%	755	15.2%	697	13.3%	299	8.8%	387	7.2%	3,031	12.5%
Vestfold	803	7.4%	697	6.2%	681	6.3%	567	5.8%	696	5.6%	3,444	6.2%
Hedmark	1,123	11.7%	1,210	12.3%	1,002	11.0%	606	9.4%	627	7.7%	4,568	10.6%
Akershus Øst	1,473	8.8%	1,599	9.4%	1,314	7.5%	954	7.4%	1,462	6.4%	6,802	7.8%
Vestre Viken	2,421	12.0%	2,298	11.0%	2,277	11.0%	1,862	12.4%	2,802	13.1%	11,660	11.9%
Fonna							394	8.7%	567	9.9%	961	9.4%
Total	18,285	8.4%	17,737	8.1%	16,953	7.6%	12,787	7.5%	18,695	7.6%	84,457	7.8%
Prevalent												
Rogaland	243	9.3%	348	10.7%	349	13.4%	275	13.8%	442	17.5%	1,657	12.8%
Hordaland	329	12.0%	491	16.1%	400	13.5%	293	15.1%	615	16.8%	2,128	14.8%
Oslo	629	18.8%	694	18.5%	653	20.5%	586	20.8%	766	18.0%	3,328	19.2%
Telemark	117	8.5%	77	8.5%	84	6.9%	52	5.5%	103	7.0%	433	7.3%
Agder	201	11.9%	258	11.8%	131	8.7%	157	9.3%	253	11.5%	1,000	10.8%
Troms og F	177	11.7%	189	12.3%	230	11.7%	167	12.8%	302	16.8%	1,065	13.1%
Østfold	301	17.9%	316	13.7%	322	16.0%	168	14.6%	458	14.3%	1,565	15.1%
Nordland	211	14.5%	185	13.7%	222	14.6%	152	10.9%	145	11.1%	915	13.0%
Trøndelag	787	27.6%	508	19.6%	490	18.0%	405	16.8%	307	12.6%	2,497	19.2%
Oppland	225	13.6%	194	12.7%	147	12.1%	132	14.4%	208	13.6%	906	13.2%
Møre og R	288	16.5%	310	20.3%	314	17.2%	177	14.4%	315	14.6%	1,404	16.5%
Sogn og F	292	34.9%	194	34.7%	196	28.3%	76	17.0%	103	14.8%	861	26.6%
Vestfold	261	17.3%	269	16.5%	216	15.1%	191	15.1%	247	13.6%	1,184	15.5%
Hedmark	377	27.1%	367	27.5%	239	19.4%	212	19.0%	190	18.5%	1,385	22.7%
Akershus Øst	525	19.0%	510	17.7%	496	16.7%	389	16.3%	538	13.9%	2,458	16.5%
Vestre Viken	748	26.5%	691	22.3%	717	22.4%	648	26.8%	1,058	27.2%	3,862	25.0%
Fonna							127	19.7%	142	18.3%	269	19.0%
Total	5,711	17.9%	5,601	16.7%	5,206	16.1%	4,207	16.1%	6,192	16.0%	26,917	16.6%
Subsequent												
Rogaland	484	2.9%	589	3.5%	815	4.8%	512	5.3%	685	5.2%	3,085	4.2%
Hordaland	1,190	6.4%	1,210	8.3%	1,338	6.9%	684	6.1%	1,297	7.8%	5,719	7.1%
Oslo	1,136	7.1%	1,053	6.3%	1,300	7.9%	1,018	8.1%	1,205	6.8%	5,712	7.2%
Telemark	197	2.9%	220	3.0%	178	2.7%	137	2.4%	199	2.5%	931	2.7%
Agder	579	5.2%	658	5.7%	435	3.8%	449	4.5%	761	5.7%	2,882	5.0%
Troms og F	519	4.9%	394	4.2%	449	4.2%	458	5.5%	742	6.7%	2,562	5.1%
Østfold	763	7.0%	648	5.7%	755	6.8%	644	6.2%	903	6.8%	3,713	6.5%
Nordland	445	4.9%	492	5.4%	395	4.4%	245	3.0%	485	4.3%	2,062	4.4%
Trøndelag	1,641	9.9%	1,230	7.4%	1,027	5.9%	668	6.0%	987	5.2%	5,553	6.9%
Oppland	427	5.4%	393	4.7%	369	4.4%	322	5.6%	456	5.2%	1,967	5.0%
Møre og R	683	7.5%	721	7.5%	579	6.1%	404	5.5%	520	5.1%	2,907	6.3%
Sogn og F	601	13.6%	561	12.7%	501	11.0%	223	7.6%	284	6.0%	2,170	10.3%
Vestfold	542	5.8%	428	4.4%	465	4.9%	376	4.4%	449	4.2%	2,260	4.7%
Hedmark	746	9.1%	843	9.9%	763	9.7%	394	7.4%	437	6.1%	3,183	8.6%
Akershus Øst	948	6.8%	1,089	7.7%	818	5.7%	565	5.4%	924	4.8%	4,344	6.0%
Vestre Viken	1,673	9.7%	1,607	9.1%	1,560	8.9%	1,214	9.7%	1,744	10.0%	7,798	9.4%
Fonna							267	6.8%	425	8.6%	692	7.8%
Total	12,574	6.7%	12,136	6.5%	11,747	6.2%	8,580	6.0%	12,503	6.1%	57,540	6.3%

3.3 Discordant interpretation scores

If one radiologist gives both breasts a score of 1 and the other radiologist gives a score of 2 or higher on one or both breasts, the interpretation is considered discordant. Examinations with discordant or concordant positive scores (both breasts scored 2 or higher by both radiologists) are discussed at consensus. About 25% of examinations with discordant interpretations and 75% of examinations with concordant positive interpretations are recalled for further assessment (*44*).

In the period from 2017 to 2021, the overall proportion of discordant scores among consensus cases was 73.2%, ranging from 63.6% in Møre og Romsdal to 81.5% in Fonna (Table 3.3). A lower proportion of discordant interpretation scores was observed for prevalently screened women compared to subsequently screened women (Table 3.4). This is expected as it is more challenging to interpret examinations with no prior mammograms available. A total of 68.5% of the prevalent examinations had a discordant score and 73.2% of the examinations for subsequently screened women.

Table 3.3: Number (n) and proportion (%) of discordant interpretation scores among cases discussed at consensus, by screening area and screening year, 2017-2021

	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	504	69.3%	642	68.5%	880	75.6%	560	71.2%	804	71.3%	3,390	71.5%
Hordaland	1,125	74.1%	1,257	73.9%	1,219	70.1%	725	74.2%	1,307	68.4%	5,633	71.8%
Oslo	1,332	75.5%	1,332	76.2%	1,468	75.2%	1,246	77.7%	1,472	74.7%	6,850	75.8%
Telemark	214	68.2%	201	67.7%	180	68.7%	119	63.0%	198	65.6%	912	66.9%
Agder	613	78.6%	761	83.1%	444	78.4%	475	78.4%	776	76.5%	3,069	79.1%
Troms og F	423	60.8%	432	74.1%	525	77.3%	461	73.8%	800	76.6%	2,641	72.8%
Østfold	840	78.9%	720	74.7%	810	75.2%	619	76.2%	1,046	76.9%	4,035	76.4%
Nordland	496	75.6%	527	77.8%	453	73.4%	310	78.1%	463	73.5%	2,249	75.5%
Trøndelag	1,956	80.6%	1,092	62.8%	1,092	72.0%	806	75.1%	960	74.2%	5,906	73.4%
Oppland	507	77.8%	445	75.8%	381	73.8%	335	73.8%	493	74.2%	2,161	75.2%
Møre og R	638	65.7%	663	64.3%	563	63.0%	360	62.0%	518	62.0%	2,742	63.6%
Sogn og F	571	63.9%	471	62.4%	546	78.3%	234	78.3%	331	85.5%	2,153	71.0%
Vestfold	619	77.1%	509	73.0%	485	71.2%	416	73.4%	518	74.4%	2,547	74.0%
Hedmark	833	74.2%	902	74.5%	769	76.7%	408	67.3%	446	71.1%	3,358	73.5%
Akershus Øst	1,155	78.4%	1,288	80.6%	981	74.7%	723	75.8%	1,088	74.4%	5,235	77.0%
Vestre Viken	1,664	68.7%	1,662	72.3%	1,609	70.7%	1,296	69.6%	1,931	68.9%	8,162	70.0%
Fonna							315	79.9%	468	82.5%	783	81.5%
Total	13,490	73.8%	12,904	72.8%	12,405	73.2%	9,408	73.6%	13,619	72.8%	61,826	73.2%

Table 3.4: Proportion (%) of discordant interpretation scores among cases discussed at consensus for prevalently (pre) and subsequently (sub) screened women, by screening area and screening year, 2017-2021

	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub
Rogaland	67.1%	70.5%	65.2%	70.5%	71.6%	77.3%	67.3%	73.2%	71.3%	71.4%	68.8%	72.9%
Hordaland	74.2%	74.0%	73.1%	74.2%	67.3%	71.0%	72.4%	75.0%	62.0%	71.4%	68.8%	72.9%
Oslo	68.4%	79.4%	72.8%	78.5%	69.7%	77.9%	73.9%	79.9%	71.8%	76.5%	71.3%	78.4%
Telemark	65.8%	69.5%	61.0%	70.0%	65.5%	70.2%	63.5%	62.8%	67.0%	64.8%	64.9%	67.8%
Agder	77.6%	78.9%	79.5%	84.5%	73.3%	80.0%	75.8%	79.3%	72.7%	77.8%	76.0%	80.1%
Troms og F	54.2%	63.0%	71.4%	75.4%	77.0%	77.5%	65.3%	76.9%	70.5%	79.1%	68.5%	74.6%
Østfold	74.4%	80.7%	71.8%	76.1%	68.6%	78.0%	77.4%	75.9%	71.6%	79.5%	72.2%	78.2%
Nordland	71.1%	77.8%	71.9%	80.1%	76.1%	71.9%	77.0%	78.8%	70.3%	74.4%	73.3%	76.5%
Trøndelag	75.2%	83.1%	56.3%	65.5%	67.6%	74.1%	71.9%	77.1%	67.8%	76.2%	68.4%	75.6%
Oppland	73.3%	80.1%	71.6%	77.9%	68.7%	75.9%	72.7%	74.2%	70.2%	76.1%	71.4%	77.0%
Møre og R	58.7%	68.7%	57.1%	67.4%	59.2%	65.1%	59.3%	63.1%	58.1%	64.4%	58.4%	66.1%
Sogn og F	55.5%	68.1%	48.5%	67.2%	73.0%	80.4%	64.5%	83.0%	82.5%	86.6%	61.9%	74.7%
Vestfold	69.7%	80.6%	72.1%	73.6%	63.4%	74.8%	75.4%	72.3%	70.9%	76.4%	70.3%	75.9%
Hedmark	68.4%	77.1%	70.3%	76.4%	69.9%	78.9%	59.9%	71.3%	60.5%	75.7%	66.8%	76.4%
Akershus Øst	75.6%	80.0%	78.6%	81.5%	73.8%	75.2%	71.5%	78.8%	74.2%	74.6%	74.9%	78.1%
Vestre Viken	60.8%	72.3%	63.0%	76.4%	61.5%	74.9%	62.0%	73.6%	62.0%	73.1%	61.9%	74.0%
Fonna							73.2%	83.1%	76.1%	84.7%	74.7%	84.1%
Total	68.6%	76.1%	68.2%	74.8%	68.5%	75.3%	69.5%	75.6%	68.1%	75.2%	68.5%	75.4%

Studies from BreastScreen Norway have reported that about 20% of screen-detected cancers have discordant interpretation scores, meaning that the examination was selected for consensus by only one of the two radiologists (*44*, *45*). What the ideal proportion of screen-detected cancers with discordant scores is, is not known. However, the observed proportion of 20% discordant cases among screen-detected cancers emphasizes the importance of independent double reading. A high rate of discordant cancers might indicate a staff of radiologists with different expertise, where some detect calcification while others detect distortions. This might be beneficial for the screening program. If the proportion was close to zero, interpretation of screening mammograms could have been performed by only one radiologist instead of two independent radiologists.

In the period from 2017 to 2021, 25.6% of the screen-detected cancers were detected after discordant interpretation scores. The lowest proportion was observed in 2019 (24.3%) and the highest in 2017 (26.7%). In Sogn og Fjordane, 7.4% of the interpretations among screen-detected cancers were discordant in 2017, while the proportion was 45.0% in 2021. It is expected that this proportion varies due to a limited number of cancers detected at each breast center each year. Breast centers with a stable workforce of breast radiologists are expected to have stable rates over time.

Table 3.5: Proportion (%) of discordant interpretation scores among screen-detected breast cancers (DCIS and invasive), by screening area and screening year, 2017-2021

	Screening year					
Screening area	2017	2018	2019	2020	2021	Total
Rogaland	35.3%	19.1%	23.3%	27.2%	16.2%	24.1%
Hordaland	31.9%	26.3%	21.5%	19.5%	17.7%	23.5%
Oslo	17.7%	29.8%	28.9%	37.1%	27.5%	28.0%
Telemark	14.0%	23.4%	20.4%	20.0%	7.4%	16.5%
Agder	33.7%	40.0%	35.4%	30.7%	32.7%	34.0%
Troms og F	13.8%	25.5%	23.6%	25.0%	25.6%	22.3%
Østfold	24.4%	16.7%	20.2%	19.7%	30.6%	22.6%
Nordland	23.2%	29.3%	22.4%	37.5%	25.0%	26.6%
Trøndelag	32.5%	19.3%	25.4%	22.7%	18.5%	23.8%
Oppland	33.3%	27.3%	35.9%	31.6%	24.6%	30.5%
Møre og R	17.6%	20.8%	21.1%	18.4%	20.5%	19.8%
Sogn og F	7.4%	11.5%	23.1%	28.6%	45.0%	21.2%
Vestfold	36.1%	20.0%	26.3%	26.4%	34.7%	28.8%
Hedmark	36.9%	26.0%	30.8%	19.1%	15.6%	26.6%
Akershus Øst	29.5%	29.4%	18.6%	20.5%	32.7%	26.8%
Vestre Viken	22.1%	33.3%	22.0%	26.7%	29.0%	26.9%
Fonna				33.3%	31.3%	32.2%
Total	26.7%	25.6%	24.3%	26.1%	25.3%	25.6%

4. Recall for further assessment

Women are recalled for further assessment due to abnormal findings on the mammogram, clinical symptoms or because of technically inadequate images. Over the last five years, approximately 4% of the screening examinations resulted in a recall due to one of the aforementioned reasons. These women are contacted and called back for further assessment, which is performed at one of the 17 breast centers. This chapter focuses on results from recalls due to abnormal mammographic findings.

4.1 Recall rates

The overall recall rate due to abnormal mammographic findings has been between 3% and 4% during the 25 years since the start-up of the program (Figure 4.1). The rate was highest for prevalently screened women, and lowest for women with a subsequent regular attendance pattern. Recall rates for prevalently screened women are typically higher than among subsequently screened women because they often lack prior screening mammograms for comparison, and because younger women often have a higher mammographic density compared to older women (*46*). Recall rates among prevalently screened women increased during the period in which digital mammography was introduced in BreastScreen Norway, and has been consistently above 6% from 2006 to 2021. Women with a regular subsequent attendance pattern had a recall rate below 3% during this period, while women with an irregular attendance pattern had a rate of about 4%.

Recall due to technically inadequate imaging varied between screening areas, but the overall rate was less than 0.1% over the last five years. The rate was higher in the initial phase of the screening program and decreased until around 2010 (Figure 4.2). Recalls due to clinical symptoms steadily decreased from the start-up of the program until today, and has stabilized around 0.25%. Higher recall rates due to inadequate imaging and symptoms at the beginning of the program could be due to the use of screen-film mammography and a high proportion of prevalent screens. Outcome of recalls due to reported symptoms are discussed in detail in a paper published in Breast in 2020 (*47*).

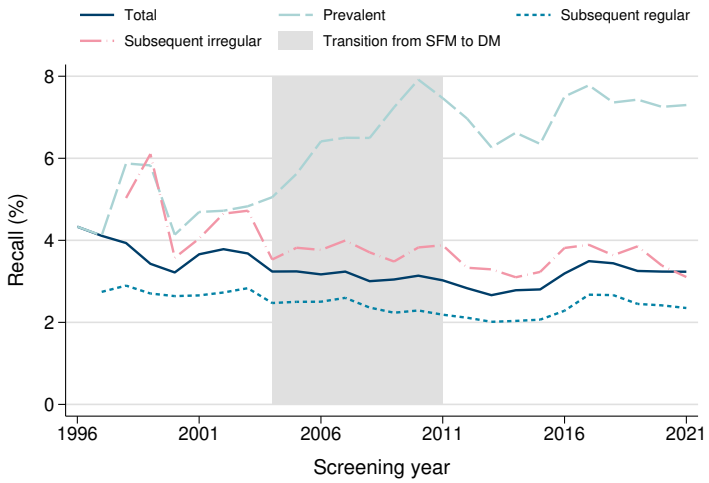


Figure 4.1: Recall rate (%) due to abnormal mammographic findings by attendance pattern and screening year, 1996-2021. SFM: Screen-film mammography, DM: digital mammography

For the period 2017 to 2021, the average recall rate due to abnormal mammographic findings was 3.3% (Table 4.1). The rate varied between screening areas, and the average rates ranged from 1.3% in Telemark, to 5.6% in Sogn og Fjordane during the last five years.

For prevalently screened women, the recall rate was on average 7.4% over the last five years (Table 4.1), varying from 2.3% in Telemark to 13.6% in Sogn og Fjordane. According to the EU guidelines, the recall rate for prevalently screened should not exceed 7% and the desirable value is less than 5% (6). The group of prevalently screened women was quite small during this period, which can explain some of the variation in recall rates for different screening areas and years. For all subsequently screened women, the recall rate was 2.6%, varying from 1.1% to 4.3% between screening areas (Table 4.1). The recommended maximum recall rate for subsequently screened women stated in the EU guidelines is less than 5%, and the desirable value is less than 3% (6).

Subsequent regular screening examinations had lower recall rates than subsequent irregular examinations, 2.5% and 3.5% in the last five years, respectively (Table 4.2). Women with an irregular attendance pattern have a longer screening interval, increasing the risk of changes in the breast when comparing with prior screening mammograms.

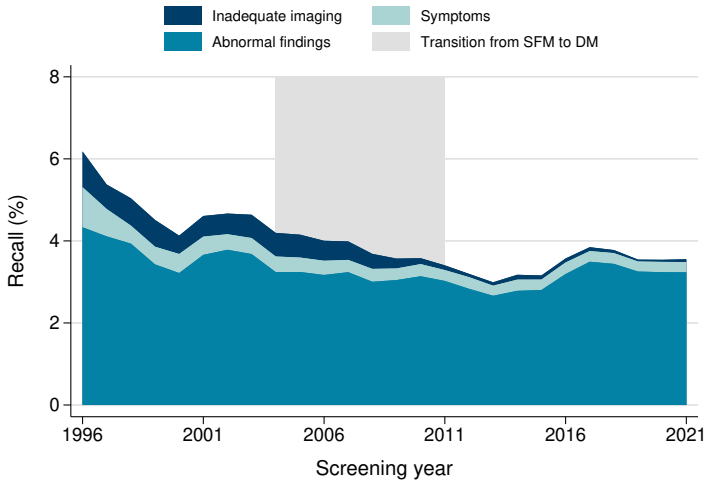


Figure 4.2: Recall rate (%) due to abnormal mammographic findings, symptoms, or inadequate imaging by screening year, 1996-2021. SFM: Screen-film mammography, DM: digital mammography

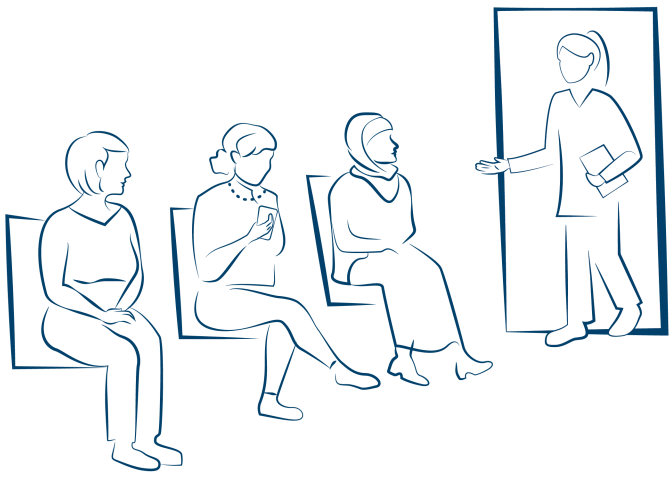


Table 4.1: Number of recalls (n) and recall rate (%) due to abnormal mammographic findings by screening area and screening year, for all screening examinations (upper table), prevalently screened (middle table) and subsequently screened (lower table), 2017-2021

Total	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	367	1.9%	439	2.2%	514	2.6%	408	3.5%	515	3.3%	2,243	2.6%
Hordaland	818	3.8%	950	5.4%	928	4.1%	490	3.7%	888	4.4%	4,074	4.3%
Oslo	684	3.6%	639	3.1%	795	4.0%	575	3.7%	823	3.7%	3,516	3.6%
Telemark	108	1.3%	125	1.5%	96	1.2%	73	1.1%	122	1.3%	524	1.3%
Agder	371	2.9%	399	2.9%	276	2.2%	325	2.8%	577	3.7%	1,948	2.9%
Troms og F	358	3.0%	287	2.6%	290	2.3%	303	3.2%	481	3.7%	1,719	3.0%
Østfold	321	2.5%	340	2.5%	346	2.6%	255	2.2%	417	2.5%	1,679	2.5%
Nordland	264	2.5%	264	2.5%	271	2.6%	158	1.7%	236	1.9%	1,193	2.2%
Trøndelag	667	3.4%	706	3.7%	563	2.8%	362	2.7%	428	2.0%	2,726	2.9%
Oppland	296	3.1%	279	2.8%	231	2.4%	182	2.7%	278	2.7%	1,266	2.8%
Møre og R	365	3.4%	412	3.7%	377	3.3%	251	2.9%	328	2.7%	1,733	3.2%
Sogn og F	363	6.9%	324	6.5%	315	6.0%	152	4.5%	194	3.6%	1,348	5.6%
Vestfold	351	3.2%	286	2.5%	310	2.8%	283	2.9%	323	2.6%	1,553	2.8%
Hedmark	395	4.1%	426	4.3%	372	4.1%	254	4.0%	231	2.8%	1,678	3.9%
Akershus Øst	781	4.7%	770	4.5%	704	4.0%	531	4.1%	898	3.9%	3,684	4.2%
Vestre Viken	1,120	5.6%	898	4.3%	873	4.2%	708	4.7%	959	4.5%	4,558	4.7%
Fonna							196	4.3%	230	4.0%	426	4.2%
Total	7,629	3.5%	7,544	3.4%	7,261	3.3%	5,506	3.2%	7,928	3.2%	35,868	3.3%
Prevalent												
Rogaland	108	4.1%	165	5.1%	158	6.1%	141	7.1%	192	7.6%	764	5.9%
Hordaland	164	6.0%	293	9.6%	224	7.6%	150	7.8%	312	8.5%	1,143	8.0%
Oslo	272	8.1%	259	6.9%	301	9.5%	208	7.4%	329	7.7%	1,369	7.9%
Telemark	29	2.1%	26	2.9%	24	2.0%	19	2.0%	38	2.6%	136	2.3%
Agder	83	4.9%	133	6.1%	68	4.5%	89	5.3%	152	6.9%	525	5.7%
Troms og F	109	7.2%	88	5.7%	108	5.5%	92	7.0%	163	9.1%	560	6.9%
Østfold	96	5.7%	114	4.9%	121	6.0%	51	4.4%	157	4.9%	539	5.2%
Nordland	93	6.4%	80	5.9%	90	5.9%	60	4.3%	51	3.9%	374	5.3%
Trøndelag	259	9.1%	200	7.7%	192	7.0%	131	5.4%	113	4.6%	895	6.9%
Oppland	96	5.8%	95	6.2%	70	5.8%	53	5.8%	92	6.0%	406	5.9%
Møre og R	122	7.0%	133	8.7%	128	7.0%	67	5.4%	129	6.0%	579	6.8%
Sogn og F	132	15.8%	105	18.8%	100	14.4%	46	10.3%	57	8.2%	440	13.6%
Vestfold	133	8.8%	107	6.6%	113	7.9%	99	7.8%	123	6.8%	575	7.5%
Hedmark	119	8.6%	131	9.8%	93	7.6%	91	8.2%	84	8.2%	518	8.5%
Akershus Øst	293	10.6%	251	8.7%	282	9.5%	243	10.2%	362	9.4%	1,431	9.6%
Vestre Viken	380	13.5%	284	9.2%	325	10.1%	278	11.5%	385	9.9%	1,652	10.7%
Fonna							72	11.2%	80	10.3%	152	10.7%
Total	2,488	7.8%	2,464	7.4%	2,397	7.4%	1,890	7.3%	2,819	7.3%	12,058	7.4%
Subsequent												
Rogaland	259	1.6%	274	1.6%	356	2.1%	267	2.7%	323	2.4%	1,479	2.0%
Hordaland	654	3.5%	657	4.5%	704	3.6%	340	3.0%	576	3.5%	2,931	3.6%
Oslo	412	2.6%	380	2.3%	494	3.0%	367	2.9%	494	2.8%	2,147	2.7%
Telemark	79	1.2%	99	1.4%	72	1.1%	54	0.9%	84	1.0%	388	1.1%
Agder	288	2.6%	266	2.3%	208	1.8%	236	2.4%	425	3.2%	1,423	2.5%
Troms og F	249	2.4%	199	2.1%	182	1.7%	211	2.6%	318	2.9%	1,159	2.3%
Østfold	225	2.1%	226	2.0%	225	2.0%	204	2.0%	260	2.0%	1,140	2.0%
Nordland	171	1.9%	184	2.0%	181	2.0%	98	1.2%	185	1.7%	819	1.8%
Trøndelag	408	2.4%	506	3.0%	371	2.1%	231	2.1%	315	1.7%	1,831	2.3%
Oppland	200	2.6%	184	2.2%	161	1.9%	129	2.2%	186	2.1%	860	2.2%
Møre og R	243	2.7%	279	2.9%	249	2.6%	184	2.5%	199	2.0%	1,154	2.5%
Sogn og F	231	5.2%	219	5.0%	215	4.7%	106	3.6%	137	2.9%	908	4.3%
Vestfold	218	2.3%	179	1.9%	197	2.1%	184	2.2%	200	1.9%	978	2.1%
Hedmark	276	3.4%	295	3.5%	279	3.6%	163	3.1%	147	2.1%	1,160	3.1%
Akershus Øst	488	3.5%	519	3.7%	422	2.9%	288	2.7%	536	2.8%	2,253	3.1%
Vestre Viken	740	4.3%	614	3.5%	548	3.1%	430	3.4%	574	3.3%	2,906	3.5%
Fonna							124	3.2%	150	3.0%	274	3.1%
Total	5,141	2.8%	5,080	2.7%	4,864	2.5%	3,616	2.5%	5,109	2.5%	23,810	2.6%

