The Norwegian Breast Cancer Screening Program 1996-2016

Celebrating 20 years of organised mammographic screening

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CANCER Registry of Norway

Breast Screen Norway

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Foreword

This report represents part of our celebration of the 20th anniversary of the Norwegian Breast Cancer Screening Program. During these 20 years the program has been through an exciting journey with triumphs and challenges. This anniversary is an excellent opportunity to reflect on the program's past as well as its achievements and future challenges.

We are very proud today to offer women a high quality screening program run according to current Norwegian and European guidelines. Screening activity has been registered in the Cancer Registry of Norway since the program's inception and 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 have never been as many ongoing quality assurance and research projects, or such a wide range of hypotheses being explored, as there are today.

Women targeted by the program are devoted: 84% of the nearly one million women invited to screening have attended at least once, resulting in a 20-30% reduction in mortality overall, and about 40% reduction in breast cancer mortality among screened women.

Today, the screening program faces a number of new challenges. Not only should the program keep up with evolving technologies and new diagnostic improvements, but it should also embrace new evidence-based developments. Any new developments that are incorporated into the program should be done in such a way that their effect can be monitored. Moreover, the need to provide understandable, evidence-based information about breast cancer and mammographic screening to women, other stakeholders, and the general population is paramount.

The aim of this report is to describe the program today, its history, and noteworthy developments. Much of the program's history has never been described, and we have attempted to gather the information here. Thank you to all who have contributed to this effort. This report also presents results from early performance measures, and shares some insights into the quality assurance, program evaluation, and research activities associated with the program, as well as our perspectives on the future development of breast cancer screening.

A 20 year old woman is full of energy, willingness to change, and has a bright future. So too is the Norwegian Breast Cancer Screening Program.

Enjoy this report!

Oslo, October 2017

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Breast cancer is the most common cancer among women worldwide and in Norway, and the second most common cause of cancer death (1, 2). Breast cancer survival is highly dependent on stage at diagnosis and mode of detection (3, 4). The causes of breast cancer are not known, but many risk factors are well established. Few of these risk factors are modifiable, however. Because of this, breast cancer screening is a well accepted strategy for the secondary prevention of breast cancer in western countries (5, 6).

The Norwegian Breast Cancer Screening Program targets women aged 50 to 69 for mammographic screening every other year. The program started as a pilot in 1995 and became nationwide in 2005. Internationally, the history of mammographic screening dates back to the early 1960s, when the first randomised trial in New York began (7). The results from this trial led to great optimism regarding the potential screening could have in reducing deaths from a disease, which at the time, had poor survival. Now, more than 50 years later, organised mammographic screening is one of the most evaluated and quality assured health care services offered in Norway, and internationally.

In Norway, an essential part of building the nationwide screening program was the establishment of specialised breast centres, with a focus on efficient work flow, centralised professional competence, and multidisciplinary teamwork. As a part of this process, systematic quality assurance tasks were developed and defined for all disciplines and institutions involved in the program. Another key factor in the program is the invitation system, which is based on personal invitations with scheduled appointments that are automatically sent to all women in the target group. This invitation system facilitates regular participation regardless of where women live.

The Norwegian model for breast screening has been successful and is quite unique internationally. This model is based on a centralised database and a shared IT system, which creates distinct opportunities for communication, quality assurance, and research. As a result, the Norwegian program is attractive to national and international researchers as well as program administrators.

Another strength of the program is its foundation in systematic quality assurance and research. A large part of this report is dedicated to early performance measures that are important for program surveillance in order to reduce future breast cancer mortality. These measures are a part of the continuous quality assurance of the program, and are regularly shared with professionals working at the breast centres.

It is well known that the concept of mammographic screening has spurred debates about its potential benefits and harms during the past decades (8–11). In recent years, international publications have strengthened the evidence for mammographic screening. A systematic review by the European Commission Initiative on Breast Cancer concluded in 2016 that there is strong evidence to recommend mammographic screening for women aged 50-69 (5). Similarly, several other institutions and research groups, such as the World Health Organization's International Agency for Research on Cancer (2015) and the UK Independent Panel on Breast Cancer Screening (2012), have concluded that there is sufficient evidence to support the benefits of mammographic screening for women aged 50-69 (6, 11, 12).

The release of an independent research-based evaluation in 2015 was an important milestone for the organised screening program in Norway. This evaluation summarised previous research and produced new evidence about the program. Highlights from this report included confirmation that the program reduced breast cancer mortality by 20-30% among invited women and affirmation of the program's cost effectiveness (13).

Today, discussions are ongoing about which age groups should be offered screening, how the service should be organised, and how women should be informed (6). The Norwegian screening program has achieved its main goal of reducing breast cancer mortality and now aims to maintain and continue to develop the quality of the program as well as increase its benefits and reduce its harms. The program faces a number of challenges today such as new screening modalities, the detection and treatment of dormant or slow growing asymptomatic tumours, stratified screening, and personalised treatment. However, changes in the program should be evidence-based and extensive research is needed in order to fill knowledge gaps before action can be taken. Political and economic support is required to make this a reality.

Figure 1.1: Mobile screening unit from the late 1960s; 70 women could be screened per day. Reproduced, with permission, from: Gold RH, Bassett LW, and Widoff BE. Highlights from the history of mammography. RadioGraphics 1990;10(6):1111-31

2. The Norwegian Breast Cancer Screening Program

The Norwegian Breast Cancer Screening Program is a part of the public health care services offered in Norway and targets women aged 50-69 for biennial screening. The program started in 1995 as a pilot, and became nationwide in 2005. The Cancer Registry of Norway administers the program, while the regional health authorities, through the local health trusts, perform screening and follow-up. Screening examination, interpretation, and any further assessment and treatment is performed at 16 specialised breast centres and 30 connected screening units. A national quality assurance manual is published by the Cancer Registry. A steering group is headed by the Norwegian Directorate of Health. This chapter presents the principles behind screening and gives a summary of the roles and areas of responsibility held by the Cancer Registry, the regional health authorities and local health trusts, as well as a description of the steering and advisory groups linked to the program.

Principles of screening

The goal of screening is to detect a disease in an early stage and thereby reduce the incidence (primary prevention), mortality (secondary prevention), and/or morbidity (tertiary prevention) of that disease. Breast cancer screening is a secondary preventative strategy to reduce breast cancer mortality by detecting the disease in an early stage. Mammography is the recommended screening technique, and the only one that has been demonstrated to reduce breast cancer mortality (*6*).

In 1968, the World Health Organization published the ten-point Wilson-Junger criteria for evaluating screening programs (Figure 2.1) (*14*). These criteria were published five years after the first randomised controlled trial with mammography started in New York, and have served as a general guideline for the establishment of screening programs since (*7*). In 2014, the Norwegian Directorate of Health added six new points to this list for Norwegian screening programs (*15*).

Cancer screening involves testing otherwise healthy people for signs of a developing cancer. The potential ethical challenges of doing so must be considered. With respect to mammographic screening, this relates to, among other things, the effectiveness of the program, the balance between benefits and harms, and how information is communicated to women to ensure an informed choice whether to participate. This also relates to how the health service is organised, taking care of both women's autonomy in their decision whether to participate, and providing an effective invitation model that ensures a cost effective program with equal and equitable access to screening regardless of where women live.

1. The condition sought should be an important health problem
2. There should be an accepted treatment for patients with recognised disease
3. Facilities for diagnosis and treatment should be available
4. There should be a recognisable latent or early symptomatic stage
5. There should be a suitable test or examination
6. The test should be acceptable to the population
7. The natural history of the condition, including development from latent to declared disease, should be adequately understood
8. There should be an agreed policy on whom to treat as patients
9. The cost of case-finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
10. Case-finding should be a continuing process and not a "once and for all" project
11. *The health benefits should outweigh the harms*
12. *The protection of personal privacy and adherence to the law be ensured*
13. *The program should be ethically acceptable*
14. *Information about participation should be evidence-based and empower making an informed choice about participation*
15. *The program should be cost-effective*
16. *There should be a plan for program administration, quality assurance and evaluation*

Figure 2.1: Modified Wilson-Junger criteria for appraising screening programs (*14*, *15*)

The Cancer Registry of Norway

The Cancer Registry is a part of the South-Eastern Norway regional health authority, organised under the Oslo University Hospital Trust. The Cancer Registry is responsible for administering the program which includes planning, design and dissemination of information, dispatch invitations, IT solutions, collection and registration of data. The data collected by the screening program are used in program evaluation and research.

Legal regulations

The Cancer Registry is a health registry (*16*). The activities at the Cancer Registry 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) of December 21, 2001, No 1477: *Forskrift om innsamling og behandling av helseopplysninger i Kreftregisteret (Kreftregisterforskriften)* (*17*, *18*).

The Cancer Registry Regulations give the Cancer Registry legal basis to collect and process personal health data about individuals who participate in the screening program (*17*). The local health trusts and health care personnel have a statutory duty to report health data to the Cancer Registry (*16*, *17*). Screening is considered a health service and breast centres must therefore comply with current legislation such as that pertaining to medical record keeping (*19*, *20*).

Women with negative screening results have the right to request that personal data be erased from the Cancer Registry after the quality of the data has been assured (*16*, *17*). See page S22 for more details. Information about this right is explicitly stated in the invitation letter. Additional information about data processing, confidentiality, and privacy, including the right to opt out is available on the Cancer Registry's website.

Invitation and response routines

The Cancer Registry ensures that invitations, reminders, and response letters from the program are sent to women targeted by the program. The Registry also provides information about the program and the screening examination together with the invitation. Details can be found in the quality assurance manual (*21*).

The planning of invitations for each screening round is performed in close cooperation with each breast centre. Plans are made for each municipality to specify which women should be invited to each screening unit in regular intervals. These plans are updated regularly to ensure a sufficient number of examinations are being performed.

The breast centres provide the Cancer Registry with information about appointment availability for each screening unit five weeks in advance. A custom IT program, the "Invitation Program", automatically assigns all eligible women a specific time and place for screening. This program prioritises finding appointments for women who have least recently attended screening, and ensures that women from municipalities with long distances to screening units are not allocated to appointments that are, for example, early in the morning.

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. As of August 2017, about 40% of women receive their invitations digitally.

If a woman does not attend her appointment, she will receive a reminder five to six weeks after her missed appointment. She must then contact her breast centre to reschedule.

All participants are notified of their screening result by a letter. Letters with information about normal results (negative findings) are sent by the Cancer Registry, while notification letters about positive screening results are sent by the breast centres.

Women who do not wish to participate in the screening program, whether entirely or for a specified time, can contact the Cancer Registry or their breast centre to register an "invitation stop" (see page S22 for more details).

Data registration

Data from the screening program are collected and stored in a national screening database at the Cancer Registry. The Cancer Registry collects, registers, and ensures the quality of these data. A network connects all of the breast centres to the Cancer Registry, and all information related to screening activities is transferred electronically over this network, with the exception of reports from some pathology laboratories. This nationwide electronic solution ensures nearly 100% data completeness.

The Cancer Registry records data on an individual level, which makes it possible to follow each woman throughout an entire screening episode, including assessment and diagnosis. Data is also captured for women who are diagnosed outside the screening program. This makes data from the Norwegian Breast Cancer Screening Program unique, both nationally and internationally.

In 2010, the national clinical registry for breast cancer (previously referred to as the Norwegian breast cancer registry) was established as a part of the Cancer Registry. Since then, this registry has been used to collect information about all breast cancers, including ductal carcinoma *in situ*, before being mapped to the screening database. Before this, pathology reports were scanned and registered separately for the Cancer Registry database and the screening program 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.

Quality assurance of the program

A quality assurance manual published by the Cancer Registry provides a foundation for the program. The manual is based on European Guidelines (*5*, *22*). The first manual was published in 1996. Revisions were released in 1998 and 2003 (*21*). Selected chapters have since been revised and are available online (*23*–*25*). Both the Norwegian and European recommendations and quality assurance guidelines for breast cancer screening and diagnosis are currently undergoing comprehensive reviews.

According to the manual, the Cancer Registry is responsible for the quality assurance of screening activities and provides regular feedback to health personnel at the breast centres. Currently, this is primarily done through reports produced three to six times yearly presenting results for each breast centre. Additionally, each breast centre is equipped with a quality assurance software, "MedStat", to monitor their own performance. In cases where the Cancer Registry identifies a deviation from set targets in the manual, a notice is sent to the breast centre. Deviations that are not followed up are reported to the steering group.

In 2017, responsibility for technical quality assurance was transferred from the Norwegian Radiation Protection Authority to the Cancer Registry and the regional health authorities. The Cancer Registry now has a coordinating role for certain aspects of this quality assurance. For more details, see page S12.

Evaluation and research activities

The quality assurance manual specifies that the Cancer Registry should evaluate a number of parameters and conduct ongoing research about the screening program. Over 160 peer-reviewed articles have been published using data from the screening program. Most of these publications evaluate early performance measures such as false positive screening results, cancer detection rates, interval cancer, or stage distribution. The Cancer Registry has been the primary driving force behind this research.

Studies from the program presenting various models to estimate the cumulative risk of a false positive screening result, and models to estimate tumour growth have had considerable impact internationally. Further, the Norwegian program has made a substantial contribution to generating evidence that led to the transition from analogue (screen film) to full field digital mammography, and is now playing a leading role in evaluating digital breast tomosynthesis as a screening technique (*26*–*28*).