Table 4.2: Number of recalls (n) and recall rate (%) due to abnormal mammographic findings by screening area and screening year, for subsequent regular screening examinations (upper table), and subsequent irregular screening examinations (lower table), 2017-2021

Subsequent regular	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	238	1.5%	251	1.6%	318	2.0%	244	2.7%	282	2.3%	1,333	1.9%
Hordaland	600	3.5%	593	4.4%	623	3.5%	282	2.8%	458	3.4%	2,556	3.5%
Oslo	353	2.4%	342	2.2%	433	2.8%	316	2.8%	395	2.6%	1,839	2.6%
Telemark	73	1.1%	87	1.3%	68	1.1%	43	0.8%	70	1.0%	341	1.1%
Agder	261	2.5%	244	2.3%	197	1.9%	212	2.3%	390	3.2%	1,304	2.5%
Troms og F	224	2.3%	178	2.1%	155	1.6%	185	2.5%	281	2.8%	1,023	2.2%
Østfold	204	2.0%	204	1.9%	199	1.9%	179	1.9%	223	1.9%	1,009	1.9%
Nordland	151	1.8%	165	1.9%	161	1.9%	83	1.1%	168	1.6%	728	1.7%
Trøndelag	374	2.4%	441	2.8%	327	2.0%	202	2.0%	192	1.4%	1,536	2.2%
Oppland	189	2.6%	172	2.2%	145	1.8%	113	2.2%	104	2.0%	723	2.2%
Møre og R	223	2.6%	257	2.9%	232	2.6%	148	2.3%	173	1.9%	1,033	2.5%
Sogn og F	201	4.9%	197	4.8%	194	4.6%	85	3.3%	123	2.9%	800	4.2%
Vestfold	204	2.4%	163	1.8%	178	2.0%	165	2.1%	167	1.7%	877	2.0%
Hedmark	251	3.2%	267	3.4%	256	3.5%	143	3.2%	126	1.9%	1,043	3.1%
Akershus Øst	443	3.4%	476	3.7%	381	2.8%	251	2.7%	385	2.7%	1,936	3.1%
Vestre Viken	660	4.1%	560	3.4%	483	3.0%	361	3.3%	377	3.1%	2,441	3.4%
Fonna							116	3.2%	137	3.0%	253	3.1%
Total	4,649	2.7%	4,597	2.7%	4,350	2.4%	3,128	2.4%	4,051	2.4%	20,775	2.5%

Subsequent irregular												
Rogaland	21	2.5%	23	2.3%	38	3.9%	23	3.2%	41	3.3%	146	3.1%
Hordaland	54	4.3%	64	5.5%	81	5.1%	58	5.0%	118	3.8%	375	4.5%
Oslo	59	4.3%	38	2.7%	61	4.7%	51	3.6%	99	4.1%	308	3.9%
Telemark	<10	1.3%	12	2.5%	<10	1.0%	11	1.9%	14	2.1%	47	1.8%
Agder	27	3.7%	22	3.0%	11	1.6%	24	2.9%	35	3.4%	119	3.0%
Troms og F	25	3.3%	21	2.7%	27	2.8%	26	3.3%	37	3.9%	136	3.2%
Østfold	21	2.6%	22	2.7%	26	3.1%	25	2.5%	37	3.0%	131	2.8%
Nordland	20	3.3%	19	3.3%	20	3.7%	15	2.5%	17	2.3%	91	3.0%
Trøndelag	34	3.1%	65	5.6%	44	3.9%	29	2.8%	123	2.2%	295	3.0%
Oppland	11	2.2%	12	2.4%	16	3.1%	16	2.7%	82	2.3%	137	2.4%
Møre og R	20	3.2%	22	3.4%	17	2.7%	36	4.1%	26	2.3%	121	3.1%
Sogn og F	30	10.1%	22	6.6%	21	7.0%	21	5.4%	14	2.9%	108	6.0%
Vestfold	14	2.1%	16	2.5%	19	2.9%	19	2.5%	33	3.4%	101	2.7%
Hedmark	25	5.3%	28	4.6%	23	4.7%	20	2.6%	21	3.9%	117	4.1%
Akershus Øst	45	4.6%	43	3.9%	41	3.8%	37	3.4%	151	3.2%	317	3.5%
Vestre Viken	80	6.8%	54	4.1%	65	5.1%	69	4.4%	197	3.6%	465	4.3%
Fonna							<10	3.4%	13	4.4%	13*	3.9%
Total	486*	3.9%	483	3.6%	510*	3.9%	488	3.4%	1,058	3.1%	3,035	3.5%

* Total number excluding screening area and year with less than 10 recalls

4.2 Recall and consensus

The overall consensus rate presented in Chapter 3.2 was 7.8% and the overall recall rate presented in Chapter 4.1 was 3.3%. Consequently, 42% of the cases discussed at consensus during the period from 2017 to 2021 were recalled for further assessment and 58% were dismissed at consensus. The lowest rate of recalls among consensus cases was observed in Østfold (32%) and the highest was observed in Akershus Øst (55%) (Figure 4.3).

The overall trend was that higher recall rates were observed for breast centers with higher consensus rates, and lower recall rates were observed for breast centers with lower consensus rates (Figure 4.4). It might be expected that breast centers with higher rates of discordant scores among consensus cases have lower rates of recalls among consensus cases. However, when comparing results from Chapter 3.3, this trend was not observed.

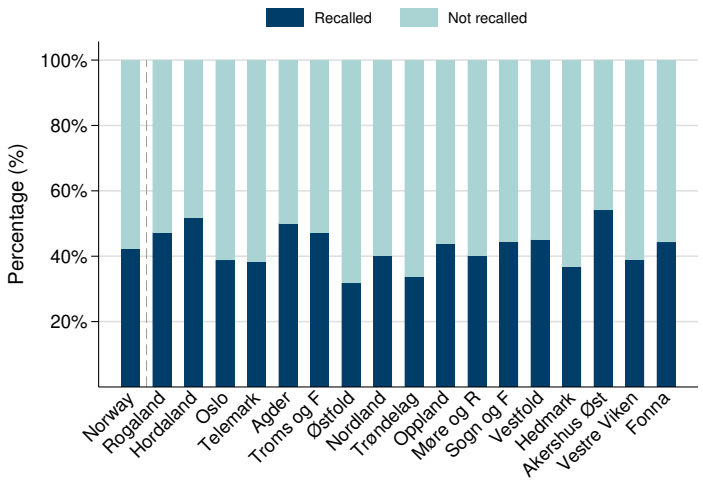


Figure 4.3: Distribution (%) of recalled and not recalled women among cases discussed at consensus by screening area, 2017-2021.

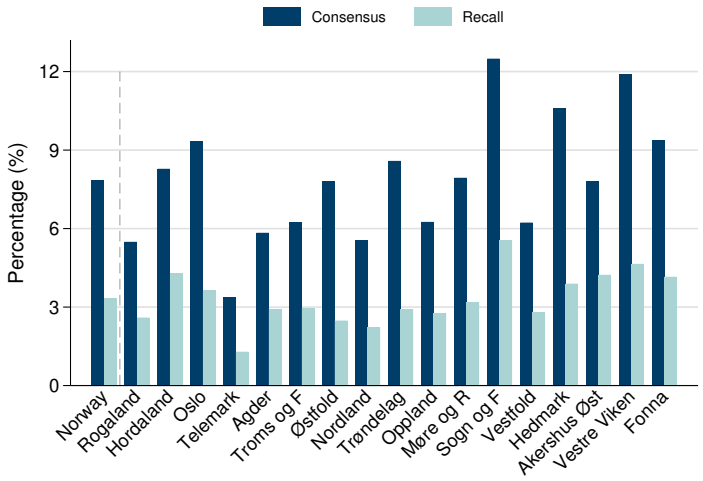


Figure 4.4: Recall rate (%) and consensus rate (%) among screened women by screening area, 2017-2021

4.3 Procedures for further assessment

BreastScreen Norway have procedures for further assessment due to abnormal mammographic findings, clinical symptoms and technically inadequate images (*5*, *48*, *49*). The procedure for abnormal findings includes triple diagnostics; imaging (digital mammography, tomosynthesis and/or ultrasound), clinical examination, and potentially a needle biopsy.

From the initiation of BreastScreen Norway through the end of 2021, 97.3% of the women with abnormal findings on the screening mammograms or with clinical symptoms had a recall for further assessment within 6 months of screening (Table 4.3). Among the women recalled, 53.8% had additional mammograms and/or ultrasound only, while the remaining women, 48.6%, had an additional biopsy. Performance of the procedures varied between the screening areas, with the lowest proportion of no follow-up within 6 months in Telemark and Fonna (Table 4.4). Telemark had the highest percentage of performance of additional mammography, ultrasound and biopsy, 61.1%, while Østfold had the lowest, 19.1%. However, Østfold had the highest percentage of performance of a biopsy in combination with ultrasound, 18.5%, and mammograms or ultrasound alone, 20.2%.

Table 4.3: Frequency of diagnostic follow-up patterns (n and %) among women with abnormal findings and symptoms, 1996-2021

	Abnormal findings		Symptoms		Total	
Procedures	n	%	n	%	n	%
Mammograms, ultrasound and biopsy	47,447	34.0%	1,140	8.6%	48,587	31.8%
Ultrasound and biopsy	8,648	6.2%	1,433	10.9%	10,081	6.6%
Mammograms and biopsy	3,115	2.2%	<10	0.0%	3,115*	2.0%
Biopsy only	699	0.5%	117	0.9%	816	0.5%
Mammograms and ultrasound	60,257	43.2%	3,801	28.8%	64,058	41.9%
Mammograms only or ultrasound only	16,122	11.6%	5,829	44.1%	21,951	14.4%
No follow-up within 6 months	3,285	2.4%	879	6.7%	4,164	2.7%

* Total number excluding groups with less than 10 observations

Table 4.4: Frequency of diagnostic follow-up patterns (n and %) among women with abnormal findings, by screening area, 2017-2021*

	Mammograms, ultrasound and biopsy		Ultrasound and biopsy		Mammograms and ultrasound		Mammograms only or ultrasound only		No follow-up within 6 months	
Screening area	n	%	n	%	n	%	n	%	n	%
Rogaland	862	38.4%	<10	0.3%	1,314	58.6%	26	1.2%	34	1.5%
Hordaland	2,022	49.6%	184	4.5%	1,634	40.1%	158	3.9%	75	1.8%
Oslo	1,504	42.8%	129	3.7%	1,694	48.2%	145	4.1%	44	1.3%
Telemark	320	61.1%	<10	0.8%	188	35.9%	12	2.3%	0	-
Agder	617	31.7%	241	12.4%	837	43.0%	244	12.5%	<10	0.4%
Troms og F	620	36.1%	20	1.2%	981	57.1%	49	2.9%	49	2.9%
Østfold	321	19.1%	311	18.5%	700	41.7%	339	20.2%	<10	0.4%
Nordland	543	45.5%	15	1.3%	607	50.9%	25	2.1%	<10	0.3%
Trøndelag	1,080	39.6%	49	1.8%	1,440	52.8%	108	4.0%	49	1.8%
Oppland	549	43.4%	24	1.9%	659	52.1%	30	2.4%	<10	0.3%
Møre og R	694	40.0%	141	8.1%	656	37.9%	238	13.7%	<10	0.2%
Sogn og F	310	23.0%	29	2.2%	876	65.0%	83	6.2%	50	3.7%
Vestfold	643	41.4%	33	2.1%	814	52.4%	55	3.5%	<10	0.5%
Hedmark	706	42.1%	<10	0.4%	944	56.3%	<10	0.4%	13	0.8%
Akershus Øst	1,640	44.5%	132	3.6%	1,760	47.8%	105	2.9%	46	1.2%
Vestre Viken	2,024	44.4%	153	3.4%	2,117	46.5%	223	4.9%	38	0.8%
Fonna	199	46.7%	<10	0.9%	218	51.2%	<10	1.2%	0	-
Total	14,654	40.9%	1,483	4.1%	17,439	48.6%	1,852	5.2%	431	1.2%

* No cases in procedure-group "Biopsy only" or "Mammograms and biopsy" in this period

4.4 Cumulative risk of a false positive screening result

As more and more women complete the screening program, more accurate estimates of the cumulative risk of different screening outcomes can be provided. For various reasons, women can be recalled due to abnormal findings on the screening mammograms without being diagnosed with breast cancer. This is called a false positive screening result. Such recall for further assessment usually includes additional mammography imaging, ultrasound and/or a biopsy of the breast (See chapter 4.3). Analyses have shown that these women have a higher risk of being diagnosed with breast cancer at a later date (*50*, *51*) and it is important to have an updated estimate of how many women this applies to. Studies have also shown increased stress and anxiety among these women (*52*). These negative effect were transient and declined three months after screening. False positive screening results are considered a harm in mammography screening and the rate should be kept as low as possible.

In a recent publication, it was estimated that 1 in 5 women attending all ten screening invitations in BreastScreen Norway will experience a false positive screening result (Figure 4.5) (*53*). About 1 in 20 women is expected to have an invasive procedure. The results are in line with previous publications that were based on smaller samples of women who had completed the program (*54*–*56*).

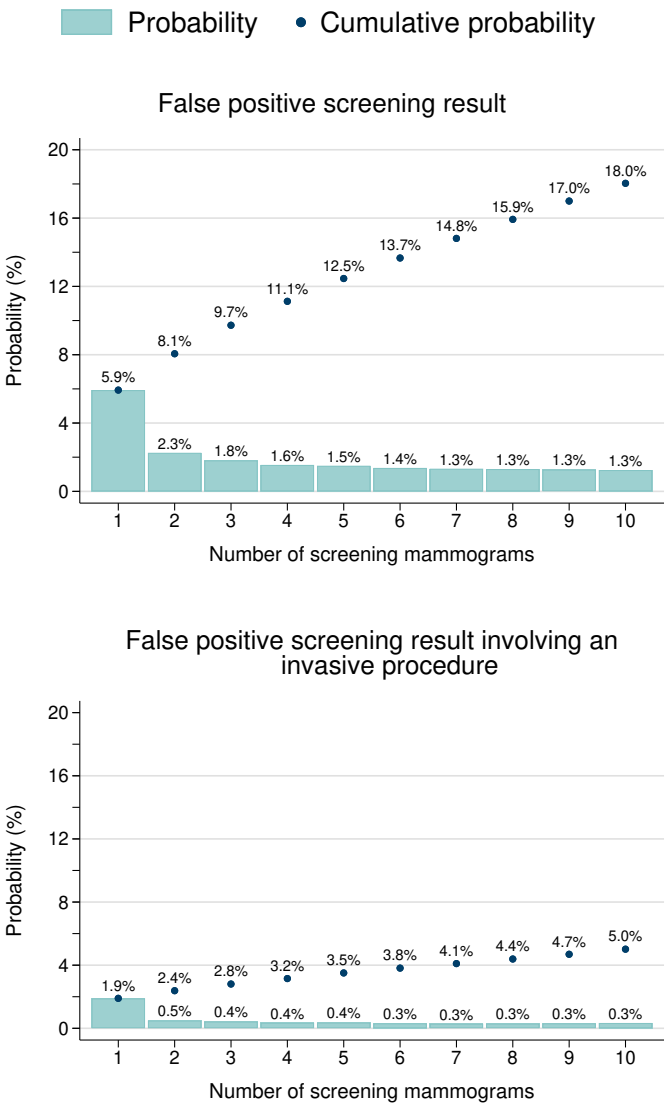


Figure 4.5: Observed risk of experiencing a false-positive screening result (upper panel) and a false-positive screening result involving an invasive procedure (lower panel) among 421,545 women attending BreastScreen Norway, 1995-2019 (Adapted from Cancer/Tsuruda et al, (*53*), this work is licensed under CC-BY-NC 4.0)

5. Breast cancer detection

In this report, screen-detected cancer was defined as a ductal carcinoma in situ (DCIS) or invasive breast cancer diagnosed as a result of a recall assessment (abnormal mammographic findings, clinical symptoms or technically inadequate images) and diagnosed within 182 days (six months) following a screening examination.

Interval cancer was defined as breast cancer diagnosed after a negative screening result or more than six months after a false-positive screening result and within two years after screening. Because of the need for a two-year follow-up period, 2019 is the last year from which data on interval cancer can currently be reported. For interval cancers, the term "the last five years" consequently means interval cancers detected among women screened in the period 2015 to 2019 in this report.

About 25,400 screen-detected cancers were diagnosed among women attending BreastScreen Norway between 1996 and 2021, of which approximately 4,600 (18%) were DCIS. Of the cancers, 98.3% were detected after recall due to abnormal mammographic findings, 1.5% due to clinical symptoms and 0.2% due to technically inadequate images. In this chapter, all cancers regardless of reason for recall are presented. Roughly 7,100 interval cancers were diagnosed between 1996 and 2019, which makes up 22% of all breast cancers detected in the screening program.

5.1 Screen-detected cancer

Since the start-up of the screening program, the overall cancer detection rate has been between 5 and 6 per 1000 screening examinations (Figure 5.1). The rates were higher among prevalently screened women compared to subsequently screened women. Due to the low numbers of women with a subsequent irregular attendance pattern, the detection rate among this group varied, but the overall trend showed a higher detection rate in this group compared to women with other attendance patterns. The detection rate in this group increased during the period when digital mammography was introduced in BreastScreen Norway and has remained higher than the rate for the other attendance patterns.

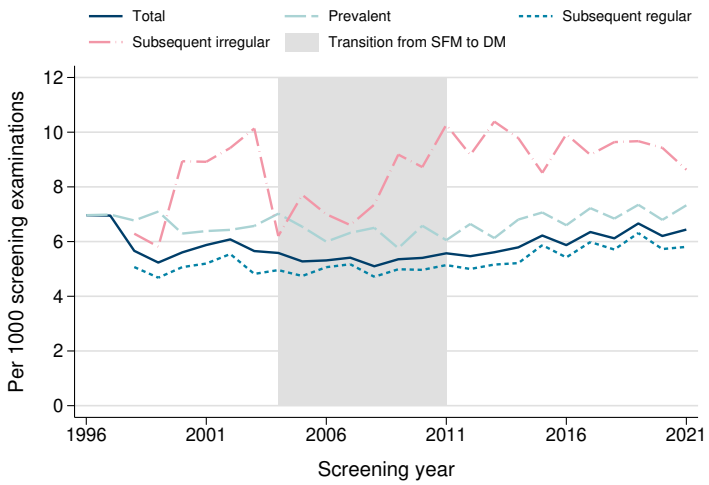


Figure 5.1: Rate (‰) of screen-detected breast cancers (DCIS and invasive) per 1000 screening examinations by attendance pattern and screening year, 1996-2021. SFM: Screen-film mammography, DM: digital mammography

Between 2017 and 2021, the average rate of screen-detected cancer was 6.4 per 1000 screening examinations (Table 5.1). In 2020, the year of the initial COVID-19 lock-down, the cancer detection rate was 6.2 per 1000 screening examinations. Although the detection rate in 2020 was similar to "normal" years, the number of screening examinations performed was lower and approximately 400 fewer breast cancers were detected compared to 2019 (see chapter 1.5 for more details about COVID-19). As of April 30, 2022, 1,578 breast cancers were reported in 2021. This number is somewhat higher than the number of cancers detected in the years prior to the COVID-19 lock-down, but perhaps not high enough to compensate for the low number in 2020. Women who were screened in the last months of 2021 have not yet been followed for six months, and some cases might still be missing. However, from 1996 to 2020, 99.3% of the screen-detected cancers were diagnosed within four months, and it can be assumed that there are few breast cancers from 2021 that are still not reported.

During the last five years, 2017-2021, the highest rate of screen-detected breast cancer was observed in Fonna, Vestre Viken and Hordaland (8.5, 7.6 and 7.5/1000 screening examinations, respectively, Table 5.1). The To-Be studies were performed in Bergen in 2016-2019, which may have affected the breast cancer detection rate in Hordaland during this period (for more details on the To-Be studies, see chapter 10.3). The lowest breast cancer detection rate was observed in Sogn og Fjordane (4.7/1000 screening examinations). The number of screened women in Sogn og Fjordane was small, and the results should be interpreted with caution. However, the range from 4.7 to 8.5 cancers per 1000 screening examinations is interesting and needs to be investigated further.

In the last five years, the detection rate among prevalently screened women was 7.1 per 1000 screening examinations (Table 5.2). The rate was lowest in Nordland (4.4/1000 screening examinations) and highest in Hordaland, Fonna and Vestre Viken (9.0, 8.5 and 8.4/1000 screening examinations, respectively). The rate was 6.2 per 1000 subsequently screened women (Table 5.2). The cancer detection rates among subsequently screened women were lowest in Sogn og Fjordane (4.5/1000 screening examinations) and highest in Fonna, Vestre Viken and Hordaland (8.5, 7.5 and 7.2/1000 screening examinations, respectively).

BreastScreen Norway has recommended the rate of screen-detected cancer to be between 5 and 7 per 1000 screening examinations, and not higher than 9 per 1000 screening examinations (*5*). Over the last five years, most of the screening areas have complied with this recommendation, but not necessarily every year (Table 5.1). This also applied to prevalent and subsequent screens, but the detection rates for these categories varied more due to a lower number of cancers per screening area and year (Table 5.2).

Among the subsequently screened women, the detection rate was lower among women with a regular (5.9/1000 screening examinations) compared to an irregular attendance pattern (9.2/1000 screening examinations) over the last five years (Table 5.3). The rate among women with a subsequent irregular attendance pattern was more than 3 cancers higher per 1000 screening examinations than the rate for all subsequent screening examinations. The rates among women with a subsequent irregular attendance pattern varied substantially between screening areas and year, probably due to the small number of cases.

Table 5.1: Number (n) and rate (‰) of screen-detected breast cancers (DCIS and invasive) per 1000 screening examinations by screening area and year, 2017-2021

	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	n	‰	n	‰	n	‰	n	‰	n	‰	n	‰
Rogaland	102	5.3	115	5.8	120	6.1	92	7.8	99	6.3	528	6.1
Hordaland	138	6.5	152	8.6	191	8.5	82	6.3	147	7.2	710	7.5
Oslo	113	5.9	114	5.6	142	7.2	97	6.3	142	6.5	608	6.3
Telemark	43	5.2	47	5.7	49	6.3	25	3.7	54	5.7	218	5.4
Agder	89	6.9	55	4.0	65	5.1	75	6.5	101	6.5	385	5.8
Troms og F	80	6.6	51	4.7	55	4.3	60	6.3	82	6.4	328	5.6
Østfold	86	6.8	84	6.1	89	6.8	76	6.6	98	5.9	433	6.4
Nordland	56	5.3	58	5.5	67	6.3	40	4.2	72	5.8	293	5.5
Trøndelag	123	6.3	114	5.9	122	6.1	75	5.6	124	5.8	558	6.0
Oppland	63	6.6	55	5.6	64	6.7	38	5.7	65	6.3	285	6.2
Møre og R	74	6.8	77	6.9	95	8.3	49	5.7	83	6.7	378	7.0
Sogn og F	27	5.1	26	5.2	26	5.0	14	4.1	20	3.7	113	4.7
Vestfold	61	5.6	60	5.3	80	7.3	53	5.4	72	5.8	326	5.9
Hedmark	65	6.8	50	5.1	52	5.7	47	7.3	45	5.5	259	6.0
Akershus Øst	122	7.3	119	7.0	129	7.4	73	5.7	150	6.5	593	6.8
Vestre Viken	145	7.2	165	7.9	141	6.8	120	8.0	176	8.3	747	7.6
Fonna							39	8.6	48	8.4	87	8.5
Total	1,387	6.3	1,342	6.1	1,487	6.7	1,055	6.2	1,578	6.4	6,849	6.4

Table 5.2: Rate (‰) of screen-detected breast cancers (DCIS and invasive) per 1000 prevalent (pre) and subsequent (sub) screening examinations by screening area and year, 2017-2021

	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub	Pre	Sub
Rogaland	5.0	5.4	6.2	5.7	5.4	6.2	5.5	8.3	6.7	6.2	5.8	6.2
Hordaland	8.0	6.3	10.5	8.3	8.8	8.5	6.7	6.2	9.9	6.7	9.0	7.2
Oslo	9.9	5.0	7.2	5.2	9.1	6.8	8.5	5.8	5.4	6.7	7.8	5.9
Telemark	5.1	5.2	7.7	5.5	8.2	5.9	5.3	3.5	5.4	5.7	6.3	5.2
Agder	5.3	7.2	5.5	3.7	5.3	5.0	5.4	6.6	7.3	6.4	5.8	5.8
Troms og F	5.3	6.8	4.6	4.7	7.1	3.8	12.2	5.3	10.0	5.8	7.8	5.3
Østfold	6.6	6.8	5.2	6.3	6.4	6.8	9.6	6.2	8.1	5.4	7.0	6.3
Nordland	4.8	5.3	3.0	5.9	5.9	6.4	3.6	4.3	4.6	5.9	4.4	5.6
Trøndelag	9.8	5.7	5.4	6.0	5.5	6.2	6.2	5.4	6.1	5.7	6.7	5.8
Oppland	6.6	6.6	4.6	5.8	8.3	6.5	3.3	6.0	7.8	6.0	6.3	6.2
Møre og R	8.6	6.5	9.8	6.5	11.0	7.8	3.2	6.1	6.0	6.9	7.9	6.8
Sogn og F	3.6	5.4	7.2	5.0	4.3	5.1	8.9	3.4	5.8	3.4	5.6	4.5
Vestfold	6.6	5.5	7.4	5.0	9.8	7.0	6.3	5.3	5.5	5.8	7.1	5.7
Hedmark	6.5	6.8	3.8	5.3	4.1	6.0	9.0	7.0	9.8	4.9	6.4	5.9
Akershus Øst	8.7	7.1	7.0	7.0	8.1	7.3	7.1	5.3	6.5	6.5	7.4	6.7
Vestre Viken	7.4	7.2	10.0	7.5	7.2	6.7	7.4	8.1	9.2	8.0	8.4	7.5
Fonna							6.2	9.0	10.3	8.1	8.5	8.5
Total	7.2	6.2	6.8	6.0	7.3	6.5	6.8	6.1	7.3	6.3	7.1	6.2

Table 5.3: Rate (‰) of screen-detected breast cancers (DCIS and invasive) per 1000 subsequent regular (reg) and subsequent irregular (irreg) screening examinations by screening area and year, 2017-2021

	Screening year											
	2017		2018		2019		2020		2021		Total	
Screening area	Reg	Irreg	Reg	Irreg	Reg	Irreg	Reg	Irreg	Reg	Irreg	Reg	Irreg
Rogaland	5.2	8.4	5.4	10.2	5.5	17.3	7.8	15.3	5.6	12.2	5.7	12.6
Hordaland	6.0	9.5	7.6	15.4	8.3	10.7	5.5	12.0	6.8	6.1	6.9	9.7
Oslo	4.5	10.2	5.0	7.1	6.4	11.5	5.9	5.0	6.1	10.9	5.6	9.1
Telemark	5.3	4.4	5.1	10.3	6.3	0.0	3.1	6.9	5.2	11.8	5.1	7.3
Agder	6.7	13.5	3.7	4.1	5.2	2.9	6.5	8.5	6.4	5.8	5.7	7.0
Troms og F	6.7	9.2	4.6	5.1	3.8	4.2	5.1	7.5	5.7	7.3	5.2	6.6
Østfold	6.8	7.5	6.1	8.5	6.5	10.9	5.6	11.9	5.1	8.1	6.0	9.4
Nordland	5.5	3.3	5.0	18.9	5.9	15.0	3.9	9.8	5.8	8.2	5.3	10.7
Trøndelag	5.5	9.1	5.7	10.4	5.8	11.6	5.2	7.8	4.2	9.5	5.3	9.6
Oppland	6.8	4.0	5.8	6.1	5.9	15.7	5.6	10.2	5.2	7.2	5.9	7.9
Møre og R	6.3	9.6	6.1	10.9	8.1	4.8	4.9	14.8	6.9	7.0	6.5	9.5
Sogn og F	5.1	10.1	5.2	3.0	4.7	10.0	3.1	5.2	3.6	2.0	4.4	5.5
Vestfold	5.5	4.6	4.7	9.2	7.0	6.1	5.4	4.0	5.0	13.3	5.5	7.8
Hedmark	6.7	8.5	4.4	16.6	6.3	2.0	7.7	2.6	4.3	12.9	5.7	8.3
Akershus Øst	6.9	9.2	7.1	6.3	7.1	9.2	4.8	10.2	6.4	7.1	6.5	7.8
Vestre Viken	6.5	16.0	7.3	10.7	6.4	11.8	7.4	13.3	7.6	9.1	7.0	11.0
Fonna							8.7	12.6	7.1	23.6	7.8	18.7
Total	6.0	9.2	5.7	9.6	6.3	9.7	5.7	9.4	5.8	8.6	5.9	9.2

5.2 Interval cancer

The rate of interval cancers has been stable at about 1.8 per 1000 screening examinations since the start-up of the screening program (Figure 5.2). Unlike screen-detected cancers, interval cancer detection rates did not differ as clearly between different attendance patterns. Subsequently screened women with an irregular attendance pattern tended to have a higher rate of detected interval cancers (Figure 5.2), but the number of cases diagnosed each year for this group was small and should be interpreted with caution.

The majority of interval cancers were detected a year or more after the previous screening examination (Figure 5.3). This distribution has been relatively stable since the inception of the program (*1*, *57*).

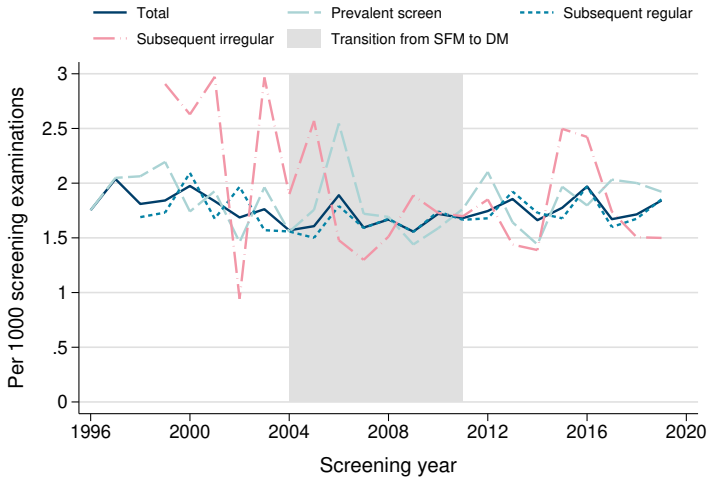


Figure 5.2: Rate (‰) of interval breast cancers (DCIS and invasive) per 1000 screened women by attendance pattern and screening year, 1996-2019. SFM: Screen-film mammography, DM: digital mammography

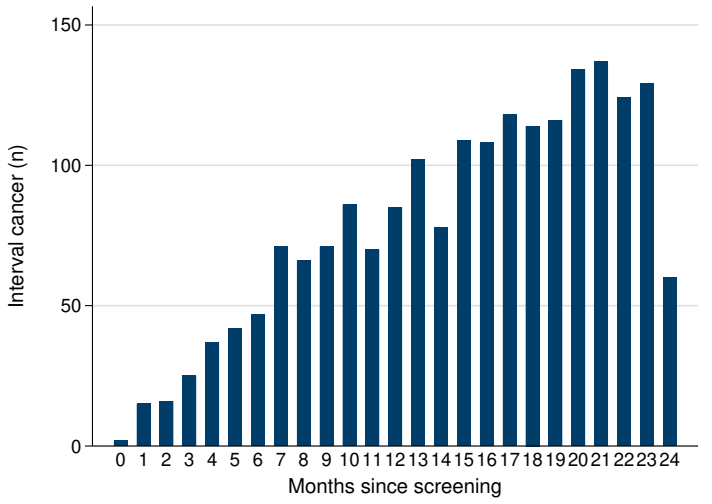


Figure 5.3: Distribution (n) of interval breast cancers (DCIS and invasive) by months since last screening, 2015-2019

On average, 1.8 interval cancers were diagnosed per 1000 screening examinations among women screened between 2015 and 2019 (Table 5.4). The rates varied across screening areas in this period. Because the number of cases diagnosed each year in single screening areas was very small, this variation must be interpreted with caution. The lowest rate of interval cancer in this period was in Hedmark and Hordaland (1.4 and 1.5/1000 screening examinations, respectively), while the highest rate was observed in Akershus Øst with 2.3 interval cancers per 1000 screening examinations. Hordaland had one of the highest screen-detected cancer rates (see section 5.1), which could explain why the interval cancer rate was lower in this area.

Interval cancer is an important parameter in the quality assurance of BreastScreen Norway since a high rate indicates low program sensitivity. Regular reviews of prior screening and diagnostic mammograms from women diagnosed with interval cancer is one way to improve the radiologists' sensitivity and reduce the interval cancer rate and the overall proportion of interval cancers. Review studies have identified some interval cancers to have visible signs on the screening mammograms prior to diagnosis (*58*, *59*). This proportion of "missed" cases ranged from 1.3% to 35.9% in the two studies, depending on the review design. Because 22% of cancers detected in BreastScreen Norway are interval cancers, and the minority of these are "missed", the number of "missed" interval cancers represents only a small proportion of all breast cancers detected among women attending BreastScreen Norway.

Table 5.4: Number (n) and rate (‰) of interval breast cancers (DCIS and invasive) per 1000 screening examinations by screening area and screening year, 2015-2019

	Screening year											
	2015		2016		2017		2018		2019		Total	
Screening area	n	‰	n	‰	n	‰	n	‰	n	‰	n	‰
Rogaland	33	1.7	38	2.0	35	1.8	40	2.0	33	1.7	179	1.8
Hordaland	28	1.3	32	1.7	37	1.7	22	1.3	34	1.5	153	1.5
Oslo	39	2.1	40	2.1	38	2.0	31	1.5	42	2.1	190	2.0
Telemark	17	2.1	14	1.7	16	1.9	16	1.9	12	1.5	75	1.9
Agder	14	1.1	24	1.8	22	1.7	20	1.5	34	2.6	114	1.7
Troms og F	19	1.5	25	2.3	16	1.3	22	2.0	19	1.5	101	1.7
Østfold	18	1.4	32	2.5	14	1.1	24	1.7	24	1.8	112	1.7
Nordland	14	1.3	15	1.5	15	1.4	18	1.7	21	2.0	83	1.6
Trøndelag	37	2.0	35	1.7	34	1.7	25	1.3	41	2.0	172	1.8
Oppland	17	1.9	22	2.3	<10	0.7	18	1.8	12	1.3	69*	1.6
Møre og R	31	2.9	21	1.9	23	2.1	13	1.2	29	2.5	117	2.1
Sogn og F	11	2.2	11	2.2	12	2.3	11	2.2	<10	1.5	45*	2.1
Vestfold	14	1.3	21	1.9	24	2.2	24	2.1	20	1.8	103	1.9
Hedmark	13	1.3	22	2.3	<10	0.7	19	1.9	<10	0.9	69	1.4
Akershus Øst	45	2.8	38	2.3	37	2.2	34	2.0	37	2.1	191	2.3
Vestre Viken	34	1.7	37	1.8	28	1.4	39	1.9	37	1.8	175	1.7
Total	384	1.8	427	2.0	365	1.7	376	1.7	411	1.8	1,963	1.8

* Total number excluding screening area and year with less than 10 interval cancers

5.3 Association between recall and cancer detection

In Chapter 4, varying recall rates between the different screening areas were described, and in Section 5.1 and 5.2, varying cancer detection rates between the screening areas were observed. When combining these results, it was observed that screening areas with higher recall rates did not necessarily have higher rates of screen-detected cancers compared to screening areas with lower recall rates (Figure 5.4). However, most screening areas with a low recall rate also had a low rate of screen-detected cancers, and a statistically significant positive association was observed between the recall rate and the rate of screen-detected cancers. Fonna was not included for interval cancers due to a limited number of cases. The rates of recall and screen-detected cancer are presented, but be aware of a limited number of screen-detected cancer cases in Fonna. When excluding Fonna from the analysis of recall and screen-detected cancers, the statistically significant positive association became non-significant.

In theory, it is expected that screening areas with higher recall rates have lower rates of interval cancers, and vice versa. This is not observed for screening areas in BreastScreen Norway (Figure 5.4). A low interval cancer rate was observed among screening areas with both low and high recall rates.

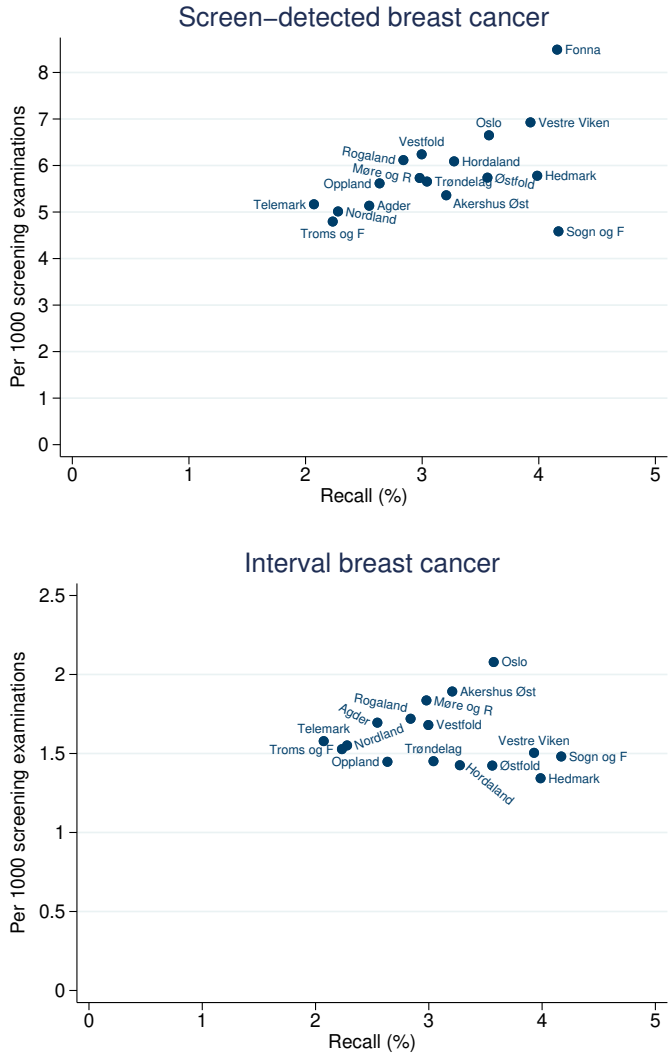


Figure 5.4: Recall Rate (%) and rate per 1000 examinations (‰) of screen-detected cancer (DCIS and invasive, upper panel), 1996-2021, and interval cancer (DCIS and invasive, lower panel), 1996-2019, by screening area

6. Positive predictive values

The positive predictive value (PPV) of a test is the probability that an event with a positive test result is a true positive (*60*). In mammographic screening this translates to a positive screening result indicating the presence of breast cancer.

In mammographic screening, PPV-1 refers to the proportion of breast cancers detected among women recalled due to abnormal mammographic findings. A high PPV-1 indicates that a high proportion of women recalled for further assessment is diagnosed with breast cancer and a low rate of false positive screening results, and vice versa. PPV-3 refers to the proportion of breast cancers diagnosed as a result of an invasive procedure. A high PPV-3 indicates that a high proportion of women who undergo an invasive procedure is diagnosed with breast cancer. PPV-2 has been used in reference to the proportion of needle biopsies yielding a breast cancer diagnosis. However, according to BI-RADS®, PPV-2 is based on a recommendation for tissue diagnosis, while PPV-3 is based on results of biopsies actually performed (*61*). In BreastScreen Norway, 1-2% of recalled women for whom a biopsy was recommended are reported to not have undergone this procedure. BreastScreen Norway is thus not reporting PPV-2 as an early performance measure.

Calculation of PPV in a screening program is reliant on a complete data material. Recall assessments, biopsies and cancer cases are reported to the Cancer Registry by radiologists and pathologists at the breast centers. BreastScreen Norway also registers results of benign biopsies to, among other things, monitor the rate of PPV-3. Due to incomplete reporting of histological reports on biopsies with a benign outcome, PPV-3 is not given for the centers Rogaland, Oslo and Fonna in 2020 and 2021, in Table 6.2. See section 7.7 for more details on reporting and completeness of data.

6.1 PPV-1

PPV-1 remained stable between 15 and 20% between 1996 and 2021 (Figure 6.1). Women with a subsequent regular and irregular attendance pattern had a higher PPV-1 compared to prevalently screened women. PPV-1 for prevalently screened women decreased during the transition from screen-film mammography to digital mammography, from about 15% in 2003 to about 10% in 2011.

For the period 2017-2021, the overall PPV-1 was 18.9% (Table 6.1). PPV-1 was lower for prevalenty screened women (9.4%) than for subsequently screened women (23.6%). PPV-1 ranged from 8.3% in Sogn og Fjordane to 41.2% in Telemark. Sogn og Fjordane had the lowest PPV-1 for prevalently (4.1%) and subsequently (10.4%) screened women, while Telemark had the highest, 27.2% and 46.1%, respectively.

According to the quality assurance manual of BreastScreen Norway, the desirable rate of PPV-1 is $\geq$16%, with an acceptable rate of >12% (*5*). All but one screening area achieved this.

Results for PPV-1 are presented for women recalled due to abnormal mammographic findings. Including women recalled due to clinical symptoms or technically inadequate images would have lowered the PPV-1 to 17.4% for all screening areas in the period 2017-2021.

6.2 PPV-3

Due to incomplete reporting of invasive procedures for 2020 and 2021, results for PPV-3 are presented until 2019 in Figure 6.1 (bottom panel), and individual screening areas are excluded in Table 6.2.

PPV-3 increased from roughly 35% in 1996 to about 45% in 2019 (Figure 6.1). Women with a subsequent regular and irregular screening pattern had a higher PPV-3 compared to prevalently screened women. PPV-3 for prevalently screened women decreased during the transition from screen-film mammography to digital mammography, from about 35% in 2003 to 20% in 2011, while it increased for subsequently screened women with both a regular and irregular screening pattern.

For the period 2017-2021, the overall PPV-3 for the included screening areas was 42.9% (not presented in table). The value ranged from 32.7% in Sogn og Fjordane to 67.3% in Telemark (Table 6.2). PPV-3 was substantially lower for prevalenty screened women than for subsequently screened women. Akershus Øst had the lowest PPV-3 (15.4%) for prevalently screened women, while for subsequently screened women the rate was lowest in Hordaland (38.6%). Telemark had the highest PPV-3 for prevalently screened women (46.3%), while Østfold had the highest PPV-3 among subsequently screened women (80.0%).