Current research initiatives focus on women's expectations and experiences of mammographic screening, risk factors that may lead to stratified screening, interval breast cancer, overdiagnosis, and overtreatment. Several studies with international collaborators are ongoing and there are currently four PhD students and one post doc working with data from the screening program. See page S57 for more details.

Representatives from the Cancer Registry have been active in European and international research networks since the inception of the program. The current leader of the screening program is active in several international breast screening networks. She is also an active member of the European guidelines development working group in the European Commission Initiative on Breast Cancer, which is in the process of updating their recommendations for breast cancer screening and diagnosis.

IT systems

The Cancer Registry is responsible for the management and development of software and database solutions for the screening program, and for ensuring that the IT systems satisfy the information security requirements as set out in the Personal Data Act. The program developed its own IT solutions between 1994 and 1996 to securely share personal information about women between the Cancer Registry, breast centres, and screening units. These solutions are also used to send invitations and response letters to women.

The IT department at the Cancer Registry manages the oversight and administration of users, networks, security, database backups, and more. IT administrators currently support roughly 120 users and 30 servers.

The IT systems currently used by the screening program were originally developed for the four-year pilot project, which covered four screening areas and roughly 160,000 women. These systems grew with the program, and by the end of 2016 they had been used to send 4.4 million invitations to nearly 1 million women.

The screening program's IT systems are based on distributed, replicated databases. Each breast centre has a database server. MedOutlook, a radiology information system (RIS) application, is used to connect to this database server. This server contains all data registered by the breast centre and its associated screening units (see Table 2.1 for an overview of breast centres and screening units). Every night these databases replicate to a main central database server at the Cancer Registry that contains all data for all centres in the program.

Information from the Cancer Registry's database is also distributed to the breast centre databases every night. This includes information about invitations, those who have requested that data related to their identity be erased after the quality of the data has been assured, user IDs in the system, and more. Information used for invitation planning is updated every month from the National Registry. The National Registry contains information about changes in names, addresses, immigration status, and deaths for past and present residents.

A DICOM work list server at the Cancer Registry provides work lists for the stationary screening units. This server synchronises continuously with the databases at the breast centre database servers and mirrors the booking lists in MedOutlook.

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 the same as the number generated for each invitation and makes it possible to link mammograms to the MedOutlook RIS information for interpretation (using MedBroker Sync).

Mobile units use a laptop with a desktop database to connect to the MedOutlook RIS. This information is sent to the breast centre via the Cancer Registry. The laptop is encrypted and uses a certificate, user name, and password to authenticate the connection to the Cancer Registry. A mobile broadband with a virtual private network (VPN) to the Cancer Registry is used to transfer data between the mobile units and breast centres. Further connection to the local database server at the breast centre from the Cancer Registry occurs in a closed environment. DICOM images are transferred to the breast centres using encrypted USB sticks.

Important components of the IT systems are:

- *Invitation program* – ensures regular invitations are sent to women across the country. Last major update was in 2005.
- *MedOutlook* – a modular radiology information system to register information about scheduled appointments, patient history, screening dates, interpretation and any consensus/arbitration results. Information is synchronised between the screening units, breast centres, and the Cancer Registry. Last major update was in 2004.

- *MedKod* - a program to register information about recall examinations and subsequent follow-up, and record which women have opted out of receiving invitations or have not consented to their negative screening data being stored at the Cancer Registry. Last major update was in 2015.
- *MedBroker* – a two-part integration solution used in screening. Used to transfer daily work lists to/from screening units (MedBroker Sync) and to synchronise workstations at the breast centres with the radiology information system (MedBroker Work List). This service is owned by Keymind, an external company, and user agreements are secured between Keymind and the local health trusts.
- *MedStat* – a data extraction and analysis program that serves as a foundation for quality assurance and program evaluation. Used by the breast centres and the Cancer Registry.
- *Teknisk kvalitetskontroll (TKK)* – a program for management of data from technical quality control procedures performed on analogue mammography equipment. Has been phased out due to the adoption of digital mammography. There is a need for a replacement.

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 analogue to digital mammography (2000-2011) are still in use today. Modernisation and updates to the screening program's IT systems are needed.

Information

The Cancer Registry is responsible for providing information to women targeted by the program, health professionals and other program stakeholders, and the general population. This is done using a number of channels.

The main purpose of information shared with women is to provide them with balanced, high quality information about mammographic screening to enable them to make an informed choice whether to participate. This information should also ensure that women have the practical information they need to make use of their screening invitation. The current information material was developed using the principle of levelled information. In this way, the most important information is presented to all in the invitation letter, while more in depth information can be obtained by visiting the Cancer Registry's website. A small portion of the Norwegian website has been translated to English. Additionally, fact sheets about the screening program are available online in Arabic and Urdu.

The screening program conveys information to women through personally addressed invitations and response letters. All letters are nationally standardised. 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 with a standardised information package when mammographic screening takes place.

Since 2014, a Facebook page, "Kreftsjekken", has been used to interact with women targeted by the Norwegian Breast Cancer Screening Program and the Cervical Cancer Screening Program. Kreftsjekken had 6500 followers during the fall of 2017. The breast screening program uses this page mainly to provide women with practical and community-specific information regarding mammography screening.

The Cancer Registry's website contains information on a variety of topics related to the screening program, such as the benefits and harms of mammographic screening, practical aspects related to participation, and the program's organisational structure, key results, and research activities. This makes the website central to all outreach activities. The website aims to educate women, health professionals, journalists, researchers and the general public about mammographic screening, the Norwegian Breast Cancer Screening Program and breast cancer. The screening program is actively working to increase information outreach through digital channels and applications.

Health professionals are an important target group for information outreach. The Cancer Registry aims to provide health professionals in the program with relevant, up to date information. A dedicated website, Mammonett, is used to share organisational and professional news to those working at the program. Employees at the screening program also take an active role in the professional education of radiographers and radiologists, and breast surgeons.

Information material developments

The screening program has provided women in the target group with nationally standardised information since the start of the pilot in 1995. The content of this information has evolved over time to reflect changes in knowledge about the program and awareness toward the potential benefits and harms of mammographic screening. Four different design themes have been used (Figures 2.2, 2.3, 2.4, and 2.5), and a fifth design update is in progress. The program logo has changed slightly during each design phase.

The first brochure from 1995 was eight pages with black and white photographs. This brochure provided information about why an invitation was being offered, why early stage diagnosis is important, what to expect at screening, how results would be shared, and the possibility of recall for further assessment.

The program's second brochure was released in 2003. Women were provided with more extensive information, which included the possibility of interval breast cancer, false positive screening results, the risk of being recalled due to breast implants, and what to do if concerned about hereditary breast cancer. More information about what to expect at screening was also added.

A third brochure was released in 2009. The information was further extended and it was made more explicit that participating in the screening program is voluntary. The leaflet provided additional information about the benefits and harms of screening, including some information on overdiagnosis/overtreatment together with additional information about the registration and use of personal data.

The fourth version was launched in 2017. A fact sheet accompanying the invitation letter replaced the brochure. This fact sheet presented the program and described what to expect during screening. An infographic was added to the fact sheet and emphasis was placed on making women aware that mammographic screening has potential benefits and harms to encourage women to make an active and informed choice whether to attend.

Figure 2.2: First information brochure produced by the Norwegian Breast Cancer Screening Program (c. 1995): "A mammography examination can save lives."

Figure 2.3: Updated information brochure from 2003: "Mammography can save lives."

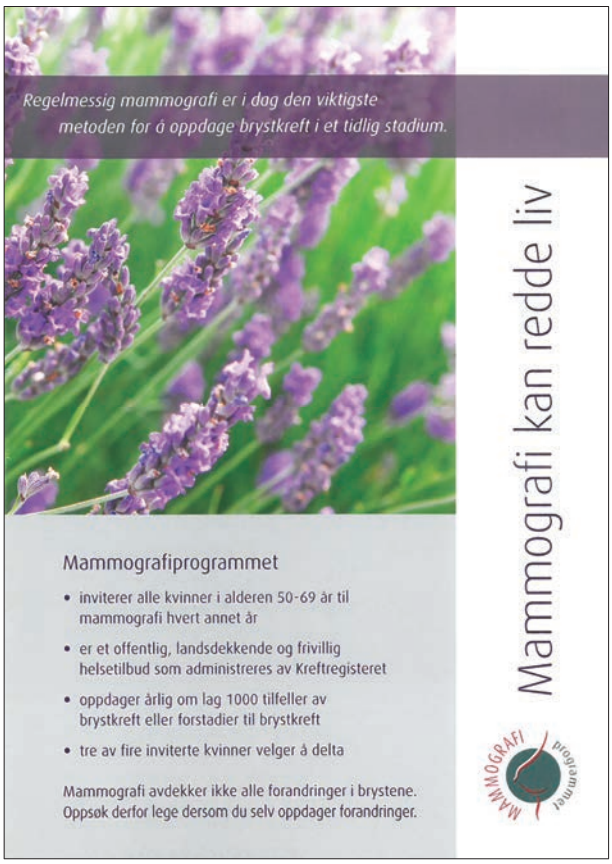


Figure 2.4: Information brochure from 2009: "Mammography can save lives."

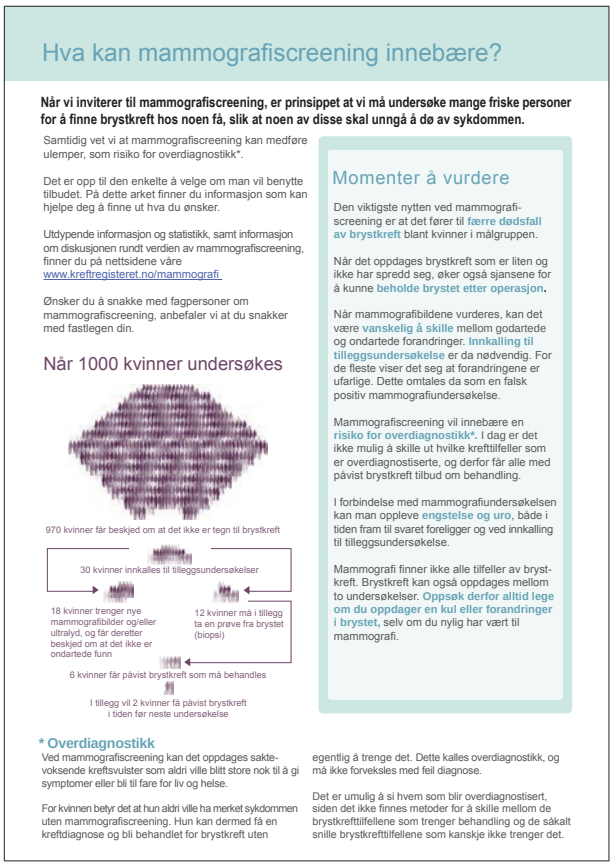


Figure 2.5: Information leaflet from 2017, "What can mammography involve?"

The regional health authorities and local health trusts

The regional health authorities are responsible for offering specialised health services. This includes facilitating mammographic screening examinations and any further assessment, including diagnostic examinations as well as treatment. For all practical purposes, the local health trusts are responsible for performing screening examinations and ensuring that adequate facilities and capacity, including personnel, are available for screening and assessment.

Breast centres and screening units

Currently, the four regional health authorities offer mammographic screening through 16 breast centres and associated screening units. These breast centres are responsible for the breast care of all women in their jurisdiction and are staffed by a professional multidisciplinary team that includes radiographers, radiologists, surgeons, nurses, pathologists, oncologists, and administrative personnel.

Women targeted by the Norwegian Breast Cancer Screening Program are currently invited to 26 stationary and 4 mobile screening units associated with the 16 breast centres (Table 2.1). Screening areas largely correspond to county borders, except for Vestre Viken, Akershus, Agder (Øst and Vest Agder), Trøndelag (Nord and Sør Trøndelag), and Troms og Finnmark. Women from some communities are invited to screening in a neighbouring county in the case that it substantially decreases their travel time.

The interpretation of screening mammograms and any further assessment takes place at the breast centres. All mammograms are independently read by two radiologists and a score between 1 and 5 is assigned to each breast. A score of 1 indicates negative for abnormality; 2, probably benign; 3, intermediate suspicion; 4, probably malignant; and 5, high suspicion of malignancy. If both radiologists give a score of 1, the screening examination is considered negative. If either radiologist gives a score of 2 or higher, a consensus or arbitration meeting is held to determine whether to recall a woman back for further assessment. Further assessment includes additional imaging (such as mammography, tomosynthesis and/or ultrasound) and potentially needle biopsy. Results from these assessments are discussed at a multidisciplinary meeting with radiologists, surgeons, and pathologists where a decision is made regarding further follow-up and treatment. Women diagnosed with breast cancer are followed-up and treated according to national guidelines (*29*).

Mobile screening

Three mobile screening units (Emma, Frøya, and James) were acquired between 1995 and 1996, and a fourth (Kaiia) was acquired in 1999, with funds from the Ministry of Health and Care Services. The local health trusts independently decide whether to offer screening at mobile units. The "department for electro-medical services" (*avdeling for mobile elektromedisinske tjenester*, Vestre Viken Health Trust) is responsible for these units.

The costs associated with staffing and running the mobile units are covered by the local health trusts' budgets. The "department for electro-medical services" is responsible for technical quality assurance and control activities, maintenance, and transportation of the mobile units between screening locations (*21*).