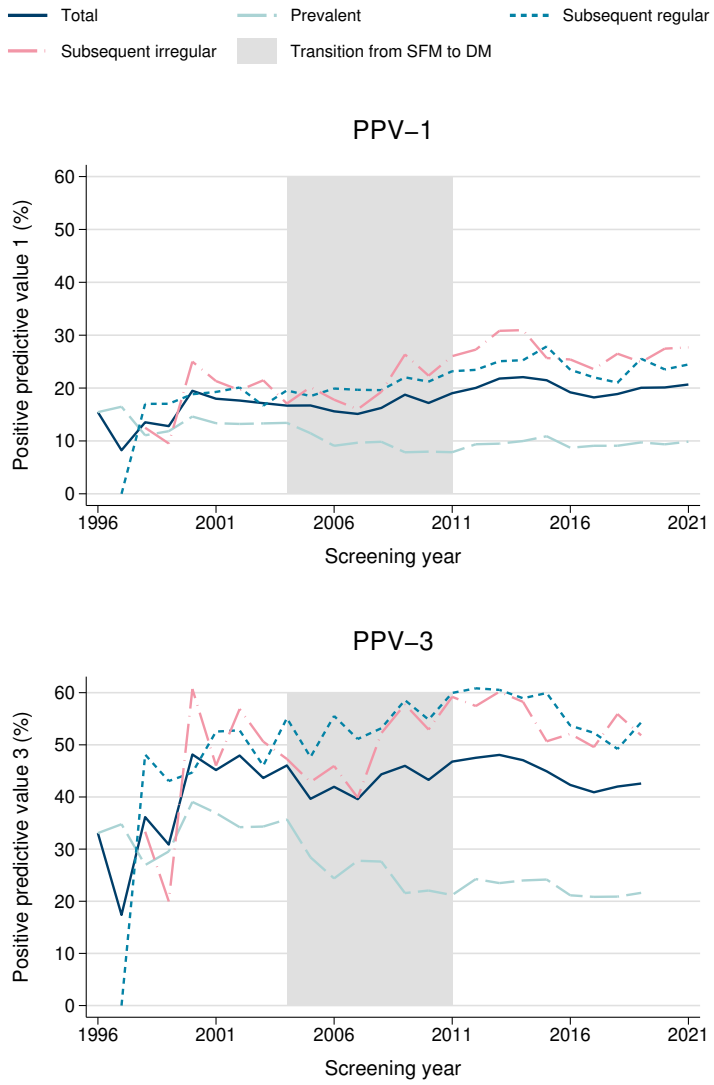


Figure 6.1: Proportion (%) of screen-detected breast cancers (DCIS and invasive) among women recalled due to abnormal findings, 1996-2021 (PPV-1, upper panel), and as a result of an invasive procedure, 1996-2019 (PPV-3, lower panel, 1996-2019), by attendance pattern and screening year. SFM: Screen-film mammography, DM: digital mammography

Table 6.1: PPV-1: Propotion (%) of screen-detected breast cancers (DCIS and invasive) among women recalled due to abnormal findings by screening area and screening year, for all screening examinations (upper table), prevalently screened (middle table) and subsequently screened (lower table), 2017-2021

Total	Screening year					
Screening area	2017	2018	2019	2020	2021	Total
Rogaland	27.0%	25.5%	23.3%	22.3%	19.0%	23.2%
Hordaland	16.5%	16.0%	20.3%	16.7%	16.6%	17.3%
Oslo	16.2%	17.5%	17.9%	16.5%	17.0%	17.1%
Telemark	39.8%	36.8%	50.0%	34.2%	44.3%	41.2%
Agder	23.7%	13.5%	23.2%	23.1%	17.0%	19.5%
Troms og F	22.3%	17.8%	18.6%	19.8%	16.4%	18.8%
Østfold	26.5%	23.8%	25.1%	29.4%	23.5%	25.4%
Nordland	20.8%	21.6%	24.7%	25.3%	30.5%	24.4%
Trøndelag	18.1%	15.7%	21.7%	20.7%	29.0%	20.3%
Oppland	20.6%	19.4%	27.3%	20.9%	22.7%	22.0%
Møre og R	20.3%	18.4%	25.2%	19.5%	25.3%	21.8%
Sogn og F	7.4%	8.0%	7.9%	9.2%	10.3%	8.3%
Vestfold	17.4%	20.6%	25.8%	18.7%	22.0%	20.9%
Hedmark	16.5%	11.5%	13.7%	18.1%	19.5%	15.3%
Akershus Øst	15.1%	15.1%	17.9%	13.7%	16.5%	15.8%
Vestre Viken	12.8%	18.2%	16.0%	16.5%	18.2%	16.2%
Fonna				19.9%	20.4%	20.2%
Total	17.9%	17.5%	20.3%	19.0%	19.7%	18.9%

Prevalent						
Rogaland	10.2%	12.1%	8.9%	7.8%	8.3%	9.4%
Hordaland	13.4%	10.9%	11.2%	8.7%	11.5%	11.2%
Oslo	12.1%	10.0%	9.6%	11.5%	7.0%	9.9%
Telemark	24.1%	26.9%	41.7%	26.3%	21.1%	27.2%
Agder	10.8%	9.0%	11.8%	10.1%	9.9%	10.1%
Troms og F	7.3%	8.0%	12.0%	17.4%	10.4%	10.9%
Østfold	11.5%	9.6%	10.7%	21.6%	16.6%	13.4%
Nordland	7.5%	5.0%	10.0%	8.3%	11.8%	8.3%
Trøndelag	10.8%	7.0%	7.8%	11.5%	13.3%	9.7%
Oppland	9.4%	7.4%	14.3%	5.7%	10.9%	9.6%
Møre og R	12.3%	10.5%	15.6%	6.0%	10.1%	11.4%
Sogn og F	2.3%	3.8%	3.0%	8.7%	7.0%	4.1%
Vestfold	7.5%	11.2%	12.4%	8.1%	8.1%	9.4%
Hedmark	7.6%	3.8%	4.3%	11.0%	11.9%	7.3%
Akershus Øst	7.8%	7.6%	8.2%	7.0%	6.9%	7.5%
Vestre Viken	5.5%	10.6%	7.1%	6.5%	9.4%	7.7%
Fonna				5.6%	10.0%	7.9%
Total	9.1%	9.1%	9.7%	9.4%	9.9%	9.4%

Subsequent						
Rogaland	34.0%	33.6%	29.8%	30.0%	25.4%	30.3%
Hordaland	17.3%	18.3%	23.2%	20.3%	19.3%	19.7%
Oslo	18.9%	22.6%	22.9%	19.3%	23.7%	21.7%
Telemark	45.6%	39.4%	52.8%	37.0%	54.8%	46.1%
Agder	27.4%	15.8%	26.9%	28.0%	19.5%	22.9%
Troms og F	28.9%	22.1%	22.5%	20.9%	19.5%	22.7%
Østfold	32.9%	31.0%	32.9%	31.4%	27.7%	31.1%
Nordland	28.1%	28.8%	32.0%	35.7%	35.7%	31.7%
Trøndelag	22.8%	19.2%	28.8%	26.0%	34.6%	25.5%
Oppland	26.0%	25.5%	32.9%	27.1%	28.5%	27.9%
Møre og R	24.3%	22.2%	30.1%	24.5%	35.2%	26.9%
Sogn og F	10.4%	10.0%	10.2%	9.4%	11.7%	10.4%
Vestfold	23.4%	26.3%	33.5%	24.5%	30.5%	27.6%
Hedmark	20.3%	14.9%	16.8%	22.1%	23.8%	18.8%
Akershus Øst	19.5%	18.7%	24.4%	19.4%	22.9%	21.0%
Vestre Viken	16.5%	21.7%	21.4%	23.0%	24.2%	21.0%
Fonna				28.2%	26.0%	27.0%
Total	22.2%	21.6%	25.5%	24.1%	25.1%	23.6%

Table 6.2: PPV-3: Proportion (%) of screen-detected breast cancers (DCIS and invasive) diagnosed as a result of an invasive procedure by screening area and screening year, for all screening examinations (upper table), prevalently screened (middle table) and subsequently screened (lower table), 2017-2021

Total	Screening year					
Screening area	2017	2018	2019	2020	2021	Total
Rogaland	60.7%	62.2%	59.4%	-	-	-
Hordaland	34.0%	30.9%	35.6%	30.7%	33.8%	33.2%
Oslo	36.0%	37.0%	41.3%	-	-	-
Telemark	67.2%	63.0%	73.8%	61.0%	69.2%	67.3%
Agder	48.6%	33.3%	50.0%	47.8%	57.0%	47.3%
Troms og F	62.5%	52.6%	50.0%	47.6%	43.8%	50.9%
Østfold	69.1%	63.8%	67.7%	71.2%	69.1%	68.1%
Nordland	55.6%	51.4%	50.4%	48.2%	67.3%	54.5%
Trøndelag	50.4%	45.5%	48.0%	49.3%	66.5%	51.2%
Oppland	46.6%	44.3%	57.8%	48.1%	51.9%	49.5%
Møre og R	47.7%	39.3%	48.5%	38.6%	51.1%	45.1%
Sogn og F	32.5%	30.2%	26.6%	36.8%	47.6%	32.7%
Vestfold	45.2%	44.4%	54.8%	43.8%	53.9%	48.6%
Hedmark	43.3%	31.6%	29.3%	37.4%	53.6%	37.3%
Akershus Øst	33.3%	31.8%	34.1%	27.2%	38.3%	33.2%
Vestre Viken	25.3%	38.5%	35.7%	33.7%	45.4%	34.9%
Fonna				-	-	-
Total	41.7%	40.4%	43.7%	-	-	-

Prevalent						
Rogaland	28.2%	37.0%	22.6%	-	-	-
Hordaland	23.4%	19.0%	19.5%	16.0%	22.8%	20.3%
Oslo	23.7%	21.3%	21.3%	-	-	-
Telemark	36.8%	46.7%	62.5%	55.6%	38.1%	46.3%
Agder	22.0%	22.2%	24.2%	22.5%	51.7%	26.9%
Troms og F	25.8%	22.6%	31.7%	35.6%	24.6%	28.2%
Østfold	31.4%	31.4%	35.1%	45.8%	50.0%	39.2%
Nordland	21.2%	15.4%	24.3%	17.2%	50.0%	22.6%
Trøndelag	37.3%	20.3%	19.2%	26.8%	30.6%	26.6%
Oppland	22.0%	19.4%	37.0%	15.0%	27.3%	24.2%
Møre og R	27.3%	20.6%	30.8%	11.4%	22.8%	23.6%
Sogn og F	10.7%	13.8%	10.0%	36.4%	44.4%	16.8%
Vestfold	18.5%	21.4%	27.5%	20.5%	23.3%	22.2%
Hedmark	19.1%	10.0%	9.3%	20.4%	37.0%	17.6%
Akershus Øst	16.1%	14.7%	16.1%	13.1%	17.0%	15.4%
Vestre Viken	10.0%	23.1%	15.2%	13.7%	24.1%	16.6%
Fonna				-	-	-
Total	20.8%	20.9%	21.6%	-	-	-

Subsequent						
Rogaland	71.0%	73.0%	75.7%	-	-	-
Hordaland	37.3%	37.0%	40.8%	37.1%	40.1%	38.6%
Oslo	46.2%	47.5%	54.3%	-	-	-
Telemark	80.0%	67.2%	77.6%	62.5%	80.7%	74.3%
Agder	56.4%	38.9%	58.9%	56.4%	58.1%	54.0%
Troms og F	74.2%	66.7%	61.2%	54.3%	56.8%	62.8%
Østfold	84.1%	76.1%	81.1%	78.8%	80.2%	80.0%
Nordland	72.7%	62.4%	60.4%	64.8%	69.6%	65.6%
Trøndelag	56.4%	55.4%	60.8%	62.5%	80.3%	62.1%
Oppland	57.8%	54.7%	64.6%	59.3%	62.7%	59.7%
Møre og R	59.0%	49.6%	57.3%	48.9%	70.2%	56.4%
Sogn og F	43.6%	38.6%	34.4%	37.0%	48.5%	39.8%
Vestfold	63.0%	61.0%	69.5%	54.9%	69.4%	63.8%
Hedmark	54.4%	41.9%	35.9%	48.6%	61.4%	46.4%
Akershus Øst	45.0%	41.1%	45.6%	40.6%	51.9%	45.1%
Vestre Viken	34.4%	45.4%	48.5%	46.0%	59.0%	45.4%
Fonna				-	-	-
Total	52.0%	49.9%	54.0%	-	-	-

7. Tumor histopathology

In this report, the first screen-detected or interval cancer diagnosed as a result of participation in BreastScreen Norway was included. Data for women diagnosed with breast cancer or recurrence prior to their first invitation were excluded. Some of the women screened in 2021 and diagnosed with DCIS or invasive cancer in 2022 are not included here due to incomplete coding of tumor histopathology information for this group. Consequently, there are slightly fewer cancer cases in this chapter compared to preceding chapters.

7.1 Histologic type

Histologic type refers to a tumor's growth patterns (*62*). These are identified through morphological and cytological patterns associated with distinct clinical characteristics and/or outcomes. This section includes ductal carcinoma in situ (DCIS), invasive cancer of no special type (NST), invasive lobular carcinoma (ILC) and other types of invasive carcinoma.

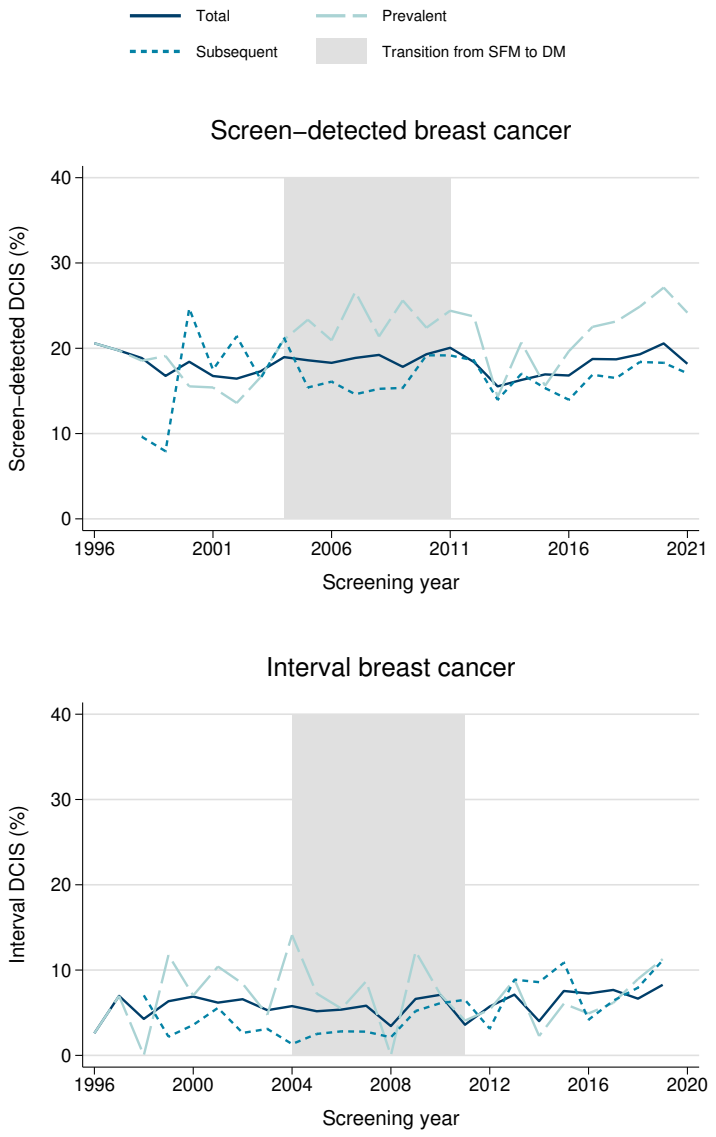


Figure 7.1: Distribution (%) of ductal carcinoma in situ (DCIS) for screen-detected, 1996-2021 (upper panel) and interval cancer, 1996-2019 (lower panel), by attendance pattern. SFM: Screen-film mammography, DM: digital mammography

From 1996 to 2021, the proportion of screen-detected DCIS was stable at 15-20% for all attendance patterns except for women with a subsequent irregular attendance pattern (Figure 7.1). Similar patterns, but at an approximately 5% lower level, were observed for women with interval DCIS. The number of cases, especially among women with a prevalent or subsequent irregular attendance pattern were small, and the results should be interpreted with caution.

The proportion of DCIS was 19.0% of screen-detected cancers in BreastScreen Norway, 2017-2021. (Table 7.1). The percentage varied from 11.0% in Troms og Finnmark to 23.7% in Oslo. Invasive cancer of no special type (NST) was the most common histologic type (68.1%) while 9.4% of screen-detected cancers were invasive lobular carcinomas and 3.4% were other invasive carcinomas. (Table 7.1).

DCIS accounted for less than 5% of all breast malignancies registered before the start of organized screening in 1996 (*63*). The rate of DCIS increased substantially after the start-up of BreastScreen Norway, which is related to the asymptomatic characteristics usually detected due to calcifications (*64*). The asymptomatic characteristics might also be one of the reasons why only 7.5% of the interval cancers are DCIS. DCIS is often associated with clinically unapparent disease. Measuring the extent of the disease is challenging even if preoperative MRI is used (*48*, *65*).

Table 7.1: Number (n) and proportion (%) of histologic type [ductal carcinoma in situ (DCIS), invasive cancer of no special type (NST), invasive lobular carcinoma (ILC) and other invasive carcinomas (Other)] for screen-detected breast cancer by screening area, 2017-2021

	DCIS		NST		ILC		Other	
Screening area	n	%	n	%	n	%	n	%
Rogaland	90	17.3%	378	72.6%	30	5.8%	23	4.4%
Hordaland	143	20.5%	456	65.2%	76	10.9%	24	3.4%
Oslo	143	23.7%	367	60.8%	61	10.1%	33	5.5%
Telemark	31	14.2%	161	73.9%	20	9.2%	<10	2.8%
Agder	73	19.2%	260	68.2%	33	8.7%	15	3.9%
Troms og F	35	11.0%	266	83.4%	13	4.1%	<10	1.6%
Østfold	69	16.1%	307	71.6%	45	10.5%	<10	1.9%
Nordland	51	17.6%	207	71.4%	26	9.0%	<10	2.1%
Trøndelag	115	20.9%	354	64.4%	48	8.7%	33	6.0%
Oppland	43	15.5%	198	71.5%	28	10.1%	<10	2.9%
Møre og R	70	19.1%	252	68.7%	42	11.4%	<10	0.8%
Sogn og F	20	17.7%	74	65.5%	12	10.6%	<10	6.2%
Vestfold	52	16.0%	225	69.4%	32	9.9%	15	4.6%
Hedmark	42	16.2%	186	71.8%	19	7.3%	12	4.6%
Akershus Øst	118	20.5%	386	66.9%	65	11.3%	<10	1.4%
Vestre Viken	174	23.5%	467	63.0%	77	10.4%	23	3.1%
Fonna	16	18.4%	58	66.7%	10	11.5%	<10	3.4%
Total	1,285	19.0%	4,602	68.1%	637	9.4%	232	3.4%

7.2 Characteristics of DCIS

DCIS includes a wide spectrum of disease ranging from low-grade lesions that are not life threatening, to widespread high-grade lesions that may harbor foci of invasive disease (*66*). Mortality from DCIS is low. In fact, women 50 years or older diagnosed with DCIS have lower all-cause mortality than the general female population. However, breast cancer mortality ten years after treatment is shown to be higher for women treated for DCIS compared to the general population (*67*).

Tumor diameter and histologic grade of DCIS are important parameters in the quality assurance of the screening program. Following cases for registration of potential relapse is of interest, but is not included in this report. Further, the proportion of women diagnosed and treated for DCIS grade I should be as low as possible (below 20%) to keep the rate of small low proliferation screen-detected cancers low.

In BreastScreen Norway in the period 2017-2021, the proportion of DCIS that were less than 11 mm was 29%, while it was 9% for DCIS greater than 50 mm (Table 7.3). The proportion of tumors larger than 50 mm was 7% in 2019 and 10% in 2020. The proportion of grade I DCIS was 18%, while it was 67% for grade III, during the period from 2017 to 2021. The proportion of reported grade III DCIS was 71% in 2017 and 64% in 2021, while the proportion of grade II DCIS was 11% in 2017 and 20% in 2021. Grade and diameter are not described for individual screening areas as the numbers are small.

Table 7.2: Distribution (%) of tumor diameter (<11 mm, 11-20 mm, 21-50 mm, >50 mm) of screen-detected ductal carcinoma in situ (DCIS), by screning year, 2017-2021

	<11 mm	11-20 mm	21-50 mm	>50 mm
2017 (n=260)	30%	28%	33%	9%
2018 (n=251)	29%	27%	35%	9%
2019 (n=287)	32%	31%	30%	7%
2020 (n=217)	28%	25%	37%	10%
2021 (n=270)	26%	32%	34%	9%
Total (n=1,285)	29%	29%	34%	9%

Table 7.3: Distribution (%) of van Nuys grade for screen-detected ductal carcinoma in situ (DCIS) by screening year, 2017-2021

	Grade I	Grade II	Grade III
2017 (n=260)	19%	11%	71%
2018 (n=251)	18%	12%	70%
2019 (n=287)	20%	14%	65%
2020 (n=217)	18%	16%	66%
2021 (n=270)	16%	20%	64%
Total (n=1,285)	18%	14%	67%

7.3 Tumor diameter

Tumor diameter is an important factor in breast cancer staging and can affect treatment and prognosis. Overall, reported tumor diameter for invasive screen-detected cancers was stable between 1996 and 2021, with 35-40% of the cases being 10 mm or smaller and 45% with a diameter between 11 and 20 mm (Figure 7.2). Invasive interval cancers with a tumor diameter under 11 mm remained stable at approximately 20% for the period 1996-2019 (Figure 7.2). Interval cancers with a tumor diameter between 11 and 20 mm or 21 and 50 mm were fluctuating around 40% in this period. There was a higher proportion of cancers with a tumor diameter of more than 50 mm among interval cancers than screen-detected cancers.

Between 2017 and 2021, 44.0% of the reported invasive screen-detected tumors were 11-20 mm, and 19.5% of the tumors were greater than 20 mm (Table 7.4). Of all interval cancers, 42.5% had a tumor diameter between 11 and 20 mm in the last five years, 2015-2019 (Table 7.4). A substantially lower proportion of interval cancers were <11 mm (19.1%) compared to screen-detected cancers (36.5%). Interval cancers showed an equivalently higher proportion of tumor diameter >20 mm (38.4% versus 19.5% for screen-detected cancer).

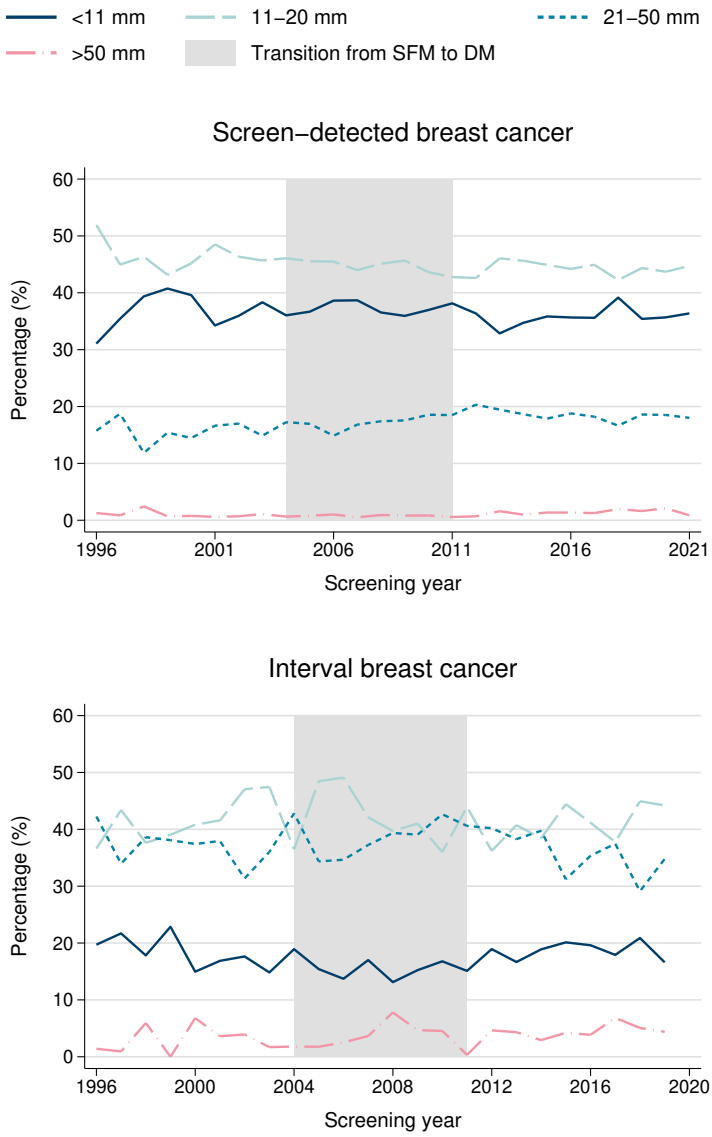


Figure 7.2: Distribution (%) of tumor diameter by groups (<11 mm, 11-20 mm, 21-50 mm, >50 mm) for invasive screen-detected cancers, 1996-2021 (upper panel) and interval cancers, 1996-2019 (lower panel). SFM: Screen-film mammography, DM: digital mammography

Table 7.4: Number (n) and proportion (%) of tumor diameter by groups (<11 mm, 11-20 mm and >20 mm) and screening area, for invasive screen-detected cancer, 2017-2021 (upper table), and invasive interval cancer, 2015-2019 (lower table)

Screen-detected breast cancer

	<11 mm		11-20 mm		>20 mm	
Screening area	n	%	n	%	n	%
Rogaland	136	32.8%	181	43.6%	98	23.6%
Hordaland	163	31.0%	227	43.2%	135	25.7%
Oslo	153	35.0%	193	44.2%	91	20.8%
Telemark	73	40.1%	76	41.8%	33	18.1%
Agder	113	38.6%	134	45.7%	46	15.7%
Troms og F	105	38.3%	131	47.8%	38	13.9%
Østfold	131	37.0%	160	45.2%	63	17.8%
Nordland	93	40.3%	104	45.0%	34	14.7%
Trøndelag	169	39.2%	188	43.6%	74	17.2%
Oppland	85	37.3%	101	44.3%	42	18.4%
Møre og R	122	41.4%	127	43.1%	46	15.6%
Sogn og F	31	34.4%	32	35.6%	27	30.0%
Vestfold	102	38.3%	125	47.0%	39	14.7%
Hedmark	83	38.4%	100	46.3%	33	15.3%
Akershus Øst	157	35.4%	195	44.0%	91	20.5%
Vestre Viken	186	33.9%	226	41.2%	137	25.0%
Fonna	28	43.1%	31	47.7%	<10	9.2%
Total	1,930	36.5%	2,331	44.0%	1,027*	19.5%

Interval breast cancer

	<11 mm		11-20 mm		>20 mm	
Screening area	n	%	n	%	n	%
Rogaland	21	13.8%	62	40.8%	69	45.4%
Hordaland	18	15.4%	44	37.6%	55	47.0%
Oslo	32	20.6%	66	42.6%	57	36.8%
Telemark	13	22.4%	27	46.6%	18	31.0%
Agder	18	19.8%	40	44.0%	33	36.3%
Troms og F	18	21.4%	39	46.4%	27	32.1%
Østfold	20	20.4%	39	39.8%	39	39.8%
Nordland	16	21.9%	31	42.5%	26	35.6%
Trøndelag	22	14.4%	64	41.8%	67	43.8%
Oppland	10	15.4%	34	52.3%	21	32.3%
Møre og R	22	22.7%	50	51.5%	25	25.8%
Sogn og F	<10	15.6%	22	48.9%	16	35.6%
Vestfold	20	24.1%	30	36.1%	33	39.8%
Hedmark	11	18.3%	29	48.3%	20	33.3%
Akershus Øst	36	22.2%	65	40.1%	61	37.7%
Vestre Viken	28	19.4%	54	37.5%	62	43.1%
Total	305*	19.1%	696	42.5%	629	38.4%

* Total number excluding screening area and year with less than 10 cancers

Median tumor diameter for invasive screen-detected cancers was 13 mm for the period 2017-2021 (Table 7.5). From 2015 to 2019, the median tumor diameter for invasive interval cancers was 18 mm (Table 7.5).

Median tumor diameter for invasive screen-detected cancers ranged from 11 mm in Fonna to 14 mm in Rogaland. Median tumor diameter among interval cancers ranged from 15 mm in Møre og Romsdal to 20 mm in Hordaland and Trøndelag (Table 7.5).

Prior analyses of tumor characteristics have demonstrated tumor diameter as the only prognostic tumor characteristics that differed between interval cancers detected in the first (18 mm) and second year (20 mm) of the screening interval (*57*). From 2015 to 2019, tumor diameter also differed between interval cancers detected in the first (17 mm) versus second year (18 mm) of the interval, but the difference was not statistically significant.

A study from BreastScreen Norway on cases diagnosed 2012-2016 has reported evidence that pathologists display a terminal digit preference for zeroes and fives for breast cancer tumors (*68*). The study found an excess of tumors recorded as 10, 20 or 50 mm, which define the border values for T1c, T2, and T3 tumors. A digit preference for zeroes and fives may increase the likelihood of under-staging of tumors in this report. This measurement error could also lead to tumor misclassification and potentially impact treatment.

Table 7.5: Median tumor diameter with the corresponding interquartile range (P25: 25th percentile, P75: 75th percentile) by screening year and screening area, for invasive screen-detected cancers, 2017-2021 (upper table) and invasive interval cancers, 2015-2019 (lower table)

Screen-detected breast cancer

	Screening year																	
	2017			2018			2019			2020			2021			Total		
Screening area	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75
Rogaland	14.0	9.0	21.0	15.5	11.0	22.0	13.0	9.0	18.0	14.0	9.0	20.0	12.0	8.0	17.0	14.0	9.0	20.0
Hordaland	15.0	10.0	21.0	14.0	10.0	20.5	15.0	10.0	22.9	14.0	10.0	21.0	11.6	8.2	18.0	14.0	10.0	21.0
Oslo	13.0	9.0	20.0	13.0	8.0	19.0	15.0	9.0	20.0	13.0	9.0	18.0	12.0	8.5	20.0	13.0	9.0	20.0
Telemark	11.0	8.0	17.0	12.0	8.0	17.0	14.0	9.0	19.0	16.0	11.0	19.0	11.0	7.0	22.0	12.0	8.0	18.0
Agder	13.0	9.0	18.5	13.0	8.0	15.0	11.0	9.0	17.0	13.0	7.0	17.0	12.0	9.0	15.0	12.0	8.0	17.0
Troms og F	11.5	8.0	15.0	11.0	8.0	14.0	14.0	9.5	20.0	12.0	9.0	19.0	11.5	8.0	14.0	12.0	8.0	16.0
Østfold	12.0	8.0	17.0	12.0	9.0	18.0	13.0	9.0	18.0	11.0	9.0	17.0	13.0	9.0	20.0	12.0	9.0	17.8
Nordland	12.0	9.0	18.0	12.0	8.0	18.0	11.0	9.0	18.0	11.0	8.0	18.0	13.0	8.5	15.0	12.0	8.5	17.0
Trøndelag	13.0	9.0	18.0	10.0	8.0	16.0	14.0	9.0	18.0	14.3	9.0	20.0	13.0	9.0	18.5	13.0	9.0	18.0
Oppland	13.0	9.0	17.0	11.0	8.0	17.0	14.0	9.0	17.0	12.0	7.0	18.0	14.0	9.0	20.0	13.0	9.0	18.0
Møre og R	12.0	10.0	17.0	12.0	7.0	18.0	12.0	9.0	18.0	11.0	7.0	15.0	12.0	8.0	18.0	12.0	8.0	18.0
Sogn og F	11.0	9.0	27.0	10.5	7.5	22.0	16.0	10.8	21.0	13.0	8.0	24.0	18.0	10.0	20.0	13.0	9.0	23.0
Vestfold	11.0	8.0	17.0	12.5	9.0	16.5	11.0	8.0	16.0	12.0	7.0	15.0	14.0	10.0	20.0	12.0	8.0	17.0
Hedmark	13.0	9.0	19.0	11.5	7.5	15.5	11.0	8.0	18.0	13.5	9.0	19.0	11.0	8.5	18.0	12.0	8.0	18.0
Akershus Øst	12.0	8.0	17.0	12.0	7.9	17.5	13.0	9.0	20.0	15.0	10.0	22.0	13.5	9.4	19.0	13.0	9.0	19.0
Vestre Viken	13.0	9.0	20.0	11.0	8.0	16.0	14.0	9.0	24.0	15.0	9.9	23.0	15.0	9.0	21.0	13.6	9.0	20.0
Fonna										11.0	8.8	14.0	10.9	8.2	15.6	11.0	8.8	15.0
Total	13.0	9.0	19.0	12.0	8.0	18.0	13.0	9.0	19.0	13.0	9.0	19.0	13.0	9.0	18.0	13.0	9.0	18.0

Interval breast cancer

	Screening year																	
	2015			2016			2017			2018			2019			Total		
Screening area	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75	Median	P25	P75
Rogaland	22.5	12.4	35.0	22.0	14.0	26.0	19.0	15.0	30.0	15.0	12.0	23.0	17.0	12.0	24.0	18.3	12.9	28.0
Hordaland	20.0	12.0	35.0	20.0	13.0	23.0	20.5	14.0	32.0	20.0	12.9	38.0	19.0	15.0	33.0	20.0	13.0	32.0
Oslo	17.5	13.0	25.0	16.5	12.0	35.0	20.0	13.0	30.0	15.0	10.5	19.5	17.0	12.0	25.0	17.0	12.0	28.0
Telemark	14.0	8.0	19.0	15.6	10.0	19.0	16.0	11.0	20.0	18.0	14.0	28.0	24.0	14.0	40.0	16.5	11.0	23.0
Agder	15.0	8.3	24.5	14.5	11.0	32.0	23.0	16.0	40.0	18.0	15.0	26.0	15.0	12.0	21.0	17.0	12.0	26.0
Troms og F	14.0	8.0	18.0	19.0	12.0	23.0	20.5	16.0	28.0	20.0	10.3	27.0	14.5	10.5	20.5	18.0	11.5	22.3
Østfold	22.0	18.0	28.0	15.0	10.0	24.0	17.5	14.0	23.0	19.0	10.5	25.0	16.0	14.0	27.0	18.5	11.0	25.0
Nordland	19.0	12.5	24.5	15.0	13.0	20.0	16.0	10.0	24.0	15.0	9.8	21.0	20.0	11.0	28.0	16.0	11.0	24.0
Trøndelag	19.5	14.0	27.0	19.0	12.0	24.0	18.0	15.0	25.0	16.5	10.0	25.0	21.5	16.0	30.5	20.0	15.0	26.0
Oppland	18.0	15.0	23.0	18.0	15.0	23.0	12.0	8.0	14.0	19.5	11.0	24.0	17.0	14.0	22.5	18.0	13.0	23.0
Møre og R	15.0	11.0	17.5	16.0	12.0	21.5	15.0	12.0	25.0	13.5	10.0	23.0	15.0	8.0	27.0	15.0	11.0	21.0
Sogn og F	18.0	12.0	40.0	17.5	13.0	30.0	15.5	12.0	26.0	14.0	7.8	47.0	19.0	11.0	40.0	16.0	12.0	28.0
Vestfold	18.5	8.0	24.0	20.0	10.5	29.5	21.0	13.0	23.5	16.0	9.0	22.0	15.5	9.5	21.5	18.0	11.0	24.0
Hedmark	14.5	9.0	18.0	18.0	11.5	30.5	14.5	9.0	30.0	17.0	15.0	20.0	21.0	12.0	23.0	16.0	12.5	25.0
Akershus Øst	18.0	13.0	25.0	19.0	9.8	26.0	15.0	9.0	27.0	15.0	12.0	22.0	16.0	13.0	24.0	16.5	12.0	25.0
Vestre Viken	18.5	15.0	25.0	19.0	10.5	27.5	22.0	10.5	27.5	16.0	14.0	24.0	18.0	11.0	30.0	18.0	12.5	26.0
Total	18.0	12.0	25.0	18.0	12.0	25.0	18.0	13.0	28.0	16.8	12.0	24.0	18.0	12.0	26.0	18.0	12.0	25.0

7.4 Histologic grade

The Nottingham histologic score system (*69*) was used for reporting histologic grade for invasive breast cancers. The proportion of grade I cancers declined from around 48% in 1996 to about 26% in 2021, while the proportion of grade II cancers was quite stable at about 50% (Figure 7.3). Grade III cancer increased steadily from about 9% in 1996 to 23% in 2021.

From 2017 to 2021, 50.1% of screen-detected cancers were classified as histologic grade II, while 23.2% were classified as histologic grade III (Table 7.6). There were substantial variations in the distribution of histologic grade between screening areas. For example, in Vestfold and Møre og Romsdal, 14.7% and 34.3% of cancers were classified as grade III, respectively. This variation is well known from the start-up of the program, and has been up for discussion several times. Whether these differences are real or related to different procedures and individual pathologists has not been investigated.

For interval cancer, the proportion of grade I cancers has decreased from above 20% at the start-up of the program to a stable value of about 15% during the last decade (Figure 7.3). Interval cancers with grade II and III fluctuated around a value of 40%, with the highest values observed for grade II cancers. During the last five years, 49.4% of invasive interval cancers were classified as histologic grade II, while 36.3% were classified as histoloic grade III (Table 7.6). Overall, histologic grade II and III was observed for about 80% of interval cancer cases in most screening areas, with substantial variation across the screening areas.

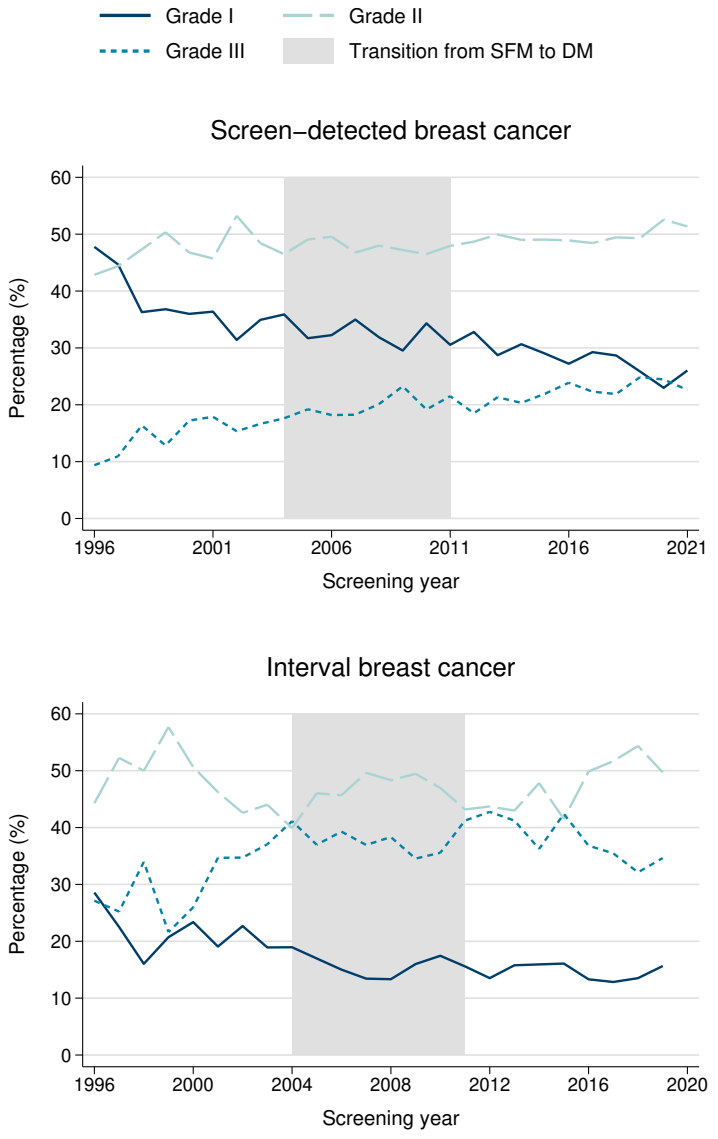


Figure 7.3: Distribution (%) of histologic grade for invasive screen-detected cancer, 1996-2021 (upper panel) and invasive interval cancer, 1996-2019 (lower panel) by screening year. SFM: Screen-film mammography, DM: digital mammography

Table 7.6: Number (n) and proportion (%) of histologic grade, by screening area, for invasive screen-detected cancers, 2017-2021, and invasive interval cancer, 2015-2019

	Screen-detected breast cancer						Interval breast cancer					
	I		II		III		I		II		III	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	125	30.1%	172	41.4%	118	28.4%	30	19.6%	60	39.2%	63	41.2%
Hordaland	172	33.0%	248	47.6%	101	19.4%	15	12.6%	66	55.5%	38	31.9%
Oslo	106	23.1%	242	52.8%	110	24.0%	32	18.6%	88	51.2%	52	30.2%
Telemark	58	31.2%	86	46.2%	42	22.6%	13	20.0%	30	46.2%	22	33.8%
Agder	89	29.6%	158	52.5%	54	17.9%	19	18.8%	48	47.5%	34	33.7%
Troms og F	99	36.3%	92	33.7%	82	30.0%	17	18.3%	37	39.8%	39	41.9%
Østfold	40	11.1%	222	61.7%	98	27.2%	<10	4.8%	56	53.3%	44	41.9%
Nordland	74	32.2%	112	48.7%	44	19.1%	13	17.1%	31	40.8%	32	42.1%
Trøndelag	97	22.5%	215	49.9%	119	27.6%	11	7.2%	85	55.6%	57	37.3%
Oppland	73	31.3%	124	53.2%	36	15.5%	<10	11.8%	43	63.2%	17	25.0%
Møre og R	87	29.3%	108	36.4%	102	34.3%	19	18.4%	40	38.8%	44	42.7%
Sogn og F	17	19.3%	53	60.2%	18	20.5%	<10	9.5%	25	59.5%	13	31.0%
Vestfold	73	26.8%	159	58.5%	40	14.7%	12	13.0%	43	46.7%	37	40.2%
Hedmark	75	34.6%	105	48.4%	37	17.1%	13	20.6%	34	54.0%	16	25.4%
Akershus Øst	106	23.1%	238	51.9%	115	25.1%	20	11.3%	93	52.5%	64	36.2%
Vestre Viken	127	22.5%	322	57.0%	116	20.5%	18	11.2%	82	50.9%	61	37.9%
Fonna	18	27.3%	35	53.0%	13	19.7%						
Total	1,436	26.7%	2,691	50.1%	1,245	23.2%	249	14.3%	861	49.4%	633	36.3%

7.5 Lymph node involvement

Lymph node involvement is an important factor in breast cancer staging and can affect treatment and prognosis. The rate of lymph node involvement for invasive screen-detected cancer fluctuated from 20% to 30% in the period from the start-up of the program to 2010 when it stabilized and remained at about 20% (Figure 7.4). A decrease in lymph node positive interval cancer was observed from the start of the screening program until 2019, from about 45% to approximately 30% (Figure 7.4). The decline might be related to increased attention to interval cancer or women being encouraged to contact their general practitioner if they observe any changes or symptoms between two screening examinations.

Overall, 21.5% of the women diagnosed with invasive screen-detected cancer between 2017-2021 had lymph node involvement (Table 7.7). This proportion varied by screening area from 16.0% in Vestre Viken to 27.2% in Møre og Romsdal. Among women with interval cancer, 37.1% of the women had lymph node involvement, ranging from 31.0% in Vestre Viken to 43.9% in Nordland for those screened 2015-2019 (Table 7.7). As for histologic grade, some of this variability may be due to different procedures and individual pathologists' assessments.

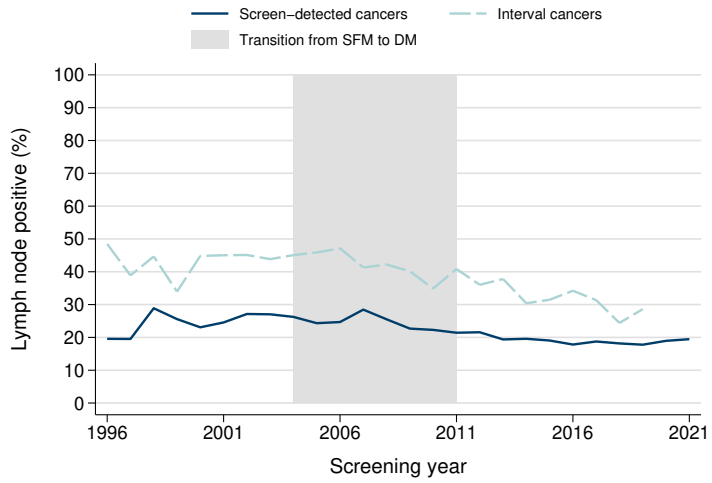


Figure 7.4: Proportion (%) of lymph node positive invasive screen-detected cancer, 1996-2021, and invasive interval cancer, 1996-2019, by screening year. SFM: Screen-film mammography, DM: digital mammography

Among women with invasive screen-detected cancer with lymph node involvement, 83.2% of the cases had 1-9 positive lymph nodes, while the remaining cases had 10 or more positive lymph nodes during 2017-2021 (Table 7.8). The proportion of cancers with 1-9 positive lymph nodes varied from 57.9% in Fonna to 89.9% in Telemark.

Of the invasive interval cancers with lymph node involvement, 76.7% had 1-9 positive lymph nodes (Table 7.8), and 23.3% had 10 or more positive lymph nodes. The proportion of cancers with 1-9 positive lymph nodes varied by screening area, from 70.0% in Hordaland to 85.9% in Hedmark.

Table 7.7: Number (n) and proportion (%) of cases with lymph node involvement, by screening area, for invasive screen-detected cancer, 2017-2021, and invasive interval cancer, 2015-2019

	Screen-detected cancer		Interval cancer	
Screening area	n	%	n	%
Rogaland	442	22.2%	249	39.3%
Hordaland	412	19.2%	210	38.3%
Oslo	427	20.0%	259	35.5%
Telemark	180	24.2%	89	39.6%
Agder	220	19.7%	135	35.9%
Troms og F	186	20.3%	119	39.5%
Østfold	281	24.0%	101	35.4%
Nordland	207	24.6%	122	43.9%
Trøndelag	386	22.7%	156	34.0%
Oppland	187	24.3%	81	39.5%
Møre og R	242	27.2%	124	40.8%
Sogn og F	83	24.9%	48	42.5%
Vestfold	203	22.2%	91	33.3%
Hedmark	164	22.3%	66	36.1%
Akershus Øst	180	18.7%	122	33.9%
Vestre Viken	179	16.0%	81	31.0%
Fonna	12	18.8%		
Total	3,991	21.5%	2,053	37.1%

Table 7.8: Number (n) and proportion (%) of cases with 1-9 positive lymph nodes, by screening area, for invasive screen-detected breast cancer, 2017-2021, and invasive interval breast cancer, 2015-2019

	Screen-detected cancer		Interval cancer	
Screening area	n	%	n	%
Rogaland	423	87.0%	234	81.0%
Hordaland	396	78.1%	191	70.0%
Oslo	404	75.2%	241	75.5%
Telemark	170	89.9%	81	78.6%
Agder	198	80.5%	119	75.3%
Troms og F	174	83.3%	99	75.6%
Østfold	259	82.5%	88	72.1%
Nordland	195	86.3%	111	77.1%
Trøndelag	364	88.8%	138	79.8%
Oppland	178	86.4%	75	80.6%
Møre og R	225	86.5%	114	82.0%
Sogn og F	77	77.0%	45	78.9%
Vestfold	195	89.0%	80	71.4%
Hedmark	151	86.8%	61	85.9%
Akershus Øst	174	83.3%	109	74.7%
Vestre Viken	166	80.2%	76	77.6%
Fonna	11	57.9%		
Total	3,760	83.2%	1,862	76.7%

7.6 Immunohistochemical subtypes

To provide more accurate treatment and prognosis, invasive breast cancers are classified into immunohistochemical subtypes. Breast cancer subtypes respond differently to various treatments, and survival for the different subtypes vary (*70*). For example, triple negative breast cancers are particularly hard to treat, and survival is poorer compared to other immunohistochemical subtypes (*71*).

Using estrogen receptor (ER), progesterone receptor (PR) and Human Epidermal Growth Factor Receptor 2 (Her2) status, invasive tumors were classified into luminal A-like, luminal B-like (Her2-), luminal B-like (Her2+), Her2+ (non-luminal) and triple negative, based on a modification of the St. Gallen surrogate immunohistochemical classification of molecular subtypes (*72*). Data on ER and PR status have been complete for screen-detected cancers since 1996, while Her2 status has sporadically been registered since 2005 in BreastScreen Norway, but systematically since 2012-2013 (see section 7.7). Expression of protein Ki67 has been partially been registered since 2010. However, Ki67 is not included due to a high proportion of cases without available information.

Table 7.9: Classification of immunohistochemical subtypes based on a modification of the St. Gallen classification (without Ki67)(*72*).

Subtype	Criteria
Luminal A-like	ER+, PR+, HER2-
Luminal B-like (Her2-)	ER+, PR-, HER2-
Luminal B-like (Her2+)	ER+, PR-/PR+, HER2+
Her2+ (non-luminal)	ER-, PR-, HER+
Triple negative	ER-, PR-, HER-

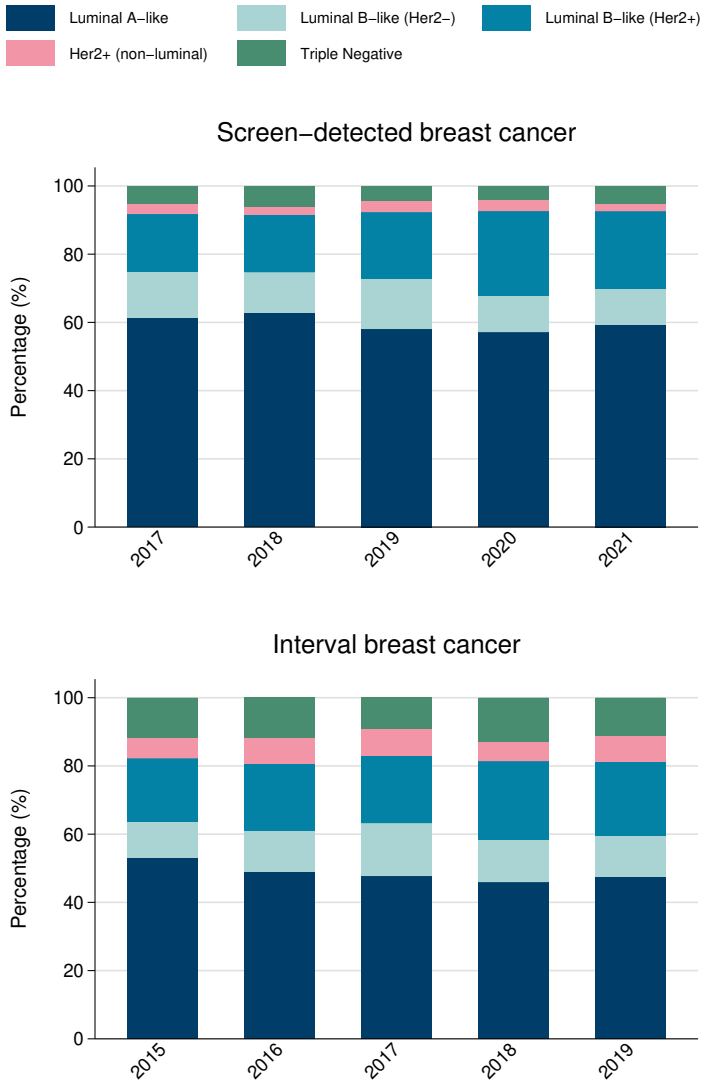


Figure 7.5: Distribution (%) of immunohistochemical subtypes of invasive screen-detected cancer, 2017-2021 (upper panel) and invasive interval cancer, 2015-2019 (lower panel)

The proportion of luminal A-like screen-detected cancers was at its highest in 2018 at about 63%, and at its lowest in 2020 at about 57% (Figure 7.5). The proportion of luminal B-like (Her2+) tumors was 17% in 2017 and 25% in 2020. Among interval cancers, the proportion of luminal A-like tumors was around 53% in 2015 and 46% in 2018. The proportion of luminal B-like (Her2+) tumors was 19% in 2015 and 23% in 2018. About 5% of the screen-detected cancers was classified as triple negative, while this proportion was 11% for interval cancers.