The results of early performance measures from mobile units compared to stationary units are presented on page S50.

Local quality assurance

The local health trusts must have authorisation for the medical use of x-ray apparatus in accordance with the Act on Radiation Protection and Use of Radiation (*30*). The breast centres and screening units are responsible for technical quality control and for quality assurance of their activities according to the manual (see page S8). The MedStat program facilitates some of these tasks.

The quality assurance manual specifies that health care personnel and other employees involved in the screening program must possess knowledge regarding the program's organisation and operations and must be familiar with the responsibilities of other health professionals (*21*).

The local health trusts are responsible for promoting multidisciplinary collaboration. Such cooperation is recommended in the quality assurance manual for delivering high quality breast care, as it lays the foundation for establishing, maintaining, and improving quality and expert knowledge of screening, diagnostics, and treatment (*21*).

Figure 2.6: Waiting room the Danmarksplass screening unit, Bergen (2017). Photo by Berit Hanestad, Hordaland breast centre

Figure 2.7: Mobile screening unit Emma with radiographers Kirsten L. Jensen (L) and Inger J. Melsbøe (R) in Hammerfest (2011). Photo by Sonja Stormo, UNN Tromsø breast centre

Table 2.1: Target population, breast centre, and screening units for past and present breast screening areas in the Norwegian Breast Cancer Screening Program

Screening area	Target population First round	Target population Latest round	Breast centre	Screening units
Rogaland	31,091	51,469	Stavanger universitetssjukehus	Gamle Stavanger sykehus Haugesund sykehus
Hordaland	38,437	56,104	Haukeland universitetssjukehus	Danmarksplass, Bergen Haukeland universitetssjukehus[1] Mobile screening unit
Oslo	46,338	65,169	Oslo universitetssykehus	Aker sykehus Galleri Oslo[1] Majorstuen[1]
Akershus[2]	44,655	-	Radiumhospitalet	Akershus Universitetssykehus[1] Galleri Oslo[1] Løkketangen, Sandvika[1] Lillestrøm sykehus[2] Mobile screening unit
Telemark	17,760	22,805	Sykehuset Telemark Porsgrunn	Sykehuset Telemark Porsgrunn Down Town kjøpesenter[1] Rjukan[1]
Agder	25,908	35,506	Sørlandet sykehus Kristiansand	Arendal sykehus Flekkefjord sykehus Kristiansand sykehus Røntgensenteret AS, Kristiansand[1] Mobile screening unit
Troms og Finnmark	22,101	32,592	UNN[3] Tromsø	UNN[3] Tromsø UNN[3] Narvik UNN[3] Harstad Mobile screening unit
Østfold	29,126	37,050	Sykehuset Østfold Kalnes Fredrikstad sykehus[1]	Sykehuset Østfold Kalnes Fredrikstad sykehus[1]
Nordland	25,334	27,774	Nordlandssykehuset Bodø	Nordlandssykehuset Bodø Mobile screening unit
Buskerud[4]	26,797	-	Drammen sykehus[4]	Drammen sykehus[4]
Trøndelag	41,455	52,866	St. Olavs Hospital	St. Olavs Hospital, Trondheim Levanger sykehus Namsos sykehus Kjøpmannsgata 17, Trondheim[1] Mobile screening unit
Oppland	21,218	26,520	Sykehuset Innlandet Lillehammer	Sykehuset Innlandet Lillehammer Mobile screening unit
Møre og Romsdal	25,221	32,091	Ålesund sjukehus	Ålesund sjukehus Molde sjukehus Mobile screening unit
Sogn og Fjordane	11,138	13,315	Førde Sentralsjukehus	Førde Sentralsjukehus
Vestfold	25,686	33,797	Sykehuset i Vestfold, Tønsberg	Sykehuset i Vestfold, Tønsberg
Hedmark	23,017	26,813	Sykehuset Innlandet Hamar	Sykehuset Innlandet Hamar Mobile screening unit
Akershus Øst[2]	39,703	48,678	Akershus universitetssykehus	Ski sykehus Lillestrøm sykehus Romerike Helsebygg[1]
Akershus Vest[2,4]	18,383	-	Radiumhospitalet	Sandvika storsenter[1]
Vestre Viken[4]	52,177	58,557	Drammen sykehus	Drammen sykehus Bærum sykehus Mobile screening unit

[1] No longer a screening location
[2] The Akershus breast screening region was split into Akershus Øst and Akershus Vest in August 2007
[3] Universitetssykehuset Nord-Norge
[4] Buskerud and Akershus Vest were merged to form a new screening area, Vestre Viken, in August 2011

Financial management

Until 2004, the financial management of the screening program was centralised at the Cancer Registry. When the regional health authorities were established in 2004 as part of a larger restructuring of the health care system, the management of finances changed to match this new organisational structure.

Since 2004, the regional health authorities have, through the the local health trusts, been responsible for financing screening activities, including follow-up assessment, diagnostics, and treatment performed within their jurisdiction. As of September 2017, women pay their local health trust a fee of NOK 245 for screening and any further assessment.

The Cancer Registry pays the wages of internal employees who work at the screening program. As of October 2017, there are nine full-time employees in the mammography section. Database management, and the development of software and database solutions for the program are integrated tasks in the IT department.

Leadership and advisory groups

Past leadership

Over the past 20 years, four individuals have been responsible for the daily operation of the screening program.

Steinar Østerbø Thoresen led the program until 2004, throughout the entire initiation and planning phase, as well as during the pilot and its later expansion to a nationwide program. He was also the leader for the Norwegian Cervical Cancer Screening program during this time, and head of the Department of screening-based research at the Cancer Registry until 2006.

Mette Kalager led the program from October 2004 to June 2006. Berit Damtjernhaug led the program from January 2007 to May 2013. Solveig Hofvind has been the leader of the program since June 2013.

Steering group

A multidisciplinary Steering Group was established in 2015. The mandate of this group is to provide high-level advice and recommendations to the Cancer Registry and the Directorate of Health. Members are appointed from the regional health authorities, the Norwegian Association of General Practitioners and the Norwegian Cancer Society. The Director of the Cancer Registry is a permanent member of the group. The person in charge of the screening program has an observer role. To ensure that the screening program maintains its high professional quality, the Steering Group reviews aspects related to data sources, early performance measures, diagnostic methods, information outreach, target groups, and ethics, among others. The Steering Group is responsible for ensuring that the screening program has a quality assurance manual. Finally, the Steering Group can recommend the initiation of an external evaluation of the program.

Advisory groups

An advisory group has guided the development of the screening program since its inception. This group provides advice to the secretariat of the program. The group's mandate and structure is currently under revision.

The Cancer Registry currently has informal working groups in the disciplines of radiology, pathology and medical physics that have provided guidance to the secretariat on subjects relevant to their professional development and the screening program.

Figure 2.8: Radiographers from around the country recently participated in "ambassador week", an initiative in preparation for a new mammography specialisation program in radiography (Oslo, August 2017). Photo by Gunhild Mangerud, Cancer Registry of Norway

3. Start-up and noteworthy developments

Following years of discussion about the merits of organised mammographic breast cancer screening in Norway, the Norwegian Breast Cancer Screening Program started as a pilot project in Rogaland in November 1995. Hordaland, Akershus, and Oslo joined the project during the first quarter of 1996. The pilot was initially intended to be a four year project, however, in 1998, after the first screening round, the government made a decision to offer mammographic screening for breast cancer nationwide. The screening program became nationwide in 2005 following a staggered implementation. This chapter describes the start-up of the program. It also presents important developments that have affected the program such as changes in legislation and organisation, as well as the transition to full field digital mammography.

Start-up of the national program

Discussions about screening, 1980-1992

A national discussion about organised mammographic screening for breast cancer started in the 1980s following the publication of results from Swedish randomised controlled trials that suggested mammographic screening reduced breast cancer mortality (*31*). These results were confirmed by other international trials and in 1985 the Directorate of Health established a working group to evaluate the potential benefits, harms, and costs of implementing mammographic screening in Norway (*32*–*35*).

No randomised controlled trials for mammographic screening were performed in Norway, but based on results from trials conducted in other countries, the working group published the Official Norwegian Report *NOU 1987:7 Mammografiscreening i Norge* ("Mammographic screening in Norway") (*36*). This report recommended biennial screening for women aged 50-74 and suggested that there may be some evidence to recommend annual screening for women aged 40-49.

In 1989, a multidisciplinary national consensus meeting was held to discuss organised screening in Norway. The outcome of this meeting was a recommendation against organised screening until the latest results on screening from the Swedish trials were published (*37*–*39*). Following the consensus meeting, the original NOU 1987:7 working group revised their report and an update was released in 1990. The updated recommendations were largely the same as those in the original report but instead recommended screening for women aged 50-69.

During this time, individual municipalities had also been discussing the merits of organised breast cancer screening. In 1986, the municipality of Oslo recommended screening for women aged 50-74 and the neighbouring municipality of Akershus recommended screening for women aged 40-70 in 1990. The municipality of Oslo updated their report in 1994 to recommend screening for women aged 50-69.

Although the debate about organised screening by now had been active for years, no concrete plans for an organised screening program had been put in place. However, it was estimated that approximately 220,000 mammograms were acquired in Norway in 1993, and about 70% of these were acquired outside of the public health system (*40*). At this time, many countries in Europe had either implemented or decided to implement an organised screening program (*41*). In the Nordic countries, organised screening was available to varying degrees in Sweden, Finland, Iceland, and Denmark (*41*).

In 1991, the Norwegian Cancer Society provided 5 million NOK to the Directorate of Health for the planning and initiation of publicly available mammographic screening. A year later the Ministry of Labour and Social Affairs (now the Ministry of Health and Care Services) asked the Directorate of Health to draw up a concrete plan for organised screening in one or more counties. This plan was delivered in the fall of 1992 and an appendix report was provided by the National Health Screening Service (now a part of the Norwegian Institute of Public Health).

Pilot project, 1993-1997

Despite the plans provided in 1992, the Ministry of Labour and Social Affairs required additional investigation related to organisational, technical, and financial resources associated with organised screening. A reference group was formed in 1993 to investigate and plan a pilot project for organised mammographic screening for breast cancer in Norway. The following year, the reference group delivered their report. Their plan was approved and approximately 25 million NOK was allocated from the state budget to implement a four-year pilot project.

The primary objective of the pilot project was to identify methods to implement screening that could reasonably be expected to reduce breast cancer mortality. The secondary objective was to assess the organisational, technical, and financial needs associated with breast cancer screening in the pilot counties and to determine the needs of a nationwide program (*42*).

The counties of Rogaland, Hordaland, and Akershus were initially selected for the pilot project. A short time later, Oslo was also included. The plan was to invite about 160,000 women, roughly 40% of women aged 50-69 in Norway, to two screening rounds during the pilot project (*42*, *43*). All four counties received national financing to support biennial mammographic screening, as recommended in the 1994 project plan. The first county, Rogaland, started screening in November 1995. Hordaland and Oslo started screening in January 1996, and Akershus started screening in February 1996. The first screening round in all four counties took place during 1996-1997.

Nationwide expansion, 1998-2005

In the spring of 1998, Parliament passed a motion to implement a nationwide program as soon as the necessary personnel were available. To this end, the 1998 state budget increased the funding allocated to mammographic screening by 20 million NOK to extend screening services to an additional four counties.

New counties joined the program through an application process to the Cancer Registry, which worked in close collaboration with the Ministry of Health and Care Services. The birth cohorts targeted for screening, planned organisation, competence and access to qualified professionals, treatment capacity, and investment needs (primarily in terms of medical equipment) were assessed as part of this process. Financing for equipment, renovations, mobile screening units, professional training, and operating expenses was obtained through grants from the Ministry of Health and Care Services. Expansion of the program continued gradually in this way until becoming nationwide in 2004/05.

Noteworthy developments

Organisational changes

Several institutions have been involved in the planning of invitations and letter dispatch throughout the program's history. From 1995 to 2001, the National Health Screening Service was responsible for invitation planning in collaboration with the breast centres, and for dispatching invitation and result letters. On January 1, 2002, *Statens Institutt for Folkehelse* and the National Health Screening Service joined to form the Norwegian Institute of Public Health. The Norwegian Institute of Public Health was then responsible for invitation planning and letter dispatch on behalf of the screening program.

After mid-2003, the Norwegian Institute of Public Health was responsible only for the dispatch of letters as the Cancer Registry took over the function of planning invitations. The Norwegian Institute of Public Health's official role in the screening program formally ended on January 1, 2016, when the screening program joined the national program for secure digital mail. Since then, letter dispatch has taken place under this agreement with other service providers.

The National Health Screening Service, and later the Norwegian Institute of Public Health, were responsible for the procurement and operation of the mobile screening units until 2004. This has since been the responsibility of the "department for electromedical services" (*avdeling for mobile elektromedisinske tjenester*, Vestre Viken Health Trust). More information on the mobile units can be found on page S12.

Multidisciplinary breast centres

The introduction of organised screening in Norway was strongly associated with optimised diagnostics, treatment and improved survival through multidisciplinary medical management and care (*44*). During the expansion period until the screening program became nationwide, 17 multidisciplinary breast centres were established across Norway, and the number of hospitals performing breast cancer surgery was reduced from over 50 to about 20. This development was closely tied to the implementation of the organised screening program.