The proportion of immunohistochemical subtypes for screen-detected cancers differed between screening areas. The proportion of luminal A-like tumors varied from 29.4% in Telemark to 69.6% in Rogaland, while triple negative tumors contributed with 2.7% in Telemark and 8.6% in Sogn og Fjordane (Table 7.10). For interval cancer, the proportion of luminal A-like tumors varied from 32.1% in Nordland to 58.3% in Sogn og Fjordane. Triple negative tumors ranged from 3.0% in Oppland to 17.0% in Østfold. (Table 7.10). The number of triple negative interval cancers were low, and results should be interpreted with care. The differences in distributions between screening areas should be further investigated as it might indicate differences in the classification of the variables included in the subtypes (ER, PR and Her2+).

Table 7.10: Number(n) and proportion(%) of immunohistochemical subtypes, by screening area, for invasive screen-detected cancers, 2017-2021 (upper table) and invasive interval cancers, 2015-2019 (lower table)

Screen-detected breast cancer

	Luminal A		Luminal B (Her2-)		Luminal B (Her2+)		Her2+ (non-luminal)		Triple negative	
Screening area	n	%	n	%	n	%	n	%	n	%
Rogaland	300	69.6%	55	12.8%	33	7.7%	<10	1.4%	30	7.0%
Hordaland	345	62.1%	61	11.0%	108	19.4%	17	3.1%	22	4.0%
Oslo	290	62.9%	59	12.8%	71	15.4%	17	3.7%	18	3.9%
Telemark	55	29.4%	17	9.1%	99	52.9%	10	5.3%	<10	2.7%
Agder	169	54.9%	61	19.8%	44	14.3%	<10	1.6%	24	7.8%
Troms og F	159	56.0%	30	10.6%	60	21.1%	<10	3.2%	18	6.3%
Østfold	189	52.5%	35	9.7%	101	28.1%	16	4.4%	18	5.0%
Nordland	105	43.9%	23	9.6%	77	32.2%	14	5.9%	18	7.5%
Trøndelag	241	55.4%	37	8.5%	122	28.0%	13	3.0%	14	3.2%
Oppland	153	65.4%	20	8.5%	45	19.2%	<10	2.1%	<10	3.8%
Møre og R	199	67.0%	63	21.2%	<10	2.7%	<10	1.0%	21	7.1%
Sogn og F	55	59.1%	13	14.0%	16	17.2%	<10	1.1%	<10	8.6%
Vestfold	184	67.6%	38	14.0%	32	11.8%	<10	2.2%	10	3.7%
Hedmark	122	56.2%	26	12.0%	55	25.3%	<10	2.8%	<10	3.7%
Akershus Øst	251	54.7%	69	15.0%	100	21.8%	15	3.3%	19	4.1%
Vestre Viken	384	67.7%	58	10.2%	84	14.8%	17	3.0%	17	3.0%
Fonna	38	53.5%	<10	7.0%	23	32.4%	0	-	<10	7.0%
Total	3,239	59.2%	665*	12.2%	1,078	19.7%	160	2.9%	264	4.8%

Interval breast cancer

	Luminal A		Luminal B (Her2-)		Luminal B (Her2+)		Her2+ (non-luminal)		Triple negative	
Screening area	n	%	n	%	n	%	n	%	n	%
Rogaland	86	50.9%	12	7.1%	33	19.5%	<10	4.7%	25	14.8%
Hordaland	66	46.2%	17	11.9%	27	18.9%	13	9.1%	15	10.5%
Oslo	93	54.1%	20	11.6%	28	16.3%	13	7.6%	18	10.5%
Telemark	22	32.8%	<10	6.0%	29	43.3%	<10	11.9%	<10	3.0%
Agder	41	39.4%	25	24.0%	16	15.4%	<10	7.7%	12	11.5%
Troms og F	43	44.8%	11	11.5%	16	16.7%	15	15.6%	<10	9.4%
Østfold	44	41.5%	7	6.6%	29	27.4%	<10	7.5%	18	17.0%
Nordland	25	32.1%	13	16.7%	23	29.5%	<10	9.0%	<10	9.0%
Trøndelag	77	48.7%	14	8.9%	37	23.4%	13	8.2%	13	8.2%
Oppland	33	47.8%	11	15.9%	17	24.6%	<10	5.8%	<10	4.3%
Møre og R	56	53.8%	28	26.9%	<10	5.8%	<10	1.9%	11	10.6%
Sogn og F	28	58.3%	<10	8.3%	<10	14.6%	0	-	<10	16.7%
Vestfold	54	55.1%	<10	8.2%	11	11.2%	<10	6.1%	16	16.3%
Hedmark	30	47.6%	10	15.9%	16	25.4%	<10	3.2%	<10	7.9%
Akershus Øst	82	46.1%	23	12.9%	47	26.4%	10	5.6%	14	7.9%
Vestre Viken	85	52.1%	15	9.2%	23	14.1%	<10	4.9%	25	15.3%
Total	865	47.6%	222	12.2%	365	20.1%	125	6.9%	201	11.1%

* Total number excluding screening area and year with less than 10 cancers

7.7 Completeness of data

The systems and processes for data collection and registration have been unchanged for invitations, attendance, recall and cancer detection since the start-up of the screening program, and data for these parameters is 100% complete. However, there have been several changes in the processes for registration of biopsies, which represent challenges for the longitudinal interpretation of histopathological tumor characteristics. Completeness of tumor characteristics data are only reported for invasive breast cancers in this section.

Since the start-up of BreastScreen Norway, the proportion of complete data has increased for all tumor characteristics for screen-detected and interval cancer, with the exception of tumor diameter (Figure 7.6). Information has been collected and registered about Her2 receptor status since 2005, but not systematically until 2012-2013. The proportion of complete data about tumor diameter for interval cancers generally decreased from 1996 and were at its lowest in 2006. This could be due to various screening areas joining the program in this period, or a change in database software around this time. The proportion of complete data decreased in 2021. This is most likely explained by the short interval between diagnosis and the publication of this report causing incomplete reporting or coding of cases. Reminders are sent from the Cancer Registry to pathology labs to submit pathology forms related to cancer cases and benign findings only after receiving information about these cases from the radiologists. The information given from the radiologists to the pathology labs should be improved, to ensure that all information about women referred from screening automatically is sent from pathology labs to the Cancer Registry. This will reduce the volume of manually sent reminders from the Cancer Registry and speed up the time to register the data in the database.

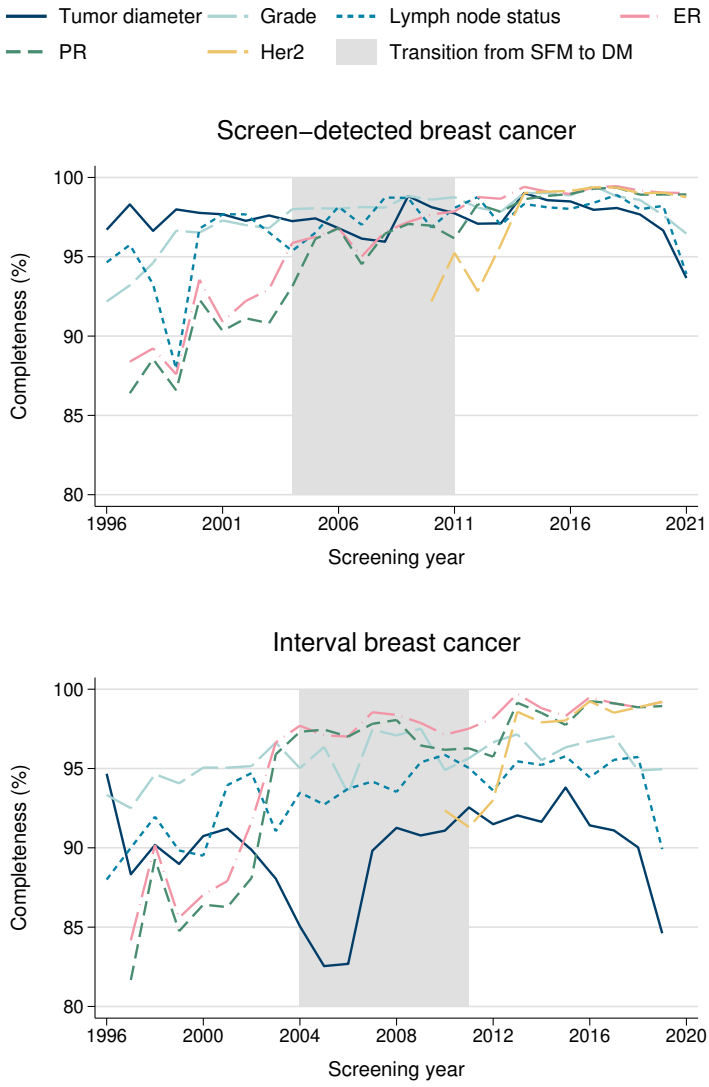


Figure 7.6: Proportion (%) of complete data on tumor characteristics for invasive screen-detected cancers, 1996-2021 (upper panel) and invasive interval cancers, 1996-2019 (lower panel). Her2 is displayed from 2010-2021. SFM: Screen-film mammography, DM: digital mammography

Over the last five years, 2017-2021, data was complete for over 96% of screen-detected cancers with respect to tumor diameter, histologic grade, and lymph node involvement (Table 7.11). Complete information about ER, PR and Her2 was available for about 99% of screen-detected cancer cases in this period.

Information regarding tumor histopathology was generally less complete for interval cancers compared to screen-detected cancers (Table 7.11). Complete information about tumor diameter has been available for 90.1% of interval cancers in the period 2015-2019. Because a higher proportion of women undergo neo-adjuvant treatment prior to surgery following a diagnosis of interval cancer than screen-detected cancer (*48*), this was not an unexpected finding. Other reasons for unavailable information on tumor histopathology can be omissions in reporting, failure to issue reminders if expected histopathology information is not received, failures in coding and registration, and failures in the extraction of data from the databases.

The proportion of completeness of tumor characteristic data differed between the screening areas (Table 7.11). Fonna had the lowest levels for tumor diameter, histologic grade and lymph node status, and the highest levels for ER, PR and Her 2 among screen-detected cancers. Fonna was established in 2020 and the total number of cancer cases was low, so these numbers should be interpreted with caution.

Table 7.11: Proportion (%) of complete data on tumor diameter, histologic grade, lymph node status, estrogen (ER) and progesterone (PR) receptor status, and Her2 status, by screening area, for invasive screen-detected cancers, 2017-2021 (upper table) and invasive interval cancers, 2015-2019 (lower table)

Screen-detected breast cancer

Screening area	Tumor diameter	Histologic grade	Lymph node status	ER	PR	Her2
Rogaland	96.3%	96.3%	98.1%	99.3%	99.1%	99.1%
Hordaland	94.4%	93.7%	97.1%	99.6%	99.6%	99.6%
Oslo	94.8%	99.3%	95.7%	98.9%	98.7%	98.9%
Telemark	97.3%	99.5%	97.9%	99.5%	99.5%	99.5%
Agder	95.1%	97.7%	97.1%	99.0%	98.7%	98.4%
Troms og F	96.5%	96.1%	97.5%	97.9%	97.5%	97.9%
Østfold	98.3%	100.0%	97.5%	99.7%	99.7%	99.7%
Nordland	96.7%	96.2%	97.5%	99.2%	99.2%	99.2%
Trøndelag	99.1%	99.1%	98.9%	98.4%	98.4%	98.4%
Oppland	97.4%	99.6%	97.0%	99.6%	99.6%	99.6%
Møre og R	99.3%	100.0%	99.7%	99.0%	99.0%	99.0%
Sogn og F	96.8%	94.6%	97.8%	100.0%	100.0%	100.0%
Vestfold	97.8%	100.0%	99.3%	99.3%	99.3%	99.3%
Hedmark	99.5%	100.0%	98.6%	100.0%	100.0%	100.0%
Akershus Øst	96.5%	100.0%	96.1%	99.6%	99.1%	98.9%
Vestre Viken	96.8%	99.6%	96.6%	99.1%	98.9%	99.1%
Fonna	91.5%	93.0%	90.1%	100.0%	100.0%	100.0%
Total	96.8%	98.2%	97.4%	99.2%	99.1%	99.1%

Interval breast cancer

Screening area	Tumor diameter	Histologic grade	Lymph node status	ER	PR	Her2
Rogaland	89.9%	90.5%	94.1%	98.2%	97.6%	98.2%
Hordaland	81.8%	83.2%	88.8%	99.3%	99.3%	98.6%
Oslo	90.1%	100.0%	93.0%	100.0%	100.0%	100.0%
Telemark	86.6%	97.0%	94.0%	97.0%	97.0%	97.0%
Agder	87.5%	97.1%	94.2%	99.0%	98.1%	98.1%
Troms og F	87.5%	96.9%	96.9%	99.0%	99.0%	99.0%
Østfold	92.5%	99.1%	94.3%	100.0%	100.0%	100.0%
Nordland	93.6%	97.4%	98.7%	98.7%	98.7%	97.4%
Trøndelag	96.8%	96.8%	98.1%	98.7%	98.7%	98.7%
Oppland	94.2%	98.6%	97.1%	98.6%	98.6%	98.6%
Møre og R	93.3%	99.0%	95.2%	99.0%	99.0%	99.0%
Sogn og F	93.8%	87.5%	93.8%	97.9%	97.9%	97.9%
Vestfold	84.7%	93.9%	89.8%	99.0%	98.0%	98.0%
Hedmark	95.2%	100.0%	96.8%	100.0%	100.0%	100.0%
Akershus Øst	91.0%	99.4%	94.4%	99.4%	99.4%	100.0%
Vestre Viken	88.3%	98.8%	92.6%	98.8%	98.2%	98.2%
Total	90.1%	96.0%	94.2%	99.0%	98.8%	98.8%

8. Mammographic features

Mammographic screening aims to detect tumors before they become symptomatic. However, to identify tumors at an early stage when they are small and difficult to recognize, the radiologist has to search not only for the conventional mammographic features of invasive tumors, but also for subtle signs of malignancy. Early detection of breast cancer requires optimal image quality and knowledge of the subtle mammographic features associated with early breast cancer. Although some early detected cancers are identified as characteristic clusters of calcification or as a spiculated mass, others demonstrate less typical and sometimes much less obvious features such as architectural distortion or asymmetry. Although these signs are nonspecific, they provide radiologists with the important opportunity to detect breast cancer at an early stage.

The radiologists working in BreastScreen Norway have reported mammographic features for all recalled women since the program started in 1996. In the beginning, lesions resulting in a recall were classified as 1) Asymmetric density; 2) Circumscribed mass; 3) Obscured mass; 4) Spiculated mass; 5) Calcification only; 6) Density and calcification; and 7) Other. The reporting system was revised and replaced with a modified BI-RADS (Breast imaging-reporting and data system) in 2013/14. The features identified at screening resulting in a recall was from that time, and is still reported as 1) Asymmetric density; 2) Architectural distortion; 3) Circumscribed mass; 4) Spiculated mass; 5) Calcification only; 6) Density and calcification; 7) Lymph node in the axilla; and 8) Other. At the recall assessment, more details are reported for the masses (shape and margin), asymmetry (global or focal), architectural distortion and calcification (benign, amorphous/coarse heterogeneous and fine pleomorphic/linear).

The completeness and distribution of mammographic features resulting in a recall and as a result of the recall assessment, vary substantially between the screening areas. In an attempt to present mammographic features of recalled cases (benign lesion with or without biopsy, and malignant cases with biopsy), the reported features were merged from both registrations into six groups, 1) Mass; 2) Spiculated mass; 3) Distortion; 4) Asymmetry; 5) Density with calcification; and 6) Calcification alone. We are well aware that the feature of interest could differ before and after recall assessment, but after intense work, we consider these six groups to best mirror the reported values.

In Figure 8.1, the features are presented for screen-detected cancers in 2017-2021. The distribution was stable for all features over time for the four groups: all recalls, recalls with a benign biopsy, recalls resulting in a diagnosis of DCIS and recalls resulting in a diagnosis of invasive breast cancer. Masses contributed to 40-50% of all recalls, above 50% for the benign lesions and about 10% of the invasive cancer cases. Calcification alone was the most common feature for DCIS, in almost 80% of the cases, while spiculated mass was most common for invasive breast cancer cases, in around 40% of the cases.

As the mammographic features did not vary remarkably over the last five years, these five years were combined in Table 8.1. The reported distribution of mammographic features varied between the screening areas.

For all recalls, the proportion of masses ranged from 29.2% in Sogn og Fjordane to 53.2% in Rogaland. Asymmetry ranged from 7.8% in Rogaland to 46.5% in Sogn og Fjordane, and calcification alone ranged from 9.5% in Sogn og Fjordane to 20.4% in Hordaland.

Among recalls resulting in a biopsy with a benign outcome, Rogaland had the highest proportion of masses, 70.9%, and Sogn og Fjordane had the lowest, 33.0% (Table 8.1). Asymmetry ranged from 7.1% in Hordaland to 49.1% in Østfold. Calcification alone was also quite common among recalls with benign biopsies, with an average of 15.9%.

For invasive cancers, the distribution of spiculated mass ranged from 28.6% in Sogn og Fjordane to 63.7% in Telemark (Table 8.1). Asymmetry was reported for an average of 14.3% of invasive cancer cases. The number of invasive cancers per screening area was low, so these numbers should be interpreted with caution.

Mammographic features of DCIS are not presented as the number of cases was too low to stratify by screening area. In total, about 76% of DCIS were classified as calcification alone, varying from 66% to 89% between screening areas.

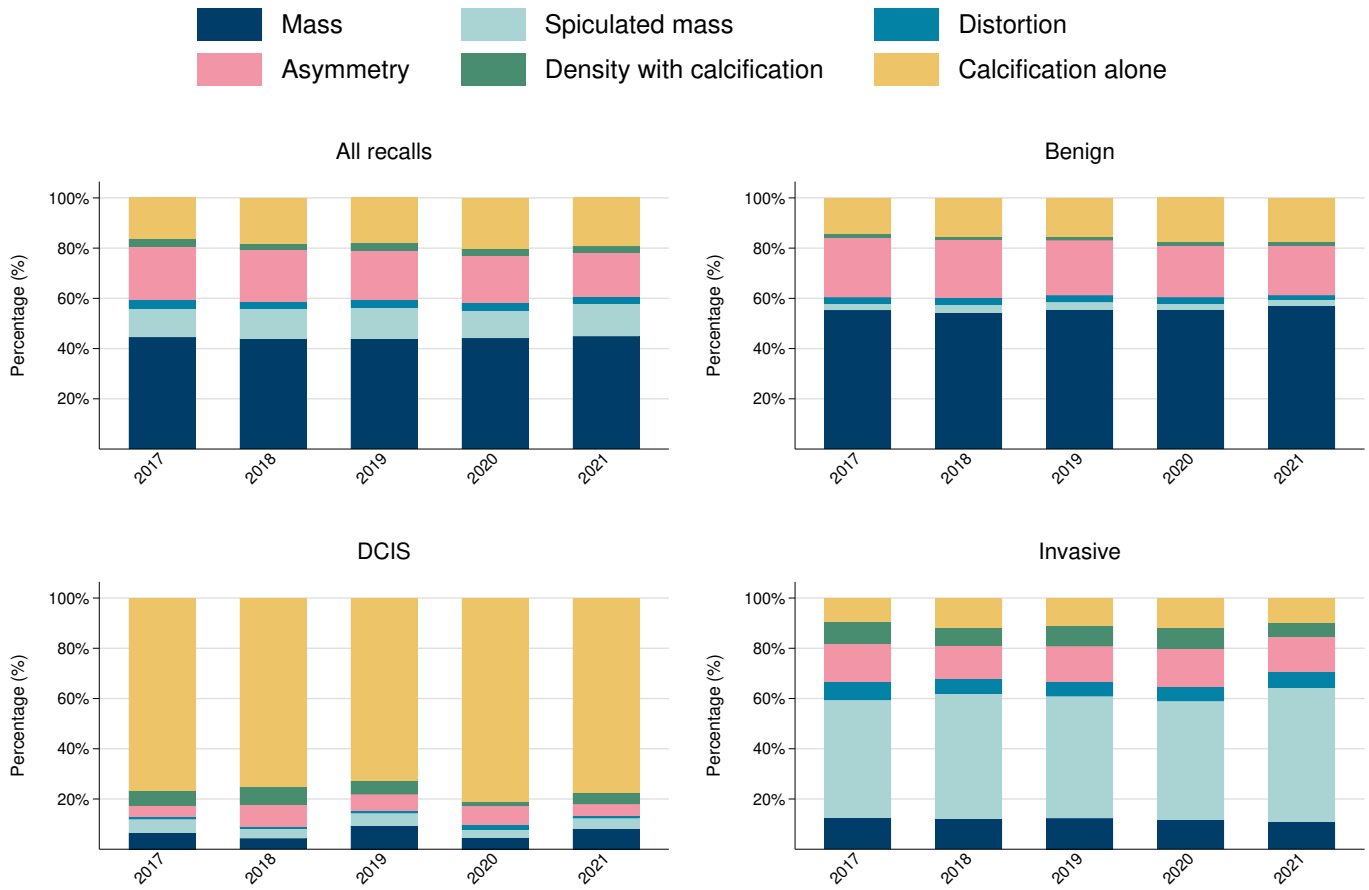


Figure 8.1: Distribution (%) of mammographic features leading to recall (upper left panel), recall with a benign biopsy (upper right panel), recall resulting in a diagnosis of DCIS (lower left panel) and recall resulting in a diagnosis of invasive screen-detected cancer (lower right panel), by screening year, 2017-2021

Table 8.1: Mammographic features for all recalls (upper table), recalls resulting in a biopsy with benign outcome (middle table) and recalls resulting in a biopsy with invasive cancers (lower table), 2017-2021, by screening area

All recalls	Mass		Spiculated mass		Distortion		Asymmetry		Density w calc.		Calcification alone	
Screening area	n	%	n	%	n	%	n	%	n	%	n	%
Rogaland	848	53.2%	236	14.8%	48	3.0%	125	7.8%	46	2.9%	290	18.2%
Hordaland	1,104	39.1%	293	10.4%	96	3.4%	666	23.6%	91	3.2%	576	20.4%
Oslo	1,282	49.6%	261	10.1%	67	2.6%	329	12.7%	68	2.6%	578	22.4%
Telemark	142	32.1%	133	30.1%	12	2.7%	71	16.1%	<10	1.8%	76	17.2%
Agder	708	45.2%	169	10.8%	80	5.1%	270	17.2%	42	2.7%	299	19.1%
Troms og F	478	47.3%	155	15.3%	52	5.1%	106	10.5%	30	3.0%	190	18.8%
Østfold	401	29.8%	165	12.3%	15	1.1%	564	42.0%	49	3.6%	150	11.2%
Nordland	400	44.5%	100	11.1%	55	6.1%	127	14.1%	49	5.5%	167	18.6%
Trøndelag	782	45.8%	192	11.3%	46	2.7%	303	17.8%	52	3.0%	331	19.4%
Oppland	432	44.9%	147	15.3%	30	3.1%	122	12.7%	43	4.5%	188	19.5%
Møre og R	750	50.5%	128	8.6%	37	2.5%	357	24.0%	34	2.3%	180	12.1%
Sogn og F	223	29.2%	46	6.0%	41	5.4%	356	46.5%	26	3.4%	73	9.5%
Vestfold	495	40.1%	149	12.1%	45	3.6%	312	25.3%	33	2.7%	200	16.2%
Hedmark	597	48.9%	111	9.1%	26	2.1%	288	23.6%	12	1.0%	186	15.2%
Akershus Øst	935	38.9%	390	16.2%	51	2.1%	557	23.2%	75	3.1%	394	16.4%
Vestre Viken	1,646	51.4%	363	11.3%	65	2.0%	333	10.4%	58	1.8%	738	23.0%
Fonna	112	36.0%	31	10.0%	11	3.5%	98	31.5%	<10	2.6%	51	16.4%
Total	11,335	44.4%	3,069	12.0%	777	3.0%	4,984	19.5%	724	2.8%	4,667	18.3%

Benign												
Rogaland	784	70.9%	40	3.6%	16	1.4%	79	7.1%	18	1.6%	169	15.3%
Hordaland	1,029	46.4%	77	3.5%	62	2.8%	573	25.8%	45	2.0%	432	19.5%
Oslo	1,251	60.5%	49	2.4%	35	1.7%	305	14.8%	27	1.3%	400	19.4%
Telemark	138	59.0%	12	5.1%	<10	3.4%	45	19.2%	0	-	31	13.2%
Agder	680	55.2%	23	1.9%	58	4.7%	230	18.7%	16	1.3%	224	18.2%
Troms og F	459	62.4%	38	5.2%	28	3.8%	81	11.0%	14	1.9%	115	15.6%
Østfold	381	38.6%	25	2.5%	10	1.0%	484	49.1%	11	1.1%	75	7.6%
Nordland	365	57.9%	19	3.0%	26	4.1%	82	13.0%	29	4.6%	109	17.3%
Trøndelag	763	60.3%	14	1.1%	29	2.3%	249	19.7%	21	1.7%	189	14.9%
Oppland	427	58.8%	25	3.4%	20	2.8%	108	14.9%	17	2.3%	129	17.8%
Møre og R	708	62.5%	12	1.1%	19	1.7%	277	24.5%	16	1.4%	100	8.8%
Sogn og F	225	33.0%	21	3.1%	39	5.7%	326	47.8%	17	2.5%	54	7.9%
Vestfold	484	50.9%	<10	0.9%	29	3.1%	286	30.1%	<10	0.7%	135	14.2%
Hedmark	581	57.2%	13	1.3%	20	2.0%	265	26.1%	<10	0.2%	135	13.3%
Akershus Øst	926	48.3%	136	7.1%	36	1.9%	528	27.5%	26	1.4%	265	13.8%
Vestre Viken	1,623	63.5%	39	1.5%	38	1.5%	305	11.9%	24	0.9%	527	20.6%
Fonna	107	45.0%	0	-	<10	1.3%	85	35.7%	<10	1.7%	39	16.4%
Total	10,931	55.5%	543*	2.8%	476	2.4%	4,308	21.9%	294	1.5%	3,128	15.9%

* Total number excluding screening area and year with less than 10 benign recalls

Invasive cancer												
Rogaland	79	16.4%	233	48.3%	40	8.3%	54	11.2%	33	6.8%	43	8.9%
Hordaland	97	17.0%	233	40.9%	34	6.0%	109	19.1%	49	8.6%	48	8.4%
Oslo	61	12.3%	253	51.1%	36	7.3%	31	6.3%	44	8.9%	70	14.1%
Telemark	<10	4.0%	142	63.7%	<10	4.0%	32	14.3%	<10	2.7%	25	11.2%
Agder	43	12.5%	175	50.9%	24	7.0%	53	15.4%	28	8.1%	21	6.1%
Troms og F	42	14.0%	133	44.5%	26	8.7%	28	9.4%	21	7.0%	49	16.4%
Østfold	34	9.3%	161	44.0%	<10	1.6%	95	26.0%	41	11.2%	29	7.9%
Nordland	51	17.7%	100	34.7%	39	13.5%	58	20.1%	20	6.9%	20	6.9%
Trøndelag	41	9.9%	193	46.7%	27	6.5%	64	15.5%	29	7.0%	59	14.3%
Oppland	15	5.8%	149	57.8%	14	5.4%	23	8.9%	23	8.9%	34	13.2%
Møre og R	45	13.6%	128	38.7%	22	6.6%	82	24.8%	21	6.3%	33	10.0%
Sogn og F	<10	7.6%	30	28.6%	<10	3.8%	47	44.8%	<10	7.6%	<10	7.6%
Vestfold	30	9.7%	166	53.9%	18	5.8%	34	11.0%	28	9.1%	32	10.4%
Hedmark	34	16.0%	110	51.6%	<10	2.8%	29	13.6%	<10	4.2%	25	11.7%
Akershus Øst	54	10.9%	280	56.7%	19	3.8%	48	9.7%	46	9.3%	47	9.5%
Vestre Viken	60	9.6%	375	59.9%	31	5.0%	39	6.2%	39	6.2%	82	13.1%
Fonna	<10	11.1%	30	47.6%	<10	12.7%	12	19.0%	<10	4.8%	<10	4.8%
Total	710	12.1%	2,891	49.2%	363	6.2%	838	14.3%	448	7.6%	628	10.7%

9. Breast cancer treatment

Surgery with sentinel node biopsy, either breast conserving therapy or mastectomy, is considered the primary treatment of breast cancer. Large clinical trials from the 1980s have shown breast conserving therapy equal to mastectomy in terms of long-term survival for women with early-stage breast cancer (*73*, *74*), and breast conserving therapy has over the years replaced mastectomy as the preferred surgical treatment (*75*, *76*). Studies from Norway have demonstrated better breast cancer-specific survival and a lower risk of dying from breast cancer for women treated with breast conserving therapy compared to mastectomy, independent of detection mode, prognostic and predictive tumor characteristics (*77*, *78*).

In this chapter, the distribution of breast conserving therapy is presented for DCIS (only as trend over time) and invasive screen-detected cancer, and invasive interval cancer. Due to a stable rate of breast conserving therapy over the past years (Figure 9.1), results for invasive screen-detected and interval cancers are combined for 2017-2021 and 2015-2019, respectively, in Table 9.1.

A substantial increase in the proportion of women who received breast conserving therapy was observed in the period 1996 to 2021, from roughly 20% to above 80% (Figure 9.1). The proportion of breast conserving therapy was higher among women with DCIS or invasive screen-detected cancer compared to invasive interval cancer.

A study using data from the Cancer Registry, found that the use of breast conserving therapy in the treatment of DCIS increased during the period 1995 to 2018, particularly for screen-detected, small lesions with low van Nuys' grade (*79*).

For the period 2017-2021, 86.0% of women with invasive screen-detected cancer underwent breast conserving therapy (Table 9.1). For women with invasive interval cancer, the proportion of breast conserving therapy was 71.1% in 2015-2019.

The proportion of breast conserving therapy for invasive screen-detected cancer ranged from 81.1% in Sogn og Fjordane to 91.9% in Fonna (Table 9.1). The proportion of breast conserving therapy for invasive interval cancer ranged from 82.6% in Troms og Finnmark to 62.4% in Oslo.

According to the Norwegian Breast Cancer Registry's report for 2020, the high performance target for breast conserving therapy is set to ≥85% for tumors 0-30 mm, with a moderate performance target of ≥70% (*29*). In total, for screen-detected breast cancer, BreastScreen Norway achieved the high target value, and all screening areas achieved the moderate target value. In total, for interval cancer, the moderate target value was achieved by the screening program, but not all screening areas achieved this goal.

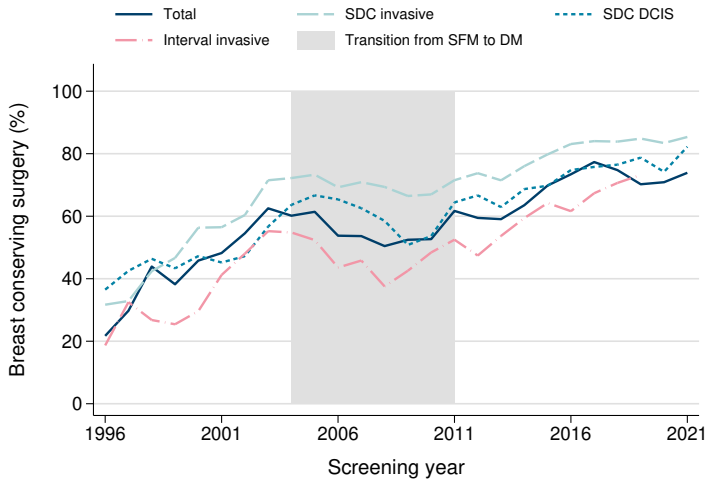


Figure 9.1: Proportion of breast conserving therapy (%) among screen-detected cancers (DCIS and invasive), 1996-2021, and invasive interval cancers, 1996-2019. SDC: Screen-detected cancer, SFM: Screen-film mammography, DM: digital mammography

The median number of days between screening and first registered treatment was 42 days among women screened in 2019 and 2020 (Table 9.2). It varied from 30 median number of days in Østfold to 57 in Hordaland. This is the first time we have had access to this data, which will be a valuable addition to the data already collected in BreastScreen Norway.

Table 9.1: Number of breast cancer surgeries (n) and proportion of breast conserving therapy (%) for invasive screen-detected breast cancers (2017-2021) and interval breast cancers (2015-2019) by screening area

	Screen-detected breast cancer		Interval breast cancer	
Screening area	n	%	n	%
Rogaland	421	82.9%	161	67.7%
Hordaland	539	83.7%	127	66.1%
Oslo	452	84.7%	165	62.4%
Telemark	183	84.2%	62	67.7%
Agder	300	86.7%	98	66.3%
Troms og F	278	89.9%	92	82.6%
Østfold	356	85.7%	99	73.7%
Nordland	235	85.1%	75	69.3%
Trøndelag	434	89.2%	154	73.4%
Oppland	231	81.4%	66	66.7%
Møre og R	296	86.5%	100	77.0%
Sogn og F	90	81.1%	46	67.4%
Vestfold	269	88.5%	90	76.7%
Hedmark	217	88.9%	62	66.1%
Akershus Øst	449	86.0%	168	71.4%
Vestre Viken	554	87.7%	156	79.5%
Fonna	62	91.9%		
Total	5,366	86.0%	1,721	71.1%

Table 9.2: Time (median, days) between screening examination and first treatment for screen-detected cancers (DCIS and invasive) among women screened 2019-2020 with the corresponding interquartile range (P25: 25th percentile, P75: 75th percentile), by screening area

Screening area	Screen-detected breast cancer (n)	Median	P25	P75
Rogaland	204	34	28	42
Hordaland	270	57	41	77
Oslo	225	55	40	77
Telemark	72	41	36	50
Agder	131	45	37	57
Troms og F	104	48	36	67
Østfold	159	30	26	35
Nordland	106	37	29	52
Trøndelag	190	55	38	67
Oppland	96	36	28	43
Møre og R	143	34	27	44
Sogn og F	37	36	28	51
Vestfold	130	42	30	57
Hedmark	96	34	28	46
Akershus Øst	193	36	28	48
Vestre Viken	241	54	42	64
Fonna	34	39	34	49
Total	2,431	42	31	57

10. Ongoing projects

Projects and research activity using data from BreastScreen Norway is diverse and include both national and international collaborators. In this chapter, currently ongoing projects where the Cancer Registry is the principal investigator are presented.

10.1 AI projects

About 200 000 women are screened in BreastScreen Norway every year. All mammograms are interpreted independently by two radiologists, resulting in about 400 000 screen-readings. As about 99.6% of screening examinations are eventually determined to have a negative screening outcome, radiologists spend a considerable amount of time reading mammograms where breast cancer is not detected.

Artificial intelligence (AI) is defined as computer systems able to perform tasks normally requiring human intelligence. AI has been introduced in numerous areas in healthcare. In mammography screening, AI has the potential to substantially reduce the radiologists' screen-reading volume without reducing breast cancer detection. In addition, about 20% of examinations positive for breast cancer are interpreted as negative by one of the two readers (*44*, *45*) and retrospective informed review studies have shown that about one in four interval and screen-detected breast cancers were visible at prior screening examinations (*58*, *80*, *81*). The sensitivity of the screening program might increase if AI can support the radiologists when interpreting these cases.

In Norway, as well as in Europe, there is a shortage of breast radiologists. Using AI in screen-reading can free up more resources. Retrospective studies using AI have shown promising results in classifying screening examinations as negative and positive for breast cancer (*82*–*85*). In addition to scoring mammograms according to the risk of breast cancer, AI can also be used in image quality analysis and mammographic breast density assessment.

AI can be utilized in different ways in a screening setting, and AI systems may be designed for use in a specific set-up. Results from retrospective and prospective studies are needed prior to implementing AI in BreastScreen Norway. To date, the performance of one AI system has been analyzed using images from BreastScreen Norway (*86*), and approvals to test systems from other vendors are in place. With data from over 4.5 million screening examinations, BreastScreen Norway might represent a unique source for international ground-breaking studies on this topic.

Retrospective evaluation

In a recently published study, mammograms from 122 969 screening examinations from 47 877 women attending screening between 2009-2011, were analyzed with the CE-marked AI system Transpara™ (ScreenPoint Medical, Nijmegen, the Netherlands). The AI system assigned the highest breast cancer risk score to a total of 87% of the screen-detected and 45% of the interval cancers (*86*). For screen-detected cancers, a high risk score was associated with less favorable histopathological tumor characteristics compared to lower risk scores. The opposite was observed for interval cancers, indicating that "true" interval cancers had a low risk score at prior screening.

Currently, results from retrospective processing of mammograms from Rogaland, Troms og Finnmark and Hordaland are being analyzed, and mammograms from Vestre Viken, Hedmark, Oppland, Østfold and Agder are being processed using Transpara™.

Randomized controlled trial

The process of testing AI prospectively in BreastScreen Norway has started, based on results from the retrospective evaluation. The trial has been approved by the Regional Committees for Medical and Health Research Ethics (Reference no.: 366405). In the trial, women will be randomized into two groups. In the control group, all screen-readings will be performed using the current standard procedure of independent double reading. In the study group, screen-reading will be performed based on the results from the AI system. Examinations assigned a low risk score of suspicious findings by the AI system will be read by only one radiologist, while examinations assigned a high risk score will be independently double read. Women participating screening at selected breast centers in BreastScreen Norway will be invited to participate in the study during 2022. Recruitment to the study will continue over several screening rounds. Parts of this project is financed by the Norwegian Cancer Society - Rosa sløyfe.

The MIM study - Machine learning in BreastScreen Norway

In addition to testing out commercially available AI systems, a research project aiming to develop an automated method to read images from screening examinations by combining machine learning-based image analysis and radiological expertise is being performed. The MIM study is a collaborative project between the Cancer Registry of Norway, the

Norwegian Computing Center, UiT The Artic University of Norway, and 7 regional health trusts, and is funded by the Research Council of Norway. The project started in 2018 and final models and plans for implementation will be finalized during the spring of 2022. Images from about 400 000 examinations from BreastScreen Norway have been used to train the algorithm, and preliminary results are comparable to results from other available AI systems. The Norwegian Computing Center have received funds from the Research Council of Norway to further develop the algorithm through the project AIforScreening. Currently, an application for funding to integrate the AI system with the IT systems in BreastScreen Norway is in progress, with the aim of testing the algorithm prospectively.

BADDI

BADDI stands for **B**reast cancer, **A**rtificial Intelligence, **D**igital Breast Tomosynthesis, **D**igital Mammography and **I**nterval Cancer. The BADDI project is based on data from the To-Be trials (see section 10.3 for more details), and the main purpose is to investigate the ability of AI to detect breast cancer at screening with digital breast tomosynthesis versus digital mammography, and to compare the AI with the performance of radiologists.

The project will examine the sensitivity and specificity of the AI system (Transpara^{TM}) using screening mammograms from the To-Be trials. In a retrospective radiological review, it will also be explored whether the AI system is able to detect breast cancers classified as missed, minimal sign or true, using screening mammograms from the examination prior to diagnosis of interval cancer and screen-detected cancer detected in the consecutive round. Results will be compared for digital breast tomosynthesis and digital mammography.

BADDI is a collaborative project between the Cancer Registry of Norway, the breast center at Haukeland University Hospital and the Mohn Medical Imaging and Visualization Center (MMIV) at Haukeland University Hospital. The project is funded by the Norwegian Cancer Society.

10.2 BERM

The aim of the project "BEdre Radiografi i Mammografiprogammet", BERM (Better mammography in BreastScreen Norway), is to improve BreastScreen Norway by focusing on quality assurance and quality improvement of the screening examinations and other radiography related aspects, as well as to acquire knowledge to establish more knowledge-based guidelines for radiographic work in mammographic screening. With BERM, we also want to increase knowledge and professional enthusiasm among radiographers and other professionals in the screening program and thereby ensure the women are participating in a safe, high-quality screening program. As a quality assurance and improvement study, BERM has received a waiver from the duty of confidentiality pursuant to the Health Personnel Act §29b from the Directorate of Health.

The invited women's experience of the information received, the screening examination, communication with the radiographers, and assessment of radiographic image quality are examples of parameters needed to be understood and assessed continuously to ensure the quality of the screening program. Many of these factors are important to achieve images of high quality, so the radiologists have the best possible starting point for making decisions on whether suspicious findings are of such a character that a woman must be recalled for further assessment.

For 97% of women attending BreastScreen Norway, the radiographers are the only professionals they encounter in the program. The ability of the radiographers to communicate with the women is crucial for providing optimal images. It will also contribute to establishing trust in the screening program, a crucial factor to ensure a high participation rate. The radiographers are responsible for ensuring optimal image quality, which is a key factor in finding small suspicious changes in the breast, to keep the rate of additional imaging at an acceptable level and to reduce the proportion of missed cancers due to sub-optimal or inadequate mammograms.

Radiographic image quality has been evaluated in BreastScreen Norway using the PGMI system (Perfect, Good, Moderate, Inadequate) since the start up in 1995. PGMI is a system to retrospectively evaluate screening mammograms according to a set of criteria into categories of Perfect, Good, Moderate and Inadequate. PGMI was established when screen-film mammography was used. It is a time consuming task and the system has never been validated (*87*). Several countries have thus replaced PGMI with other quality assurance systems during the past years. Radiographers in BreastScreen Norway have developed a new system, PAI (Perfect, Adequate, Inadequate), for immediate quality assurance of screening mammograms before the woman leaves the screening unit. PAI includes a positioning system including step-by-step checkpoints. The majority of the sub-projects in BERM are related to testing and validation of PAI.

In BERM, information from the breast centers PACS (Picture Archiving and Communication System) and the women's medical records will be collected. The PACS contains DICOM image data (mammograms) and technical information about the screening examinations, such as radiation dose, compression force and compressed breast thickness. Results of BERM will be beneficial for all women attending BreastScreen Norway and all other women with breast conditions, both in and outside of Norway.

The seven substudies in BERM are: 1) Testing of the PAI system; 2) Establishing an image bank, with learning and test sets; 3) Analyzing parameters to improve radiographic image quality; 4) Artificial intelligence and radiographic image quality; 5) Mapping and reducing retakes and additional images 6) Mapping and minimizing motion blur in the mammograms; 7) Mapping the women's experience of being invited to and participating in BreastScreen Norway.

10.3 The To-Be trials

Digital breast tomosynthesis (DBT, hereafter referred to as tomosynthesis) is a mammographic imaging technique that differs from 2D digital mammography in that the x-ray tube moves in an arch over the breast during image acquisition and the multiple exposures are reconstructed into a pseudo three-dimensional examination. Tomosynthesis was expected to be the new screening tool for breast cancer in the early 2010s. Non-randomized studies have demonstrated lower recall rates and higher rates of screen-detected breast cancer when screening with tomosynthesis compared to digital mammography (*88*, *89*). However, lack of reduction in interval cancers (*90*) have held back implementation, particularly in European screening programs.

The ECIBC guidelines suggest that organized breast cancer screening programs may use either tomosynthesis or digital mammography, but not in combination (*7*). The recommendation, however, is conditional. This is based on the balance between desired and undesirable effects, which probably favors tomosynthesis, however with very low certainty in the evidence and no data on long-term effects of the use of tomosynthesis on mortality and morbidity of breast cancer.

The Tomosynthesis trials in Bergen, the To-Be trials, aims to investigate whether tomosynthesis as a screening tool is equal or better than standard digital mammography in BreastScreen Norway. The To-Be trials are a collaboration between the Cancer Registry of Norway, Haukeland University Hospital and the University of Oslo, and consist of two separate studies performed over two screening rounds. The project is funded by the Research Council of Norway and the Norwegian Cancer Society.

To-Be 1

To-Be 1 was a randomized controlled trial, where all women who attended screening at the screening unit Danmarksplass in Bergen between January 2016 and December 2017 were invited to participate. The participants were randomly assigned to screening with tomosynthesis or digital mammography and were followed for two years to investigate early performance measures and rates of interval cancer and breast cancer in the consecutive screening round. The trial was completed in May 2021. The main findings were lower consensus and recall rates for women screened with tomosynthesis versus digital mammography (*43*), but no significant difference in cancer detection or histopathological tumor characteristics between the two study arms (*91*). Cost analyses found a higher cost for tomosynthesis versus digital mammography (*92*).

To-Be 2

The follow-up study, To-Be 2, is a single-group clinical trial where all women attending screening at Danmarksplass in Bergen were offered screening with tomosynthesis. The recruitment period was January 2018 to January 2020, and the women were followed for events of interval cancer for two years after screening. The main aim of the study is to investigate the effect of screening with tomosynthesis after a previous screening with tomosynthesis or digital mammography. The main findings was that rates and tumor characteristics of interval breast cancer from To-Be 1 or consecutive round screen-detected cancers from To-Be 2 did not differ between women originally screened in To-Be 1 with tomosynthesis versus digital mammography (*93*).

Current efforts in the To-Be trials focus on a review of interval cancers detected in To-Be 1 and screen-detected cancers detected in To-Be 2 among women who participated in To-Be 1, to classify the cases as missed, minimal sign and true cancers, based on the prior tomosynthesis mammograms from To-Be 1. This will increase our knowledge about mammographic features and histopathological findings of tumors classified into the different groups. The results will also be compared with results of an AI system (see chapter 10.1 for more details).

10.4 Quality of life following breast cancer treatment

There is limited evidence about differences in long-term quality of life among breast cancer survivors whose cancers were detected by screening and those whose cancers were detected due to symptoms. The Cancer Registry therefore started the postdoctoral project "Long-term effects following treatment of screen-detected versus symptomatic breast cancer" in 2019. The purpose is to investigate the quality of life after breast cancer diagnosis and subsequent treatment for women with breast cancer detected in BreastScreen Norway compared to women with breast cancer detected due to symptoms.

The results from a review study indicated that the long-term quality of life among breast cancer survivors eligible for screening did not differ from that of women who have never been diagnosed with breast cancer (*94*). Further, a study based on a survey among 4500 Norwegian women aged 50-69 years showed that women with screen-detected

breast cancer reported a significantly higher quality of life score compared to women who had been diagnosed with breast cancer due to symptoms (*95*). This finding suggests that early detection of breast cancer is beneficial, not only for longevity, but also for quality of life after diagnosis. Less aggressive treatment of women with screen-detected breast cancer compared to those who have had breast cancer detected due to symptoms is a possible explanation for the differences between the groups. The project is funded by the Dam Foundation, through the Norwegian Women's Public Health Association.

10.5 ImmigrantScreen

ImmigrantScreen is a collaborative project between BreastScreen Norway and ColorectalScreen Norway. One of the main purposes is to investigate whether sending an invitation to screening in the invitees' presumed native language, in addition to Norwegian, will affect attendance rates among immigrants. This will be examined with a randomized controlled trial where attendance among those who have received invitations both in their presumed native language and Norwegian will be compared with attendance among those who have only received invitations in Norwegian. Another main purpose is to investigate which factors may influence the decision of immigrants from Poland and Pakistan to attend in ColorectalScreen Norway. Similar studies related to breast cancer screening have been carried out earlier in a PhD project in BreastScreen Norway (see chapter 10.6). The project is funded by the Norwegian Cancer Society.

10.6 Recently completed PhD projects

The following PhD projects using data from BreastScreen Norway have been conducted in the last five years.

Mammographic screening among immigrant women in Norway; disparities in attendance and selected screening outcomes

Sameer Bhargava (Cancer Registry of Norway) defended his PhD in 2019. The aim of the project was to describe attendance in BreastScreen Norway among immigrant women and the outcome of screening examinations in the period 1996-2015. The project was carried out at the Cancer Registry of Norway, and funded by the Dam Foundation, through the Norwegian Breast Cancer Society.