Another driving force in this development was the publication of national recommendations for breast cancer diagnosis and treatment, which have been published regularly since 1981 (*29*, *45*). These guidelines, in combination with the specialised, multidisciplinary breast centres, have been critical in ensuring women, regardless of where they are live in Norway, in principle are offered the same diagnostics and treatment for breast cancer. This development has served as a model for other areas of cancer diagnosis and treatment in Norway.

Figure 3.1: Radiologists Stanimir Yanakiev (L) and Hanna Bjerke (R) at work, Oslo breast centre (2017). Photo by Gunhild Mangerud, Cancer Registry of Norway

Technical quality assurance

During the pilot project, and later in the national program until 2017, the Norwegian Radiation Protection Authority was responsible for technical quality assurance. As a result, the Radiation Protection Authority has been central in the development of quality assurance procedures in the screening program to ensure an optimal balance between image quality and exposure to ionising radiation. Also, in preparation for the pilot project, the Radiation Protection Authority developed two technical quality control manuals for the quality assurance of equipment used for patient exposure and film development in mammography. One of these manuals addressed comprehensive acceptance and status controls, while the other addressed frequently conducted quality control activities.

A survey group at the Radiation Protection Authority has been responsible for all acceptance and status control testing of the equipment used for screening or diagnostic mammography during most of the programs' history. Acceptance and status control activities were typically performed by medical physicists from this survey group following the installation of new equipment and then at annual intervals thereafter (Figure 3.2). When analogue images were in use, acceptance testing also included the evaluation of film developers.

The breast centres were initially responsible for frequent quality control activities on screening and diagnostic equipment. Each breast centre named a quality control radiographer who was in contact with the Radiation Protection Authority and who reported quality control results biennially. The Radiation Protection Authority was also actively involved in training radiographers in the screening program.

As changes in rules and regulations lead to the establishment of local medical physics departments, the Norwegian Radiation Protection Authority withdrew from its operative role in the screening program. On January 1, 2017, responsibility for technical quality assurance in the screening program was transferred to the regional health authorities with the Cancer Registry taking on a coordinating role.

Figure 3.2: Medical physicist Silje Flatabø performing technical quality controls (2011). Photo by Kirsti Bredholt, Norwegian Radiation Protection Agency

From informed consent to opt-out model

Legislation concerning health care services and the screening program has increased the focus on privacy and information security during the last 20 years. When the screening program started, it was based on a licence from the Norwegian Data Protection Inspectorate. This gave the Cancer Registry a legal basis to run the pilot provided that informed consent was obtained from participating women. This licence was extended in 1999 to cover the national screening program.

The Cancer Registry Regulations replaced this license in 2002 (*17*). These provisions give the Cancer Registry legal basis to collect and process personal health information about women who participate in the program.

In 2009, the Norwegian Data Inspectorate stated that consent from women participating in the screening program had not obtained in accordance with the requirements in the law. The Cancer Registry was required to obtain new consent that met the statutory requirements and was required to delete information collected on women who had not given valid consent. To meet the requirements from the Data Inspectorate, the screening program established new routines at the screening units for collecting written informed consent from attending women.

Further, the Cancer Registry and the local health trusts entered into separate data processing agreements in December 2011 to ensure that information on negative findings was recorded as required by law.

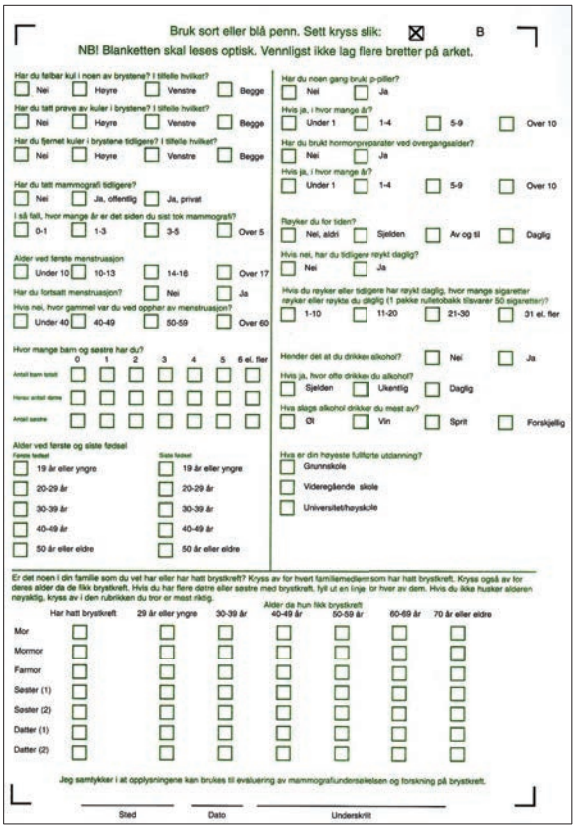
On January 1, 2014, a change was made in the Personal Health Data Filing System Act. The consent requirement was changed to a reservation right (*16*). This change meant that instead of giving their explicit informed consent, women with negative screening results were given the opportunity to request that personal data should be erased after the quality of the data has been assured. As of December 31, 2016 less than 2% of women in the target group have made such a request. See page S22 for more details.

Routine collection of epidemiologic data

Data about risk factors for breast cancer has been systematically collected during most of the screening program's existence. From 1995 to 2006, a one page questionnaire was sent alongside invitation letters (Figure 3.3). This form consisted of questions about past mammography use and risk factors for breast cancer such as alcohol use, family history of breast cancer, and hormone replacement therapy use. Women were asked to complete this questionnaire ahead of their first appointment and bring completed forms to their screening appointment. About 490,000 questionnaires were returned from over 420,000 women from 1996 to 2006.

In 2006, an extended questionnaire replaced the earlier one. The new questionnaire consisted of two forms: Form A pertained to sociodemographic factors, stable health indicators such as age at menarche, and health-related behaviours before age 50. This questionnaire was administered only once. Form B pertained to health indicators at the time of completion such as weight and height, and was included with each invitation to screening. Women were asked to bring completed questionnaires to their screening appointment. About 1.7 million questionnaires were returned from over 600,000 women from 2006 to 2015.

Information from these questionnaires is used for quality assurance activities and research projects.


Bruk sort eller blå penn. Sett kryss slik: ☒ B

NB! Blanketten skal leses optisk. Vennligst ikke lag flere bretter på arket.

Har du fått mammografi tidligere?
Nei | Ja, offentlig | Ja, privat

Har du tatt prøve av kuler i brystene? I tilfelle hvilket?
Nei | Høyre | Venstre | Begge

Har du fjernet kuler i brystene tidligere? I tilfelle hvilket?
Nei | Høyre | Venstre | Begge

I så fall, hvor mange år er det siden du sist tok mammografi?
0-1 | 1-3 | 3-5 | Over 5

Alder ved første menstruasjon
Under 10 | 10-13 | 14-16 | Over 17

Har du fortsatt menstruasjon?
Nei | Ja

Hvis nei, hvor gammel var du ved opphør av menstruasjon?
Under 40 | 40-49 | 50-59 | Over 60

Hvor mange barn og søstre har du?
0 | 1 | 2 | 3 | 4 | 5 | 6 el. flere

Alder ved første og siste fødsel
19 år eller yngre | 20-29 år | 30-39 år | 40-49 år | 50 år eller eldre

Har du noen gang brukt p-piller?
Nei | Ja

Hvis ja, i hvor mange år?
Under 1 | 1-4 | 5-9 | Over 10

Har du brukt hormonpreparater ved overgangsalder?
Nei | Ja

Hvis ja, i hvor mange år?
Under 1 | 1-4 | 5-9 | Over 10

Røyker du for tiden?
Nei, aldri | Sjelden | Av og til | Daglig

Hvis nei, har du tidligere røykt daglig?
Nei | Ja

Hvis du røyker eller tidligere har røykt daglig, hvor mange sigaretter røyker eller røykte du daglig (1 pakke rulletobakk tilsvarer 50 sigaretter)?
1-10 | 11-20 | 21-30 | 31 el. flere

Hender det at du drikker alkohol?
Nei | Ja

Hvis ja, hvor ofte drikker du alkohol?
Sjelden | Ukentlig | Daglig

Hvis slags alkohol drikker du mest av?
Øl | Vin | Sprit | Forskjellig

Hva er din høyeste fullførte utdanning?
Grunnskole
Videregående skole
Universitet/høyskole

Er det noen i din familie som du vet har eller har hatt brystkreft? Kryss av for hvert familiemedlem som har hatt brystkreft. Kryss også av for deres alder da de fikk brystkreft. Hvis du har flere døtre eller søstre med brystkreft, fyll ut en linje for hver av dem. Hvis du ikke husker alderen nøyaktig, kryss av i den rubrikken du tror er mest riktig.

	Har hatt brystkreft	Alder da hun fikk brystkreft: 29 år eller yngre	30-39 år	40-49 år	50-59 år	60-69 år	70 år eller eldre
Mor							
Mormor							
Farmor							
Søster (1)							
Søster (2)							
Datter (1)							
Datter (2)							

Jeg samtykker i at opplysningene kan brukes til evaluering av mammografiundersøkelsen og forskning på brystkreft.

Sted | Dato | Underskrift

Figure 3.3: Breast cancer risk factor questionnaire used at the screening program from 1995 to 2006

Transition to digital mammography

The arrival of full-field digital mammography systems (digital mammography) on the market coincided with the gradual implementation of organised screening in Norway. This sparked a debate over whether counties joining the screening program should invest in screen-film mammography (analogue mammography), or the newer digital systems. At the time, there were no established procedures for technical quality control or functionality evaluation for digital mammography.

When a GE Senographe 2000D full-field digital mammography machine was installed at Galleri Oslo in 1999, not only was it the first full-field digital mammography unit in Norway, but also the first intended for screening. By the time a second machine was installed at Ullevål University Hospital about four months later, a project plan had been developed to compare full-field digital mammography to analogue mammography in screening. This project would become known as the Oslo I study (*26*, *46*). Later on, the Oslo II study was conducted (*27*, *47*). When Oslo I started in early 2000, 12 counties had yet to join the screening program. Four years later in 2004, Vestfold was the last county to join the screening program, the second to offer full-field digital mammography, and the first to screen exclusively with full-field digital mammography (*48*). Table 3.1 summarises when digital mammography was implemented at each screening unit in the program. More information on the Oslo I and II studies can be found on page S57.

The implementation of digital mammography presented a broad range of challenges, from purely technical, to knowledge-based and procedural. In addition to the requirements for equipment training and the time needed to gain interpretative experience with digital images, there was a need to develop a new framework for storing, transferring, retrieving and presenting studies and images. Furthermore, workplace routines needed to be adapted to suit and take advantage of this new technology. Some of these topics were addressed early on by two working groups, which published their opinions on challenges and solutions in two reports (*49*, *50*).

In 2009, a protocol for routine quality control, developed in close cooperation with radiographers, was published (*24*, *51*). A year later a national protocol for acceptance and status control testing was published, based both on European guidelines and acquired experience in quality control of digital mammography systems (*23*). The transition from analogue to full-field digital mammography in the screening program was completed when Møre og Romsdal implemented full-field digital mammography in the fall of 2011.

Figure 3.4: Radiographer Sonja Stormo hanging analogue mammograms, UNN Tromsø breast centre (2003). Photo by Kristin Pedersen, UNN

Figure 3.5: Radiologist Jan Ole Frantzen reading digital mammograms, UNN Tromsø breast centre (2003). Photo by Kristin Pedersen, UNN

Table 3.1: Installation of full-field digital mammography equipment at stationary and mobile screening units by screening area

Screening area	Stationary screening units	FFDM start
Rogaland	Gamle Stavangersykehus	01.2007
	Haugesund sykehus	05.2007
Hordaland	Danmarksplass, Bergen	09.2014
	Haukeland universitetssjukehus[1]	08.2007
Oslo	Aker sykehus	08.2013
	Galleri Oslo[1,2]	01.2000-01.2005
	Majorstuen[1]	-
Akershus[3]	Akershus Universitetssykehus	-
	Galleri Oslo[1,2]	01.2000-01.2005
	Løkketangen, Sandvika	-
	Lillestrøm sykehus	08.2007
Telemark	Sykehuset Telemark Porsgrunn	08.2008
	Downtown kjøpesenter[1]	-
	Rjukan[1]	-
Agder	Arendal sykehus	08.2010
	Flekkefjord sykehus	02.2011
	Kristiansand sykehus	09.2010
	Røntgensenteret AS, Kristiansand	-
Troms og Finnmark	UNN[4]Tromsø	09.2004
	UNN[4]Narvik	01.2011
	UNN[4]Harstad	02.2013
Østfold	Sykehuset Østfold Kalnes	-
	Fredrikstad sykehus[1]	08.2008
Nordland	Nordlandssykehuset Bodø	09.2009
Buskerud[5]	Drammen sykehus[5]	04.2009
Trøndelag	St. Olavs Hospital, Trondheim	11.2008
	Levanger sykehus	09.2009
	Namsos sykehus	09.2009
	Kjøpmannsgata 17, Trondheim[1]	-
Oppland	Sykehuset Innlandet Lillehammer	01.2010
Møre og Romsdal	Ålesund sjukehus	08.2011
	Molde sjukehus	08.2011
Sogn og Fjordane	Førde Sentralsjukehus	08.2006
Vestfold	Sykehuset i Vestfold, Tønsberg	02.2004
Hedmark	Sykehuset Innland Hamar	10.2009
Akershus Øst[3]	Ski sykehus	01.2009
	Lillestrøm sykehus	08.2007
	Romerike Helsebygg[1]	08.2012
Akershus Vest[3,5]	Sandvika storsenter[1]	-
Vestre Viken[5]	Drammen sykehus[5]	04.2009
	Bærum sykehus	08.2011
	Mobile screening units	FFDM start
	Emma	08.2008
	Frøya	04.2010
	James	04.2008
	Kaiia	05.2009

[1] No longer a screening locaion

[2] The Oslo I and II trials were performed from 2000-2001 (see page S57 for more information). Women were randomly allocated to screening with digital mammography between 2002 and 2005.

[3] The Akershus breast screening region was split into Akershus Øst and Akershus Vest in August 2007

[4] Universitetssykehuset Nord-Norge

[5] Buskerud and Akershus Vest were merged to form a new screening area, Vestre Viken, in August 2011

4. Early performance measures, 1996-2016

This chapter presents the results of early performance measures for the Norwegian Breast Cancer Screening Program. The following early performance measures are reported: attendance, recall, and cancer detection rates, positive predictive values, histopathologic tumour characteristics, and surgery rates. A number of these are considered to be important for program surveillance in order to reduce future breast cancer mortality.

Data considerations

Data used for this report were extracted from the Cancer Registry during June 2017. Results are presented for all of Norway and for each screening area. Although all analyses were population-based, some screening areas serve rural populations and some results are therefore based on small cell counts. This can also be the case in years when individual screening areas joined the screening program or were merged with other areas (Table 4.1). The number of women invited to screening and diagnosed with breast cancer in each screening area can give an idea of the magnitude of this issue (see Tables 4.4, 4.8 and 4.11).

Results pertaining to invitations, attendance, recalls, and screen-detected breast cancers are presented for the period 1996-2016. Results pertaining to interval breast cancers are presented for women screened between 1996-2014 and diagnosed between 1996-2016, as a two-year period is required to diagnose all interval breast cancers following a screening examination. Information about needle biopsies with malignant outcomes is presented for 1996-2016, while information about benign outcomes is presented for 1996-2015. While figures may present data on a yearly basis, tables present this data using the following categories: 1996-2000, 2001-2005, 2006-2010, 2011-2015, and 2016.

The transition from screen-film to digital mammography took place between 2000 and 2011. Table 3.1 outlines when each screening unit began screening with digital mammography.

The screening program targets women aged 50-69. However, women aged 48-71 are invited due to the staggered implementation of the screening program (Table 4.1). Age at diagnosis can range from 48-73 years because women are followed for interval breast cancer for two years after their last screening examination.

Since the screening program rolled out nationwide, the majority of prevalently screened women have been 50-51 years old and the subsequently screened women have been 52 years or older. Age-stratified results are presented based on either age at invitation, screening, or diagnosis.

Lastly, the screening program's databases are continuously updated and corrected. Results presented in this report may therefore deviate slightly from those in previous publications.

Table 4.1: The Norwegian Breast Cancer Screening Program was implemented gradually on a per-county basis between 1995 and 2005. Different birth cohorts are screened in different years depending on the screening area. Women are generally sent invitations to attend ten screening rounds between the ages of 50 and 69

Screening area	Screening start		Screening round										
			1	2	3	4	5	6	7	8	9	10	11
Rogaland	11.1995	Screening years	1996-1997	1998-1999	2000-2001	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017
		Birth cohorts	1927-1946	1927-1948	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966
Hordaland	01.1996	Screening years	1996-1997	1998-1999	2000-2001	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017
		Birth cohorts	1927-1946	1927-1948	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966
Oslo	01.1996	Screening years	1996-1997	1998-1999	2000-2001	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017
		Birth cohorts	1927-1946	1927-1948	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966
Akershus[1]	02.1996	Screening years	1996-1997	1998-1999	2000-2001	2002-2003	2004-2005						
		Birth cohorts	1927-1946	1927-1948	1931-1950	1933-1952	1935-1954						
Telemark	09.1999	Screening years	1999-2001	2001-2003	2003-2005	2005-2007	2007-2009	2009-2011	2011-2013	2013-2015	2015-2017		
		Birth cohorts	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966		
Agder	11.1999	Screening years	1999-2001	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017		
		Birth cohorts	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966		
Troms og Finnmark	05.2000	Screening years	2000-2002	2002-2004	2004-2006	2006-2008	2008-2010	2010-2012	2012-2014	2014-2016	2016-2018		
		Birth cohorts	1931-1950	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966		
Østfold	04.2001	Screening years	2001-2003	2003-2005	2005-2007	2007-2009	2009-2011	2011-2013	2013-2015	2015-2017			
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966			
Nordland	05.2001	Screening years	2001-2003	2003-2005	2005-2007	2007-2009	2009-2011	2011-2013	2013-2015	2015-2017			
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966			
Buskerud[2]	09.2001	Screening years	2001-2003	2003-2005	2005-2007	2007-2009	2009-2011						
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960						
Trøndelag	09.2001	Screening years	2001-2003	2003-2005	2005-2007	2007-2009	2009-2011	2011-2013	2013-2015	2015-2017			
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966			
Oppland	01.2002	Screening years	2002-2003	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017			
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1967			
Møre og Romsdal	04.2002	Screening years	2002-2004	2004-2006	2006-2008	2008-2010	2010-2012	2012-2014	2014-2016	2016-2018			
		Birth cohorts	1933-1952	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966			
Sogn og Fjordane	01.2003	Screening years	2003-2004	2005-2006	2007-2008	2009-2010	2011-2012	2013-2014	2015-2016				
		Birth cohorts	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966				
Hedmark	08.2003	Screening years	2003-2005	2005-2007	2007-2009	2009-2011	2011-2013	2013-2015	2015-2017				
		Birth cohorts	1935-1954	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966				
Vestfold	02.2004	Screening years	2004-2005	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017				
		Birth cohorts	1935-1954	1937-1957	1939-1959	1941-1961	1943-1963	1945-1965	1947-1967				
Akershus Øst[1]	01.2006	Screening years	2006-2007	2008-2009	2010-2011	2012-2013	2014-2015	2016-2017					
		Birth cohorts	1937-1956	1939-1958	1941-1960	1943-1962	1945-1964	1947-1966					
Akershus Vest[1]	01.2006	Screening years	2006-2007	2008-2009	2010-2011								
		Birth cohorts	1937-1956	1939-1958	1941-1960/61								
Vestre Viken[2]	08.2011	Screening years	2011	2012-2013	2014-2015	2016-2017							
		Birth cohorts	1941-1961	1943-1962	1945-1964	1947-1966							

[1] The Akershus breast screening region split into Akershus Øst and Akershus Vest in 2006

[2] Buskerud and Akershus Vest were merged to form a new screening area, Vestre Viken, in August 2011

The right to withdraw from data storage

Women with a negative screening result have the right to request that data relating to their identity be erased from the screening database after the quality of the data has been assured. As of December 31, 2016, roughly 15,385 women had made such a request. These women represent approximately 1.6% of all invited women and 1.9% of all participating women (Table 4.2). Information about these women is excluded from this report.

The right to opt out from being invited

Women invited to the screening program may opt out of receiving future invitations. As of December 31, 2016, roughly 3.8% of women invited to the program had opted out (Table 4.2). Although it is voluntary to cite a reason for requesting an invitation stop, over 40% of women cited a diagnosis of breast cancer as the reason for their request. These women are typically followed up with mammography outside of the screening program. It is also expected that some women opt out of receiving invitations to the screening program because they attend screening at private clinics, or because they consider the potential harms associated with mammographic screening to outweigh the benefits.

In Hordaland, only 1.1% of invited women had opted out. This is likely associated with the fact that Hordaland has unique follow-up procedures for women diagnosed with breast cancer.

Møre og Romsdal has the highest proportion of invited women who had opted out, 7.3%. It is also well known that women residing in Kristiansund and surrounding areas have an attendance rate below 30% among those invited. This may be due to a higher rate of opportunistic screening at private centres in this area.

Table 4.2: Approximate number (n) and proportion (%) of women who have ever requested that data about their negative screening examinations should be erased or who have opted out from receiving future invitations, as of December 31, 2016

Screening area	Invited	Attended	Requested negative data be erased			Opted out from the program	
			n	% of invited	% of attended	n	% of invited
Rogaland	84,740	73,865	1355	1.6 %	1.8 %	2845	3.4 %
Hordaland	95,590	83,395	2155	2.3 %	2.6 %	1035	1.1 %
Oslo	123,330	87,710	2720	2.2 %	3.1 %	7110	5.8 %
Akershus	73,615	46,760	1850	2.5 %	4.0 %	3030	4.1 %
Telemark	36,540	31,165	515	1.4 %	1.7 %	920	2.5 %
Agder	54,005	47,180	790	1.5 %	1.7 %	1565	2.9 %
Troms og Finnmark	48,725	41,590	965	2.0 %	2.3 %	1670	3.4 %
Østfold	54,945	45,525	535	1.0 %	1.2 %	2780	5.1 %
Nordland	43,055	39,690	545	1.3 %	1.4 %	1445	3.4 %
Buskerud	41,500	27,030	640	1.5 %	2.4 %	1955	4.7 %
Trøndelag	79,085	69,035	945	1.2 %	1.4 %	2175	2.8 %
Oppland	38,255	32,050	500	1.3 %	1.6 %	1285	3.4 %
Møre og Romsdal	45,725	37,000	630	1.4 %	1.7 %	3370	7.4 %
Sogn og Fjordane	18,900	17,245	195	1.0 %	1.1 %	375	2.0 %
Vestfold	41,955	36,175	395	0.9 %	1.1 %	1885	4.5 %
Hedmark	37,160	31,375	465	1.3 %	1.5 %	1430	3.8 %
Akershus Øst	24,765	34,070	85	0.3 %	0.2 %	710	2.9 %
Akershus Vest	5605	5465	55	1.0 %	1.0 %	280	5.0 %
Vestre Viken	17,095	28,525	40	0.2 %	0.1 %	405	2.4 %
Total	964,590	814,850	15,380	1.6 %	1.9 %	36,270	3.8 %

Screening intervals

The program's screening interval is two years. That is, appointments are scheduled every 2 years ± 6 months (730 days ± 180 days). Practically, individual screening intervals are determined based on the date of a woman's last screening examination. From 1996 to 2016, the average (mean) time between two screening invitations was 741 days (median 731 days, Table 4.3).

Women who do not respond to their ordinary invitation are sent a reminder. Women who attend screening as a result of the reminder are invited to screening two years following the date of their screening examination. This increases the average screening interval for those women and the program. Those who do not attend following the reminder are sent a new invitation two years after the original appointment date.

The use of mobile screening units can also affect screening intervals. These units are stationed for up to 16 weeks. Opportunities for attending a mobile unit in response to a reminder are dependent on the length of a mobile unit's stay at a given site. Once a mobile unit has moved, women must attend their local stationary unit for screening.

Table 4.3: Mean and median number of calendar days between invitations and screening examinations

Time between	Mean	Median	Interquartile range
Dispatch of two ordinary invitations	741	731	720-746
Two consecutive screening examinations following ordinary invitations	730	730	719-742
Two consecutive screening examinations following an ordinary invitation and a reminder	806	785	769-801
Two screening examinations regardless of attendance pattern	785	733	720-748

Invitations and attendance

From the initiation of the screening program in 1996 through to the end of 2016, over 4.4 million personal invitations were sent to 947,933 women across the country. Approximately 3.3 million screening examinations were taken during this time and, on average, three out of four women (76%) attended the program.

The number of invitations sent to women increased almost every year, from 61,577 in 1996, to 299,040 in 2016 (Figure 4.1). During this time, the yearly number of women attending screening increased from 49,526 to 223,266. Increases between 1996 and 2004 largely reflect the expansion of the screening program, while increases between 2005 and 2016 reflect the growing number of women in the target group.

After becoming a nationwide program in 2005, the attendance rate declined from a high of 77% in 2006 to a low of 73% in 2012. However, it has been stable at 75% in the years since. Over the past 20 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 helping the screening program achieve the desired attendance rate of at least 75% (Figure 4.2).

On average, women of all ages attend screening at a rate that exceeds the target level of 70%. Women receiving a prevalent invitation (primarily younger women) and women aged under 55 receiving a subsequent invitation have the lowest attendance (73%). Women between the ages of 60-64 have the highest attendance rate on average (78%) (Figure 4.3).

Rogaland, Hordaland, Nordland, and Sogn og Fjordane have the highest attendance rates (≥80%, Table 4.5). To access the screening program, some women in Rogaland and Sogn og Fjordane must travel to Stavanger/Haugesund and Førde, respectively. Women in Sogn og Fjordane may have to travel as many as three hours to reach the screening unit. This is in stark contrast to Oslo which frequently has the lowest attendance rates, dating back to the inception of the program (64% overall with a high of 71% in 1996 and lows of 60% in 2003, 2007, and 2012). Since 2013, screening in Oslo has taken place at Aker sykehus, which is relatively close to the city centre and accessible by public transport. It is thought that attendance may be low in Oslo because a higher proportion of women may obtain screening through private clinics. Moreover, a higher percentage of immigrant women live in Oslo than elsewhere. Attendance rates have been shown to be lower among immigrants than non-immigrants (*52*). Mammographic screening taking place outside the screening program is difficult to accurately quantify (*13*, *53*), however such information would be of great interest for estimating the program's effectiveness.