The results showed that immigrants had lower attendance in BreastScreen Norway than Norwegian-born women, independent of country of birth, also after adjusting for various socio-demographic factors (*38*). Further, Bhargava and colleagues showed that breast cancer tumors among immigrant women were more often larger and of a higher histologic grade than those among Norwegian-born women, even after adjusting for age and screening history (*96*). This was interpreted to indicate that immigrant women were diagnosed with breast cancer at a more advanced stage. In a qualitative study, the authors showed that a number of factors, such as family life or the gender of the radiographer, influence Pakistani immigrant women in Norway when they consider whether to attend screening, and that these factors may influence individuals differently (*39*). To increase the likelihood of providing an equitable offer for mammographic screening, the authors concluded that measures should be taken to give immigrant women a more tailored offer to increase their awareness of, and attendance in, mammography screening.

Breast compression in mammography – from experience-based to evidence-based practice

Gunvor Gipling Waade (Oslo Metropolitan University) defended her PhD in 2020. The aim of the project was to investigate how breast compression is performed in clinical practice of breast cancer screening today. The project was funded by the Oslo Metropolitan University.

The project revealed large variation in the use of breast compression between breast centers in BreastScreen Norway, and also within the breast centers (*97*). Women screened with tomosynthesis (in the To-Be trial, see chapter 10.3) received slightly lower compression force compared to women screened with digital mammography (*98*). Furthermore, an increase in breast compression was observed for women at consecutive screening examinations (*99*). This project also found that the radiation dose increased by quartiles of compression force and compressed breast thickness, where the highest values of compression force and compressed breast thickness had the highest radiation doses (*97*).

Based on this project, Waade and colleagues concluded that there was a need for increased awareness of the use of breast compression in mammographic screening. The guidelines for breast compression valid at the time should be revised with the aim of establishing evidence-based guidelines. This should be done as a collaboration between radiographers, radiologists, medical physicists and women in the target group of the screening program.

Overdiagnosis and underdiagnosis in BreastScreen Norway

Kaitlyn Tsuruda (Cancer Registry of Norway) defended her PhD in 2021. The PhD project investigated aspects of overdiagnosis and underdiagnosis in BreastScreen Norway. The goal of the project was to add to what is known about the potential harms of mammographic screening. The project was funded by the Dam Foundation, through the Norwegian Breast Cancer Society.

Organized breast cancer screening can detect early-stage breast cancer and reduce deaths caused by the disease. However, screening also involves harms, such as the potential detection of a slow growing breast cancer that would never present symptomatically during a woman's lifetime (overdiagnosis). "Underdiagnosis" can also occur, which was defined as "failing" to diagnose a breast cancer that would present symptomatically during a woman's lifetime. The thesis aimed to generate knowledge about these harms through three studies.

The first study demonstrated that radiologists and pathologists preferentially round tumor diameter measurements, which can lead to understaging but not overstaging (*68*). The second study considered whether women with "missed" cancers that were diagnosed at a subsequent screening examination could be underdiagnosed (*100*). Based on their tumor characteristics and survival profile, it was posited that these women received a timely diagnosis. The last study indicated that women have less knowledge about overdiagnosis than other topics related to mammographic screening (*101*). This study highlights some of the challenges related to communicating information about overdiagnosis and screening.

Improved breast cancer screening for women and society: A radiological approach

Tone Hovda (Drammen Hospital) defended her PhD in 2022. The overall aim of the PhD project was to investigate ways to improve early detection of breast cancers and included analyses of mammographic techniques and radiologists performance. The project was funded by the South-Eastern Norway Regional Health Authority.

In the first study, women residing in Oslo were screened with tomosynthesis, while women from Vestfold or Vestre Viken were screened with digital mammography during the period 2014-2015. A 50% increase in cancer detection was observed for those screened with tomosynthesis versus digital mammography (*102*). No difference in rates of interval cancer was observed (*103*). Cancers detected with tomosynthesis were mainly smaller and less aggressive compared to those detected with digital mammography. Thus, whether the increased cancer detection represents clinically significant cancers remains debatable, and as of today, the basis of knowledge for implementing screening with tomosynthesis in BreastScreen Norway is considered insufficient.

In the second study, panels of five radiologists performed retrospective reviews at all breast centers in BreastScreen Norway of mammograms from diagnosis and prior screening of women diagnosed with screen-detected and interval breast cancer. In the majority of the reviewed cases, no abnormalities at all, or only minor, non-specific findings were retrospectively visible at the later cancer site (*80*, *81*). However, in about 20% of the reviewed cases, findings that were more obvious were observed on prior screening mammograms, with a potential for earlier diagnosis. Education, increased awareness and regular self-audits may increase radiologists' performance and reduce cancers missed at screening.

Age at menopause: Associated factors and temporal trends

Marthe Sørli Gottschalk (Akershus University Hospital) defended her PhD in 2022. In this PhD project, data from the questionnaire collecting information from women attending BreastScreen Norway, 2006-2016, was used in two of a total of three studies. The first study investigated if age at natural menopause had changed over time and the second study looked into if age at natural menopause increased by number of childbirths. A minor decrease in mean age at menarche was found, but an increase of approximately three years in mean age at menopause (*104*). The mean age at natural menopause increased from 50.3 years among women born in 1936 to 52.7 years among women born in 1964. Thus, the mean number of years of reproduction increased by more than three years. The authors also found that women with three childbirths had the highest age at menopause and women with no childbirths had the lowest (*105*). Beyond three childbirths, no further increase in age at menopause was observed. More than 55% of the women with early menopause gave birth within 10 years before menopause, whereas this was true for less than 1% of the women with late menopause. Almost no women gave birth after the age of 45 years. The project was funded by the South-Eastern Norway Regional Health Authority and by the Norwegian Cancer Society.

10.7 Ongoing PhDs, postdocs and master's

PhD, postdoctoral and master's projects using data from BreastScreen Norway are continuously ongoing. Below, the ongoing projects are described in short. Three PhD studies are planned to start during 2022 and 2023, while two postdocs will be employed at the Cancer Registry during the fall of 2022.

PhD projects

Digital Breast Tomosynthesis - the future screening tool for breast cancer?

Hildegunn Siv Aase (Haukeland University Hospital) is a breast radiologist and has been working on her PhD alongside her work as the leader of the breast center at Haukeland University Hospital. The doctoral defence is planned to take place in 2022. The topic of the PhD is related to the To-Be 1 trial where screening outcome of tomosynthesis was compared to digital mammography. The studies included

in the thesis presents results for consensus and recall rates, screen-reading and consensus time, radiations doses, mammographic breast density and mammographic features. The thesis includes three published papers (*43*, *106*, *107*). The PhD project is funded by the Research Council of Norway and Haukeland University Hospital.

Use of machine learning in mammographic screening - challenges and consequences

Marit Almenning Martiniussen (The Hospital in Østfold Kalnes) is a breast radiologist and started her PhD work in May 2021. She will be working on her PhD in a 50% position alongside her work as a radiologist at the Hospital in Østfold Kalnes. The PhD project will investigate AI and machine learning in mammographic screening, and one paper have been published (*44*). The following substudies will also be performed:

- Ethical, legal and social implications of implementing AI in BreastScreen Norway
- Mammographic screening outcome of a CE-marked AI system versus independent double reading, using data from BreastScreen Norway.

The PhD project is funded by the South-Eastern Norway Regional Health Authority.

Lifestyle factors, age at menopause and subsequent health outcomes

Julie Røgler Langås (Oslo Metropolitan University) conducts her PhD project at the Oslo Metropolitan University. The project aims to study temporal changes in age at menopause, identify factors associated with the timing of age at menopause, study the relationship between length of the reproductive period with hormone related cancers and the risk of cardiovascular death and all-cause death. This will be done using data from the questionnaire used in BreastScreen Norway 2006-2016, which will be linked to the Cancer Registry and Cause of Death Registry of Norway. The project is a collaboration between Oslo Metropolitan University, the Cancer Registry and Akershus University Hospital. The project is funded by the Norwegian Cancer Society and the South Eastern Norway Regional Health Authority.

Postdoctoral projects

Long-term effects following treatment of screen-detected versus symptomatic breast cancer

Nataliia Moshina (Cancer Registry of Norway) is employed as a postdoc at the Cancer Registry of Norway, working on a project about quality of life after breast cancer (see 10.4 for more details). She did her PhD at the Cancer Registry of Norway, on the topic mammographic breast density.

Two papers have been published (*94*, *95*). The following substudies will also be performed:

- Quality of life among breast cancer survivors who attended screening compared to non-attendees
- Detection mode versus tumor characteristics as the main predictor of long-term quality of life among women diagnosed and treated for breast cancer.

The project is funded by the Dam Foundation, through the Norwegian Women's Public Health Association.

Facilitators and barriers apart from language for attending breast and colorectal screening among Pakistani and Polish immigrants

Sameer Bhargava (Bærum Hospital/Cancer Registry of Norway) is working on his postdoc in a 40% position at the Cancer Registry of Norway, alongside his position as an oncologist at Bærum Hospital. The project is included in ImmigrantScreen (see page 62), and Sameer is leading the qualitative study investigating the reasons for attending and not attending screening programs among Polish and Pakistani born individuals. He did his PhD at the Cancer Registry of Norway focusing on immigrant women and participation in BreastScreen Norway (see chapter 10.6 for more details). The project is funded by the Norwegian Cancer Society.

Master's degree project

Artificial intelligence and quality control of breast positioning

Linn Tøsdal (Stavanger University Hospital) is chief radiographer at the breast center at Stavanger University Hospital, and is doing her master's degree on AI and quality control of breast positioning in BreastScreen Norway at the University of Stavanger. A group of radiographers have reviewed mammograms according to specific positioning criteria and Linn have compared the results of the review with results from AI. She will finalize her work during 2022.

11. Summing up, and future perspectives for BreastScreen Norway

Early screening outcomes in BreastScreen Norway are within the recommended levels of the EU and Norwegian guidelines (*5*, *7*). The screening program continuously focuses on presenting balanced information, facilitating an informed choice about participation. The program has a complete database with information available for quality assurance and research projects and several projects have been or are focusing on improving the program, for the benefit of the women, society, and the health care system. Studies from BreastScreen Norway have shown a reduced breast cancer mortality after implementation of the screening program, the most recent with an estimate of about 40% among invited women (*108*). The screening program was estimated to have contributed to about half of this reduction, with better treatment contributing to the other half. In addition, breast cancer mortality has been found to be further reduced among women who participated versus those who did not (*109*, *110*). Studies from BreastScreen Norway have also shown a higher quality of life among women after treatment of screen-detected breast cancer versus symptomatic breast cancer in adjusted analyses (*94*, *95*). Based on these results, the following conclusion could be easy to draw; the program is well organized and performs well.

However, the consensus, recall and cancer detection rates, screen-detected as well as interval cancers, and histopathological tumor characteristics, have been more or less the same during the 25 years of population-based screening in Norway. What are the lessons learned and what direction could and should the program take after more than 4.3 million screening examinations and 17 million screen-readings in BreastScreen Norway? Are we satisfied with the 2022 version of BreastScreen Norway?

BreastScreen Norway has carried out a substantial number of studies aimed to improve the program. Recent studies have focused on preparing for testing, studying and implementing artificial intelligence (AI) in the screening program, particularly in the image interpretation phase. Unfortunately, the IT systems currently used in BreastScreen Norway, largely unchanged since 1995, do not communicate well with modern IT systems. Several ad hoc solutions have been developed both for running the program and for quality assurance and research. However, an upgraded IT system is crucial to make necessary changes and ensure that women are offered participation in a modern screening program for breast cancer.

Privacy legislation has changed in recent decades. The introduction of the GDPR and subsequent changes in national legislation has led to several changes in the procedures for performing quality assurance and research projects. It has proven particularly challenging to manage screening in this environment as screening basically involves healthy individuals, despite being performed within health trusts by health care personnel using medical equipment. Several ethical and legal questions relevant to screening are discussed either in the context of healthy or sick individuals, while screening does not fit well into either of these two categories. Also, as screening is offered to all women in the target group, it is important to continuously carry out quality assurance and research that contribute to safeguarding and improving all parts of the program; information and invitations, imaging, screen-reading, assessment and treatment. If either of these components fails, the quality of the program will be compromised. The changes in privacy legislation also represent challenges regarding information to the health care personnel performing the work and thereby the program's opportunities for surveillance of important quality measures on a national level. Individual feedback to all professional groups involved in the screening program is crucial for quality assurance and improvement of the program.

Breast tumors are heterogeneous and may appear and develop differently in different women. Some tumors may be clearly visible in fatty or dense breasts, while others may be hidden in dense tissue or may not be visible on mammograms at all. This means that stratification of the screening population based on risk factors might be a more effective approach than the current "one-size fits all" model. Construction of risk stratification models requires data and biological samples from large cohorts, ideally in prediagnostic populations that are followed for breast cancer diagnosis (*111*). Various strategies have been proposed. Stratification will result in different screening plans for individual women, where some may be offered annual screening, possibly with different modalities, while others may be offered screening with mammography only every three years. Regular updates of the individual risk profiles will be necessary as risk factors such as the use of hormone therapy and mammographic density, change over time.

New international recommendations must also be considered by modern screening programs. In February 2022, the European Society of Breast Imaging (EUSOBI) published a paper recommending that women with extremely

dense breasts should be offered screening with MRI rather than mammography every two to four years (*112*). They also recommended that women should be informed about their mammographic density at screening. Women with extremely dense breasts have an increased risk of breast cancer and mammography has low sensitivity when it comes to dense breast parenchyma because tumors can be masked in dense tissue. EUSOBI considers screening with MRI to be a cost-effective method that enables an important reduction in breast cancer mortality for women with dense breasts. Such a change in the program would require substantial resources both at the 17 breast centers and centrally, both to facilitate and run. The recommendation will be presented to the Steering Group during the first half of 2022.

What might BreastScreen Norway launched in 2023 have looked like?

The basis for starting organized breast cancer screening today differs from that of 25-30 years ago when BreastScreen Norway was started. Knowledge about the biology of cancer tumors has increased significantly, and equipment and techniques for screening and follow-up of suspicious findings have higher sensitivity. Methods and systems for collecting and processing data are more effective and formal information and privacy requirements are considerably higher and more stringent.

Given the current knowledge, an organized breast cancer screening program would most likely have been initiated and implemented differently today compared with 1995. The text below presents ideas on how such an imaginary program could have been planned and run, and hopeful perspectives on how it might appear in a bright future. The text is intended to inspire thoughts and discussions, innovations, improvements and to contribute to streamlining breast cancer screening for women in Norway in the future.

Prerequisites

An imagined organized screening program for breast cancer starting in 2023 would have a modern IT system connecting all its parts and with sufficient flexibility to allow for updates whenever needed to allow for continuous improvement caused by administrative or urgent needs (i.e. a pandemic) or by new insights gained through quality assurance and research.

A substantial prerequisite to starting, running and maintaining a future screening program would be political motivation and support. The program would have sufficient resources earmarked for professional growth and development. Further, one would envisage a tight collaboration between health care professionals and authorities, representatives from a varied field of stakeholders, i.e the users, both in relation to the administration and to the quality assurance and further development of the program. The program would be knowledge-based, constantly seeking out new knowledge and developments to guide its activities.

Basic aspects

Planning and implementation of a future screening program for breast cancer in Norway would be based on evidence from modern screening programs. However, to fill some of the evidence gaps, a substantial number of studies with a broad specter of goals and interventions would be required. Studies on AI, retrospective as well as prospective, for image interpretation and other purposes would be a part of these studies. A substantial number of these studies would be conducted in Norway and performed as randomized controlled trials. After 4-6 years, the results would be evaluated, and largely determine the design of the future screening program.

The future program would have a centralized administration responsible for day-to-day operation, economy, data collection, quality assurance and research. It would work in close partnership with the various groups of specialists at local breast centers, responsible for the imaging, screen-reading, assessment, treatment and follow-up, but also quality assurance and research.

Targeted information campaigns would disseminate information about breast cancer according to the current EU Guidelines (*7*), about the benefits and harms of screening in general and breast cancer screening in particular. This effort would prepare women in the target group, the society, and academics for a stratified screening program, including different screening techniques, modalities, and procedures depending on individual risk profiles. This would give the women the opportunity to make an informed choice about participation from their first invitation. Any treatment and follow-up after screening would be tailored to the individual woman. Continuous, short- and long-term objectives for the program would be clearly described in guidelines. Formal requirements for reporting, storage, use and publication of data would be clear and pre-approved, which would allow timely and continuous monitoring, maintenance, development and research related to the program.

Mapping of risk factors

For all the women, the future screening program would start with an invitation to a basic interview to map risk factors, around the age of 46-47. This personal interview, where risk factors for breast cancer and other diseases would be mapped, and blood tests, collection of saliva including polygenetic risk score, and basic mammograms would be included, would form the foundation for the screening scheme for the women until the age of 60. Then a new interview

would be conducted, and adjustments to procedures would be made to provide the best possible individual screening strategy until the women turned 75. After that, the women would have the opportunity to decide whether they wanted further invitations to screening. The invitation systems would be based on algorithms that could communicate with all institutions that might be involved in this initial process, the central administration of the program, breast centers, general practitioners, and others.

The basic interview would include the dissemination of information about breast cancer, and the benefits and harms of participating in personalized screening. This information would refer to further information videos, websites, and other information tools. An app using standardized translations to other languages would be used to assist in interviews with non-Norwegian speaking women. A professional group within the screening team, including trained experts in information and dissemination, would be responsible for the information material and research would be an integral part of their work. The interviews would be conducted by trained radiographers and nurses and could include risk analysis for other cancers in addition to breast cancers, such as cervix, colorectal, lung, and melanoma. Further procedures for other cancer types are not discussed in this text.

Risk assessments

This future screening program would use saliva and/or blood samples for analyses of polygenetic risk scores and mammograms would be analyzed for density and glandular pattern (radiomics), using AI. The proportion of women with dense breasts is expected to be about 5% of the screened women. Based on these results and other risk factors, including genetics, family history and other diseases, AI would be used to stratify women for breast cancer screening at various intervals and with adjusted techniques; mammography, standard or breast tomosynthesis, MRI, or mammography followed by automated breast ultrasound or MRI.

Procedures for invitations and information

Invitations to the interview and risk assessment would be sent to the individual woman, in Norwegian or another preferred language, from the central administration of the program, like today. After the interview, they would receive a written summary of the results, a description of their personal risk profile and proposed screening strategy. General practitioners and others involved in the women's health profile would be informed of the outcome of the survey. Invitation to screening would include time and place for a scheduled appointment, like the procedures in BreastScreen Norway today, as this is cost-effective and in line with what women have expressed that they value in a screening program (*113*). The women would be able to change their appointments themselves, and everyone would receive a reminder of the appointment by SMS. If the women had any questions, the information team would be able to respond by phone and e-mail, all days, all weeks, personally or using chat boxes.

The screening examination

Future screening examinations, mammography, ultrasound and/or MRI would be performed by trained radiographers who used standard techniques and AI to ensure images of the highest quality. All screening units would have the same type of equipment and a central, national system for storing images. This would ensure uniform examinations, enable examinations across screening areas and simplify technical quality control and maintenance of equipment for the radiographers as well as for the medical physicists. At the screening units, previous examinations would be available at the time of screening to provide mammograms and other images for comparison. Based on results from the studies performed before the start-up of the program, this is shown to increase the sensitivity and reduce false positive screening examinations. The risk assessment would direct the women to the most efficient screening technique(s).

Interpretation of the screening examination

All screening examinations, be it mammography, ultrasound or MRI, would be interpreted by AI immediately after screening. Two or more AI systems would select about 20% of the screening examinations for interpretation by radiologists and less than 5% should be selected for consensus. This means that about 80% of the women would be informed that there were no signs of breast cancer before they left the screening unit.

Alongside being immediately informed about the result of their screening examination, the women would be informed about their mammographic density and next screening appointment. The results of the screening examination and from additional follow-up would be automatically stored in systems familiar and accessible to the women, the breast centers and general practitioners.

Mammography, ultrasound and MRI examinations interpreted as positive by AI would be further interpreted by dedicated radiologists. There would be a central unit to which all images would be sent directly after the screening examination. Screening examinations from throughout the country would be read by 7-8 dedicated screening radiologists. There should be a rotation scheme for radiologists, to increase their competence, reduce vulnerability, and make the work attractive. The work would amount to a maximum of 1.5-2 full-time positions and the 7-8 screening radiologists would spend a maximum of 20-25% of their working time on interpreting screening examinations. The screening radiologists would read examinations from randomly

selected centers and if independent double reading still is proven effective, the pairs of radiologists would be random, to achieve the optimal selection of screening examinations for consensus. Such an interpretation procedure would reduce bias that may occur when the same pairs of radiologists interpret and perform consensus year after year. The performance of the screening radiologists should be subject to continuous monitoring, and regular courses, quality assurance and improvement measures would be an integrated part of the work. Today, there are close to 100 radiologists interpreting screening mammograms in BreastScreen Norway, and there is a considerable shortage of breast radiologists. Breast radiologists interpret both screening and clinical mammograms and are often dedicated to the breast center. Central interpretation would be attractive and open up for combined positions for radiologists, at breast centers and other units in radiology departments, for example MRI.

The consensus rate would be about 5% and consensus would be carried out by two local radiologists and one screening radiologist. Consensus would be conducted according to a fixed schedule, on specific days of the week to ensure predictability and reduce waiting time for assessment for the women. The consensus would deselect 60-70% of the cases discussed, resulting in a recall rate of 2% or lower and a positive predictive value of recall close to 50%. This would release significant resources at the breast centers and fewer women would experience a false positive screening test, without a reduction in the detection of breast cancer.

Triple diagnostics and cancer detection

Recall assessments after positive screening examinations would be performed and reported at the dedicated breast centers according to standardized procedures. Reporting of screening activity would be 100% electronic, with opportunities for immediate extraction for analyses at the central administration unit, but also for each breast center. Standardized diagnostic procedures will ensure that all women could be offered equal opportunities for tailor-made treatment. Standardized reporting would provide unique opportunities for immediate quality assurance and further development of the procedures as well as assessment of short- and long-term effects of the treatment. The radiologists would use speech recognition systems to describe the outcome of further assessment and an AI system would be used to extract the information needed for reporting to different databases. This procedure would reduce the workload for the professionals, ensure comparable reporting and make data immediately available for analysis.

The outlined screening design is expected to result in an increased rate of screen-detected breast cancer, from about 6 to 8 breast cancer cases per 1000 screening examinations, while the interval cancer rate would be reduced to less than 0.75 per 1000 screening examinations. Due to the increased risk of being diagnosed with interval and screen-detected cancer later among women with false positive screening tests, all women with a negative recall assessment would be invited to a new screening examination after one year.

Women with symptoms, both within and outside the target group, would be able to refer themselves to triple diagnostics by filling in a form, for example using HelseNorge, the electronic health portal for all residents in Norway. The woman's information would be evaluated by an AI system that immediately prioritized the woman for an appointment at the nearest breast center or the one with the first available appointment, or for seeking their general practitioner. All assessments based on symptoms would be performed according to standardized procedures with assistance from AI and reported the same way as further assessments in the screening program to ensure high quality and comparable data for quality assurance and research.

Treatment and follow-up

The outlined screening design would probably increase the risk of detecting small, non-progressive tumors, also called overdiagnosed cancers. However, increased knowledge about tumor biology would allow histological and molecular characteristics to define "small slow-growing tumors" and the use of tailored treatment would eliminate or substantially reduce the harms of detecting such tumors.

The primary treatment would be immediate, with local excisions on all small and non-progressive tumors. Re-excisions would no longer be relevant, and there would be an absence of relapse after 10 years as well as 15 years due to the tailored treatment and use of risk prediction models for recurrence. The latter would be a part of the tailored follow-up. More than 90% of all women needing surgery would receive breast-conserving surgery. Radiation and any additional treatment would be tailored to the individual woman and the few who underwent mastectomy would have implants inserted in the same surgical procedure, in line with the women's personal choice. All women would be able to remain in their jobs during and after treatment, and those who were treated would report having a long-term quality of life at the same level as women without breast cancer.

The goal of the future screening program for breast cancer in Norway would be to detect tumors at an early stage to reduce negative effects during and after treatment. Further, the future screening program would be a continuation of the program we are running today, which has proven to reduce breast cancer mortality. BreastScreen Norway 2023 might thus not be able to further reduce mortality from the disease per se; however, in combination with improved treatment, the main long-term goal of the program would be to reduce breast cancer mortality to less than 100 women every year in Norway in 2050.

We are really looking forward to planning this screening program in detail and starting the work!

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