Women who have opted out from receiving invitations to screening have not been included in these analysis. Attendance figures presented here are therefore slightly inflated. Moreover, these results do not include women who have requested that their data related to normal mammography findings not be saved by the screening program. These women collectively make up a small proportion of women targeted for screening (see page S22 for more details).

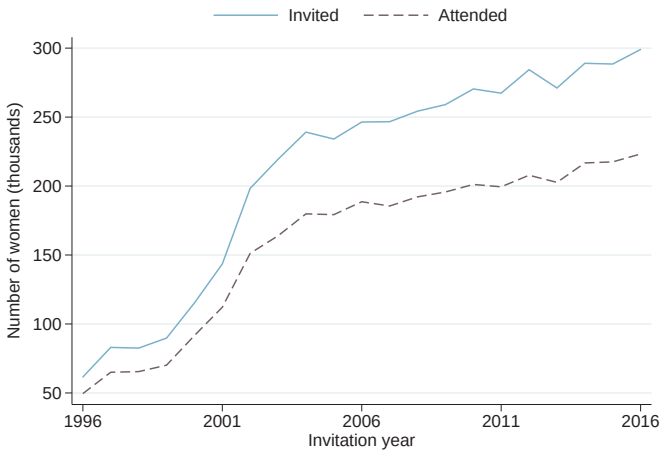


Figure 4.1: Yearly number of women invited to and attending the screening program by invitation year, 1996-2016

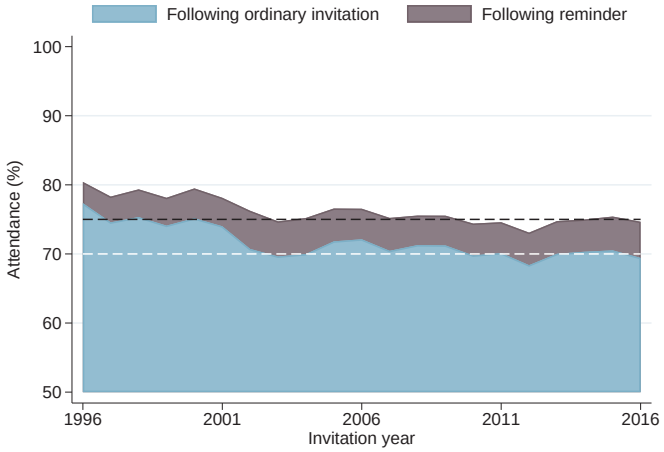


Figure 4.2: Attendance rate (%) following an ordinary invitation and a reminder by invitation year, 1996-2016

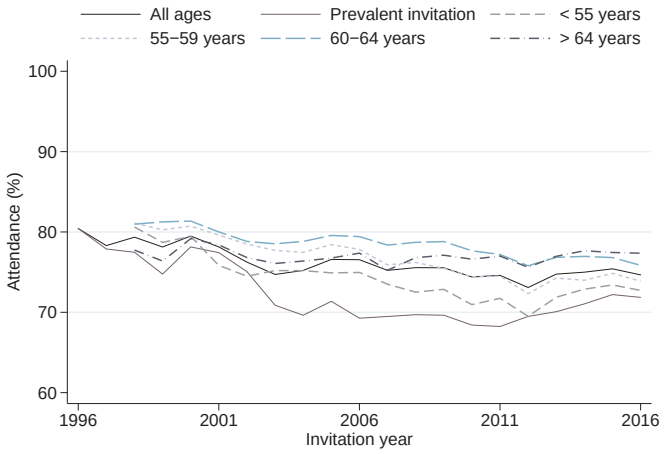


Figure 4.3: Attendance rate (%) among women invited to screening by age group and year of invitation dispatch, 1996-2016

Table 4.4: Number of invitations dispatched by screening area and invitation year, 1996-2016

Screening area	Invitation year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	78,779	88,271	102,351	114,079	25,033	408,513
Hordaland	95,558	106,048	118,427	128,899	27,308	476,240
Oslo	115,092	110,100	122,992	139,589	29,925	517,698
Akershus	108,727	127,819	53,119			289,665
Telemark	12,958	45,782	51,069	54,105	11,230	175,144
Agder	14,168	65,306	74,415	80,420	18,207	252,516
Troms og Finnmark	6853	55,637	61,178	75,634	14,943	214,245
Østfold		66,639	76,073	84,575	17,858	245,145
Nordland		58,158	65,919	64,887	12,976	201,940
Buskerud		60,241	76,892			137,133
Trøndelag		93,577	114,138	123,315	26,766	357,796
Oppland		42,126	55,501	58,353	13,158	169,138
Møre og Romsdal		43,761	65,055	70,832	14,947	194,595
Sogn og Fjordane		17,241	28,929	31,516	6507	84,193
Vestfold		25,793	66,148	71,439	15,677	179,057
Hedmark		28,020	58,814	63,038	12,599	162,471
Akershus Øst			58,416	109,084	23,342	190,842
Akershus Vest			27,411			27,411
Vestre Viken				130,553	28,564	159,117
Total	432,135	1,034,519	1,276,847	1,400,318	299,040	4,442,859

Table 4.5: Attendance rate (%) at the screening program by screening area and invitation year, 1996-2016

Screening area	Invitation year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	88 %	86 %	83 %	80 %	79 %	84 %
Hordaland	85 %	83 %	80 %	77 %	74 %	81 %
Oslo	68 %	63 %	62 %	62 %	66 %	64 %
Akershus	79 %	74 %	71 %			75 %
Telemark	81 %	79 %	75 %	73 %	74 %	76 %
Agder	81 %	80 %	79 %	78 %	77 %	79 %
Troms og Finnmark	83 %	82 %	80 %	77 %	77 %	79 %
Østfold		72 %	74 %	74 %	73 %	74 %
Nordland		81 %	81 %	80 %	80 %	81 %
Buskerud		75 %	77 %			76 %
Trøndelag		78 %	78 %	76 %	78 %	78 %
Oppland		69 %	74 %	75 %	75 %	73 %
Møre og Romsdal		72 %	72 %	72 %	74 %	72 %
Sogn og Fjordane		82 %	84 %	81 %	78 %	82 %
Vestfold		73 %	76 %	73 %	74 %	74 %
Hedmark		64 %	69 %	72 %	75 %	70 %
Akershus Øst			72 %	74 %	73 %	73 %
Akershus Vest			72 %			72 %
Vestre Viken				74 %	75 %	74 %
Total	79 %	76 %	75 %	75 %	75 %	76 %

Recall for further assessment

Women can be recalled for further assessment due to abnormal mammographic findings, clinical symptoms, or technically inadequate images (unsatisfactory image quality). The recall rate decreased over 40% during the study period, from a high of 6.1% in 1996 to 3.6% in 2016 (Figure 4.4). Between 1996 and 2016 over 96% of all screening examinations were interpreted as negative. Women with a negative screening result receive a letter telling them that there were no signs of abnormal findings on their screening mammogram.

On average 3.2% of all screening examinations resulted in a recall due to abnormal mammographic findings (Table 4.6). Recall due to clinical symptoms and unsatisfactory image quality were each associated with 0.3% of all screening examinations. Women who are recalled due to clinical symptoms or technically inadequate images have a lower risk of breast cancer than those who were recalled due to abnormal mammographic findings (see page S34 for more details). Although the switch from screen film mammography to digital mammography had limited or no effect on recall rates due to abnormal mammographic findings, a decrease in the proportion of technical recalls has been observed (*54*). The majority of this decrease is likely attributable to under-reporting since radiographers can preview the digital mammograms at the time of acquisition and decide to retake images without saving or reporting unsatisfactory images.

Recall rates due to abnormal mammographic findings were over twice as high for prevalently versus subsequently screened women (an average of 5.5% versus 2.6% respectively from 1996-2016; Figure 4.5 and Table 4.7). Prevalently screened women typically have a higher recall rate than subsequently screened women because of the unavailability of prior mammograms against which to make a comparison, and because mammographic density is higher in this group of younger women. Recall rates for prevalently screened women were consistently above 6% after 2005. There was little variation in recall rates due to abnormal findings among subsequent screening examinations when stratified by age.

Recall rates varied by county. The lowest recall rate was observed in Troms og Finnmark (2.5%), which also reported the lowest overall rate due to abnormal mammography findings (2.0%) (Figure 4.6).

False positive screening results are screening examinations leading to a recall for assessment that turns out to be negative. False positive screening results are widely considered a harm of mammographic screening and are associated with anxiety while waiting for diagnostic results. Studies have shown that this is temporary and typically diminishes to normal levels after three months (*55*–*57*). For women who participate in ten screening rounds between ages 50-69, the cumulative risk of a false positive screening results leading to additional imaging such as diagnostic mammography or ultrasound is roughly 15%, while the cumulative risk of a false positive screening result leading to an invasive procedure is 4% (*58*).

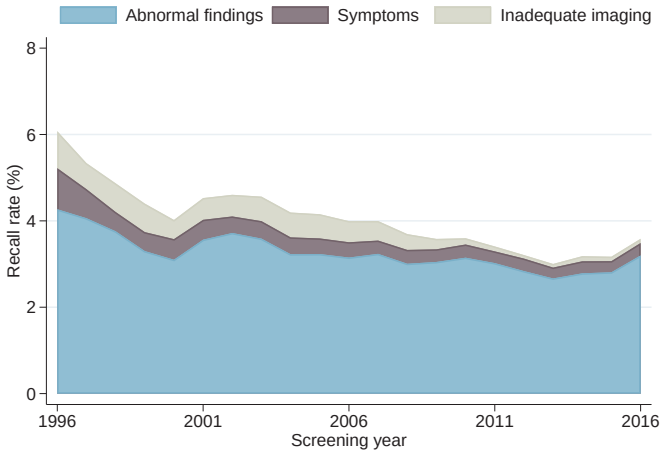


Figure 4.4: Recall rates (%) due to abnormal mammographic findings, symptoms or technical reasons (inadequate imaging), 1996-2016

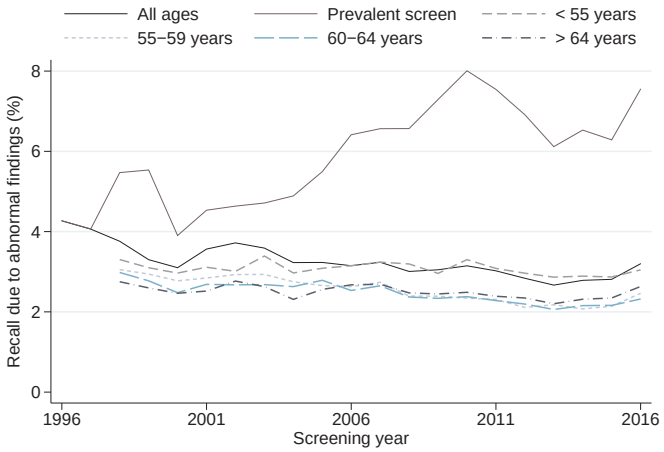


Figure 4.5: Recall rate (%) due to abnormal mammographic findings by age groups, 1996-2016

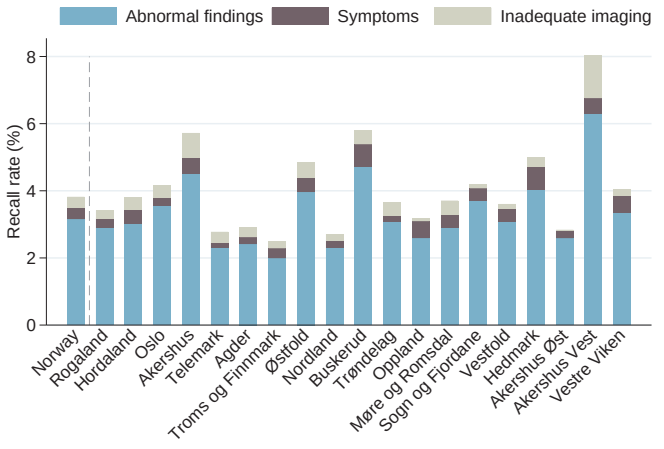


Figure 4.6: Recall rate (%) due to abnormal mammographic findings, clinical symptoms, and inadequate imaging by screening area, 1996-2016

Table 4.6: Number (n) and percent (%) of recall examinations due to abnormal mammographic findings by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)
Rogaland	2697	4.0 %	1965	2.6 %	2369	2.8 %	2367	2.6 %	446	2.3 %	9844	2.9 %
Hordaland	2627	3.3 %	2037	2.3 %	2593	2.7 %	3441	3.4 %	810	4.2 %	11,508	3.0 %
Oslo	2407	3.2 %	2311	3.3 %	3303	4.3 %	2906	3.4 %	765	3.9 %	11,692	3.6 %
Akershus	3396	4.1 %	4462	4.7 %	1897	5.0 %					9755	4.5 %
Telemark	358	3.7 %	1114	3.1 %	842	2.2 %	629	1.6 %	125	1.5 %	3068	2.3 %
Agder	351	3.3 %	1400	2.7 %	1237	2.1 %	1452	2.3 %	326	2.4 %	4766	2.4 %
Troms og Finnmark	121	2.5 %	1231	2.7 %	836	1.7 %	894	1.5 %	278	2.5 %	3360	2.0 %
Østfold			2759	5.9 %	1817	3.2 %	2233	3.6 %	295	2.3 %	7104	4.0 %
Nordland			852	1.9 %	1503	2.8 %	1114	2.1 %	256	2.4 %	3725	2.3 %
Buskerud			2565	5.8 %	2330	3.9 %					4895	4.7 %
Trøndelag			2332	3.3 %	2745	3.1 %	2861	3.0 %	560	2.7 %	8498	3.1 %
Oppland			824	2.9 %	996	2.4 %	1103	2.5 %	247	2.6 %	3170	2.6 %
Møre og Romsdal			839	2.8 %	1182	2.5 %	1651	3.2 %	364	3.3 %	4036	2.9 %
Sogn og Fjordane			469	3.5 %	662	2.7 %	1112	4.4 %	275	5.5 %	2518	3.7 %
Vestfold			741	4.1 %	1393	2.8 %	1568	3.0 %	350	3.1 %	4052	3.1 %
Hedmark			864	5.0 %	1751	4.3 %	1551	3.4 %	396	4.1 %	4562	4.0 %
Akershus Øst					1353	3.2 %	1616	2.0 %	585	3.5 %	3554	2.6 %
Akershus Vest					1247	6.3 %					1247	6.3 %
Vestre Viken							2942	3.0 %	948	4.5 %	3890	3.3 %
Total	11,957	3.6 %	26,765	3.4 %	30,056	3.1 %	29,440	2.8 %	7026	3.2 %	105,244	3.2 %

Table 4.7: Percent (%) of recall examinations due to abnormal mammographic findings at prevalent and subsequent screening examinations by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub
Rogaland	5.3 %	2.9 %	5.1 %	2.2 %	5.6 %	2.4 %	6.4 %	2.1 %	4.9 %	1.9 %	5.5 %	2.3 %
Hordaland	4.5 %	2.3 %	4.4 %	2.0 %	6.4 %	2.3 %	7.0 %	3.0 %	8.0 %	3.6 %	5.2 %	2.5 %
Oslo	3.7 %	2.7 %	4.5 %	3.1 %	7.5 %	3.9 %	6.9 %	2.8 %	9.9 %	2.9 %	5.1 %	3.2 %
Akershus	4.8 %	3.3 %	9.0 %	4.2 %	9.7 %	4.4 %					6.0 %	4.0 %
Telemark	3.7 %	<0.1 %	4.9 %	2.5 %	4.8 %	1.9 %	3.5 %	1.4 %	2.3 %	1.5 %	4.2 %	1.8 %
Agder	3.3 %	1.9 %	4.2 %	2.1 %	5.4 %	1.7 %	5.5 %	1.9 %	4.5 %	2.1 %	4.4 %	1.9 %
Troms og Finnmark	2.5 %	8.3 %	3.8 %	2.1 %	3.7 %	1.5 %	2.9 %	1.3 %	5.4 %	2.1 %	3.5 %	1.6 %
Østfold			8.3 %	3.6 %	6.2 %	2.8 %	8.1 %	3.0 %	5.1 %	1.8 %	7.8 %	3.0 %
Nordland			2.4 %	1.3 %	7.5 %	2.2 %	5.6 %	1.7 %	6.1 %	2.0 %	3.9 %	1.9 %
Buskerud			6.9 %	4.7 %	11.4 %	3.0 %					8.0 %	3.5 %
Trøndelag			4.0 %	2.5 %	8.0 %	2.4 %	7.3 %	2.5 %	6.7 %	2.2 %	5.4 %	2.5 %
Oppland			3.3 %	2.5 %	4.3 %	2.2 %	5.6 %	2.1 %	6.3 %	1.9 %	4.1 %	2.2 %
Møre og Romsdal			3.2 %	2.2 %	5.5 %	2.1 %	8.0 %	2.6 %	7.3 %	2.9 %	4.6 %	2.4 %
Sogn og Fjordane			4.2 %	1.7 %	7.8 %	2.1 %	12.6 %	3.4 %	17.1 %	4.3 %	6.7 %	2.8 %
Vestfold			4.1 %	5.3 %	6.4 %	2.2 %	7.3 %	2.5 %	8.5 %	2.4 %	5.3 %	2.4 %
Hedmark			5.2 %	4.1 %	8.6 %	3.7 %	7.4 %	3.0 %	10.8 %	3.4 %	6.5 %	3.4 %
Akershus Øst					8.1 %	2.6 %	6.1 %	1.4 %	8.5 %	2.6 %	7.0 %	1.9 %
Akershus Vest					11.4 %	5.3 %					11.4 %	5.3 %
Vestre Viken							7.9 %	2.5 %	10.8 %	3.5 %	8.5 %	2.6 %
Total	4.4 %	2.8 %	4.8 %	2.8 %	7.0 %	2.6 %	6.7 %	2.3 %	7.6 %	2.6 %	5.5 %	2.6 %

Breast cancer detection

Screen-detected breast cancer was defined as a ductal carcinoma *in situ* (DCIS) or an invasive breast cancer diagnosed as a result of a recall assessment diagnosed within 182 days (6 months) following a screening examination.

Interval breast cancer was defined as breast cancer diagnosed after a negative screening result or more than 6 months after a false-positive screening result and within 2.5 years after screening.

Over 18,600 screen-detected breast cancers were diagnosed among women attending the screening program between 1996 and 2016 (Table 4.8), of which approximately 3200 (17%) were DCIS. Roughly 5100 interval breast cancers were diagnosed between 1996 and 2014 (Table 4.11).

Screen-detected breast cancer

Between 1996 and 2016, 5.6 screen-detected breast cancers were detected per 1000 screening examinations (Table 4.8). The rates were relatively stable within each age group, and increased with increasing age among subsequently screened women (Figure 4.7).

Detection rates varied by screening area. In 2016 the rate was highest in Vestfold (6.9/1000 screening examinations) and lowest in Troms and Finnmark (4.1/1000 screening examinations, Table 4.8). The highest rate of screen-detected cancer was observed in Oslo between 2011-2015 (8.4/1000 screening examinations, Table 4.8). This period includes both the Oslo Tomosynthesis Trial and the Oslo, Vestfold, and Vestre Viken study. Both studies used digital breast tomosynthesis which can increase the rate of screen-detected breast cancer (*59*, *60*). For more information about these studies see page S57.

Detection rates were higher for prevalent (6.4/1000) than subsequent screening examinations (5.3/1000, Tables 4.9 and 4.10). Among prevalently screened women, the highest detection rate (9.4/1000 screening examinations) was observed in Vestfold in 2016, while the lowest rate was observed in Telemark (1.1/1000 screening examinations) during the same year. The numbers of prevalent screen-detected cancers were small and these results should be interpreted with caution. There was less variation in detection rates among subsequently screened women.

The majority of screen-detected cancers are detected following a recall examination due to abnormal findings. On average, only 1.7% of screen-detected breast cancers were diagnosed following clinical symptoms at time of screening mammography, while 0.3% were diagnosed following a recall examination due to technically inadequate images (Figure 4.8).

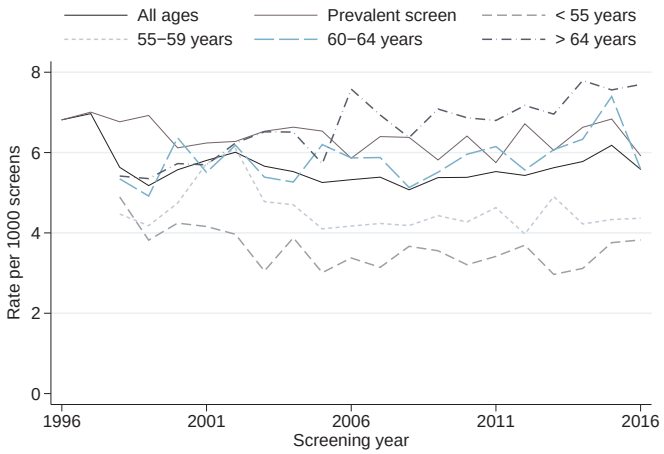


Figure 4.7: Rate of screen-detected breast cancer per 1000 screening examinations (‰), 1996-2016

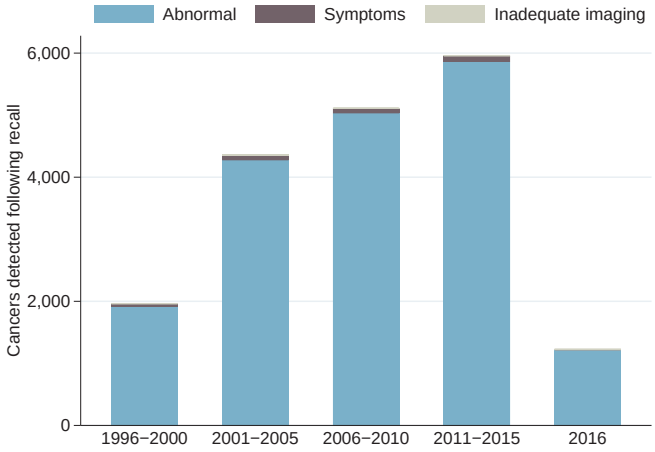


Figure 4.8: Number of screen-detected breast cancers based on reason for recall, 1996-2016

"The rate of screen-detected breast cancers was stable between 5 and 6 per 1000 screening examinations between 1996 and 2016"

Table 4.8: Number (n) and rate per 1000 screening examinations (‰) of screen-detected breast cancers by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)
Rogaland	478	7.0	444	5.9	476	5.6	554	6.0	112	5.7	2064	6.1
Hordaland	445	5.6	450	5.1	536	5.7	597	6.0	116	6.0	2144	5.6
Oslo	457	6.0	456	6.5	475	6.2	725	8.4	100	5.1	2213	6.7
Akershus	438	5.2	557	5.9	237	6.2					1232	5.7
Telemark	64	6.6	204	5.6	163	4.2	202	5.1	46	5.6	679	5.1
Agder	56	5.3	248	4.8	254	4.4	333	5.3	78	5.8	969	4.9
Troms og Finnmark	27	5.5	211	4.7	180	3.7	294	5.0	46	4.1	758	4.5
Østfold			242	5.2	310	5.5	346	5.5	73	5.6	971	5.4
Nordland			214	4.7	266	4.9	255	4.9	53	5.1	788	4.9
Buskerud			336	7.6	328	5.5					664	6.4
Trøndelag			365	5.1	492	5.5	558	5.9	109	5.3	1524	5.5
Oppland			156	5.5	206	5.1	252	5.7	46	4.8	660	5.4
Møre og Romsdal			150	5.0	229	4.9	280	5.5	65	5.9	724	5.2
Sogn og Fjordane			70	5.2	108	4.4	104	4.1	27	5.4	309	4.5
Vestfold			142	7.9	304	6.1	312	5.9	78	6.9	836	6.3
Hedmark			123	7.1	220	5.4	235	5.2	57	5.9	635	5.6
Akershus Øst					206	4.9	312	3.9	96	5.7	614	4.4
Akershus Vest					130	6.6					130	6.6
Vestre Viken							602	6.2	124	5.9	726	6.2
Total	1965	5.9	4368	5.6	5120	5.3	5961	5.7	1226	5.6	18,640	5.6

Table 4.9: Number (n) and rate per 1000 prevalent screening examinations (‰) of screen-detected breast cancers by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)
Rogaland	264	8.4	79	7.2	83	6.8	114	9.1	12	3.9	552	7.9
Hordaland	277	7.1	74	5.8	88	7.1	85	6.3	21	6.9	545	6.7
Oslo	254	6.5	75	6.5	101	7.9	138	8.9	24	6.1	592	7.1
Akershus	261	6.0	87	6.1	44	7.9					392	6.2
Telemark	64	6.6	67	7.1	10	2.0	29	5.5	1	1.1	171	5.6
Agder	56	5.3	84	5.0	33	4.3	47	5.3	9	4.5	229	5.0
Troms og Finnmark	27	5.5	109	5.9	38	5.8	36	4.6	7	4.9	217	5.5
Østfold			146	5.8	60	7.1	58	6.6	17	7.9	281	6.3
Nordland			142	5.8	52	7.0	43	6.1	5	3.7	242	6.0
Buskerud			226	9.2	58	6.6					284	8.5
Trøndelag			248	6.3	64	5.2	73	5.7	16	5.4	401	5.9
Oppland			100	5.9	30	5.0	48	7.8	10	5.4	188	6.1
Møre og Romsdal			109	5.5	34	4.6	46	6.3	9	5.6	198	5.5
Sogn og Fjordane			55	5.6	16	4.6	11	3.4	2	3.6	84	4.9
Vestfold			138	7.8	66	6.8	38	5.5	15	9.4	257	7.2
Hedmark			106	7.3	38	4.8	40	5.9	7	5.5	191	6.3
Akershus Øst					40	6.2	57	4.6	19	6.4	116	5.3
Akershus Vest					33	8.3					33	8.3
Vestre Viken							90	6.7	30	8.3	120	7.0
Total	1203	6.8	1845	6.4	888	6.2	953	6.4	204	5.9	5093	6.4

Figure 4.9: Radiographer Nina Vårdal in action in Røros, Trøndelag (2015).
Photo by Signe Blix, Trøndelag breast centre

Table 4.10: Number (n) and rate per 1000 subsequent screening examinations (‰) of screen-detected breast cancers by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)
Rogaland	214	5.9	365	5.7	393	5.4	440	5.5	100	6.1	1512	5.6
Hordaland	168	4.2	376	4.9	448	5.5	512	5.9	95	5.8	1599	5.3
Oslo	203	5.5	381	6.5	374	5.9	587	8.3	76	4.8	1621	6.6
Akershus	177	4.4	470	5.9	193	5.9					840	5.5
Telemark	0	0	137	5.1	153	4.6	173	5.1	45	6.2	508	5.0
Agder	0	0	164	4.7	221	4.4	286	5.3	69	6.0	740	4.9
Troms og Finnmark	0	0	102	3.8	142	3.4	258	5.1	39	4.0	541	4.2
Østfold			96	4.4	250	5.2	288	5.4	56	5.1	690	5.1
Nordland			72	3.4	214	4.6	212	4.7	48	5.3	546	4.5
Buskerud			110	5.6	270	5.3					380	5.4
Trøndelag			117	3.7	428	5.5	485	6.0	93	5.3	1123	5.4
Oppland			56	5.0	176	5.1	204	5.4	36	4.7	472	5.2
Møre og Romsdal			41	3.9	195	4.9	234	5.4	56	5.9	526	5.1
Sogn og Fjordane			15	4.1	92	4.4	93	4.2	25	5.6	225	4.4
Vestfold			4	8.7	238	5.9	274	6.0	63	6.5	579	6.0
Hedmark			17	6.0	182	5.5	195	5.1	50	6.0	444	5.4
Akershus Øst					166	4.6	255	3.8	77	5.5	498	4.3
Akershus Vest					97	6.1					97	6.1
Vestre Viken							512	6.2	94	5.5	606	6.0
Total	762	5.0	2523	5.1	4232	5.2	5008	5.6	1022	5.5	13,547	5.3

Interval breast cancer

On average, 1.8 interval breast cancers were diagnosed per 1000 screening examinations (Table 4.11). Detection rates have been relatively stable since the inception of the screening program. Unlike screen-detected cancers, interval breast cancer detection rates were similar across all age groups (Figure 4.10).

Interval breast cancer detection rates varied across screening areas (Table 4.11). However, this variation must be interpreted with caution because the number of cases diagnosed each year in individual screening areas is very small. The highest rate of interval breast cancer was observed in Oslo (2.3/1000 screening examinations). This might be due to the availability and use of private clinics in the time between two screening examinations.

The majority of interval breast cancers (roughly 70%) were detected more than a year following screening (Figure 4.11). This distribution has been relatively stable since the inception of the program (*61*, *62*).

Interval breast cancers accounted for nearly a quarter (24%) of all breast cancers detected in the screening program from 1996 to 2014 (Table 4.12). The lowest proportion of interval breast cancers was observed in Hedmark (20%), while the highest was observed in Akershus Øst (34%).

Interval breast cancer detection rates are important in the evaluation of organised screening programs because a high rate results in low program sensitivity. Regular reviews of screening and diagnostic mammograms from women diagnosed with interval breast cancer is one way to improve radiologist sensitivity and to reduce the rate and their overall proportion. Informed, consensus-based retrospective reviews from Norway have demonstrated that 20-25% of interval breast cancers showed abnormalities on the screening mammograms prior to the diagnosis (*63*, *64*). In these reviews both screening and diagnostic images, and histopathological results were available. An informed review strategy makes it easier for radiologists to detect abnormalities on the screening mammograms. This result therefore does not represent clinical practice, but rather offers an opportunity for learning. Blinded reviews, where only screening mammograms are available and cancer cases are mixed with normal screening mammograms, have demonstrated a lower rate of missed cases (*63*). Regardless of the review method used, the rate of missed interval breast cancers represented only a small proportion of all breast cancers detected among women attending screening. The review of interval breast cancer cases plays an important role in the education and professional development of breast radiologists and such reviews may help to minimise the overall rate of interval breast cancers.

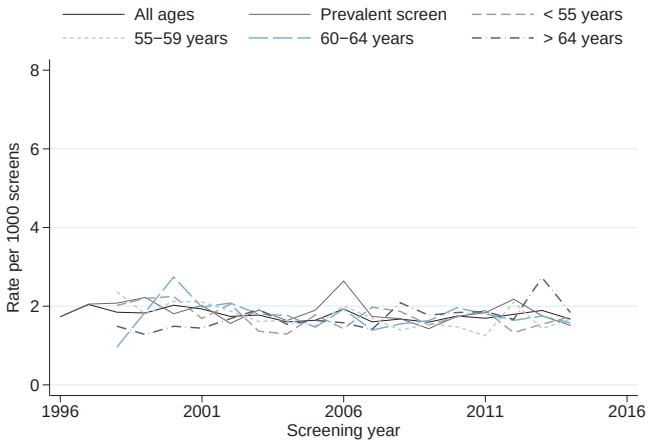


Figure 4.10: Interval breast cancer detection rate per 1000 screening examinations (‰), 1996-2014

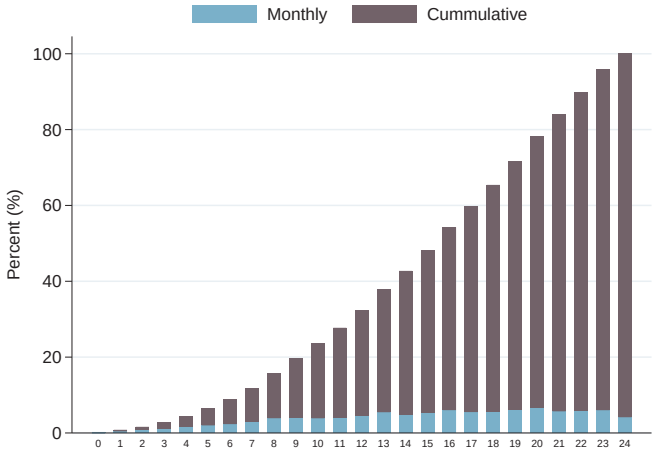


Figure 4.11: Distribution of interval breast cancer from time of screening examination, 1996-2014

"Interval breast cancers constituted 24% of the breast cancers diagnosed among women screened in the Norwegian Breast Cancer Screening Program between 1996 and 2014"

Table 4.11: Number (n) and rate per 1000 screening examinations (‰) of interval breast cancers by screening area and year, 1996-2014

Screening area	Screening year 1996-2000		2001-2005		2006-2010		2011-2014		Total	
	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)	(n)	(‰)
Rogaland	93	1.4	132	1.8	158	1.9	142	2.0	525	1.7
Hordaland	136	1.7	127	1.4	137	1.5	122	1.6	522	1.5
Oslo	181	2.4	173	2.5	157	2.1	147	2.2	658	2.3
Akershus	175	2.1	159	1.7	65	1.7			399	1.8
Telemark	22	2.3	59	1.6	66	1.7	46	1.5	193	1.7
Agder	20	1.9	98	1.9	114	2.0	95	1.9	327	1.9
Troms og Finnmark	7	1.4	77	1.7	61	1.3	92	2.0	237	1.6
Østfold			64	1.4	88	1.6	69	1.4	221	1.4
Nordland			86	1.9	89	1.7	64	1.5	239	1.7
Buskerud			68	1.5	117	2.0			185	1.8
Trøndelag			110	1.5	132	1.5	102	1.4	344	1.5
Oppland			36	1.3	67	1.6	59	1.7	162	1.6
Møre og Romsdal			61	2.0	92	2.0	82	2.0	235	2.0
Sogn og Fjordane			15	1.1	31	1.3	32	1.6	78	1.3
Vestfold			41	2.3	96	1.9	76	1.8	213	1.9
Hedmark			30	1.7	59	1.4	45	1.3	134	1.4
Akershus Øst					78	1.8	149	2.4	227	2.1
Akershus Vest					42	2.1			42	2.1
Vestre Viken							130	1.7	130	1.7
Total	634	1.9	1336	1.7	1649	1.7	1452	1.8	5071	1.8

Table 4.12: Proportion of interval breast cancers among all breast cancers detected in the screening program by screening area and year, 1996-2014

Screening area	Screening year 1996-2000	2001-2005	2006-2010	2011-2014	Total
Rogaland	16 %	23 %	25 %	25 %	22 %
Hordaland	23 %	22 %	20 %	20 %	22 %
Oslo	28 %	28 %	25 %	22 %	26 %
Akershus	29 %	22 %	22 %		25 %
Telemark	26 %	22 %	29 %	23 %	25 %
Agder	26 %	28 %	31 %	28 %	29 %
Troms og Finnmark	21 %	27 %	25 %	30 %	27 %
Østfold		21 %	22 %	20 %	21 %
Nordland		29 %	25 %	24 %	26 %
Buskerud		17 %	26 %		22 %
Trøndelag		23 %	21 %	18 %	21 %
Oppland		19 %	25 %	23 %	23 %
Møre og Romsdal		29 %	29 %	28 %	29 %
Sogn og Fjordane		18 %	22 %	27 %	23 %
Vestfold		22 %	24 %	24 %	24 %
Hedmark		20 %	21 %	20 %	20 %
Akershus Øst			28 %	38 %	34 %
Akershus Vest			24 %		24 %
Vestre Viken				22 %	22 %
Total	24 %	23 %	24 %	24 %	24 %

Positive predictive values

The positive predictive value (PPV) of a test is the probability that a positive screening result indicates the presence of breast cancer (65). PPV is important in mammographic screening because it is directly related to false positive mammographic findings: a high PPV indicates a low rate of false positive screening results and vice versa.

In mammographic screening, PPV-1 refers to the percentage of breast cancers detected among women recalled due to abnormal mammographic findings. A high PPV-1 indicates that many women recalled for further assessment have breast cancer. PPV-2 refers to the percentage of breast cancers detected among recalled women who had an invasive procedure (needle biopsy). A high PPV-2 indicates that many women who undergo an invasive procedure have breast cancer.

PPV-1

Since the inception of the screening program, 18% of women recalled due to abnormal mammographic findings were diagnosed with breast cancer (PPV-1 = 18%, Table 4.13). PPV-1 increased from 15% in 1996 to 17% in 2016 (Figure 4.12). There was substantial variation in PPV-1, both over time and between screening areas. In Troms og Finnmark, PPV-1 varied from 33% during 2011-2015 to 16% in 2016. While across the screening areas, PPV-1 ranged from 10% in Akershus Vest to 22% in Troms og Finnmark for all years combined (Table 4.13).

PPV-1 was lower for prevalent screening examinations (11%) than for subsequent screening examinations (22%) (Table 4.14). Among subsequent screening examinations, PPV-1 increased with age from 13% for women younger than 55 to 29% for women older than 64 (Figure 4.13).

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 lowered the PPV-1 to 15% overall. This is because the overwhelming majority of women diagnosed with screen-detected breast cancer had abnormal findings on their screening mammogram (Figure 4.8). The overall PPV-1 among women recalled due to clinical symptoms was 2.8%, and for women with technically inadequate images 0.5%. It should be noted that in the past 20 years of organised screening, 315 women had symptoms of breast cancer that were mammographically occult. Moreover, 51 women with screen-detected breast cancer were diagnosed following a recall examination due to technically inadequate screening images. Most of these women were diagnosed during the transition period from analogue to digital mammography.

PPV-2

Results for PPV-2 are presented until 2015, as the coding for invasive procedures that took place in 2016 was not complete at the time of data extraction for this report.

Between 1996 and 2015, 44% of screened women who underwent an invasive procedure were diagnosed with breast cancer (PPV-2 = 43%). PPV-2 also varied over time and between screening areas. PPV-2 increased from 32.3% in 1996 to 48.1% in 2015 (Figure 4.12). The overall highest PPV-2 during the past 20 years was observed in Oppland (58%) and the lowest in Akershus Vest (25%) (Table 4.16). The highest PPV-2 during 2011-2015 was observed in Telemark (68%), while the lowest was observed in Akershus Øst (32%).

Like PPV-1, PPV-2 was lowest for prevalently screened women (29%) and increased with age for subsequently screened women, from 40% for women younger than 55, to 62% for women older than 64 (Table 4.17 and Figure 4.13).

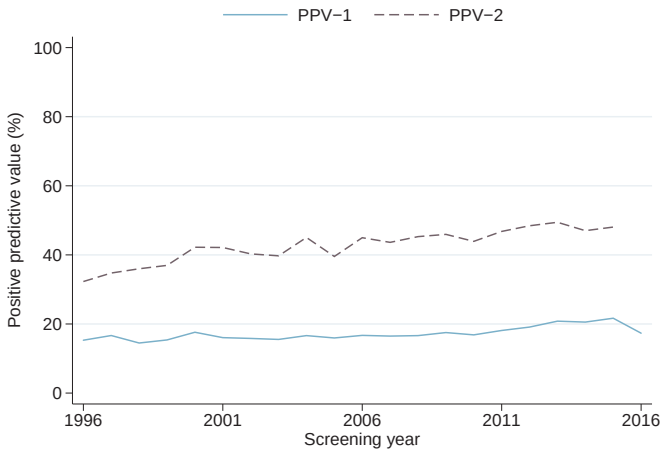


Figure 4.12: Proportion of breast cancer cases diagnosed as a result of a recall due to abnormal mammographic findings (PPV-1; 1996-2016) and as a result of an invasive procedure (PPV-2; 1996-2015)

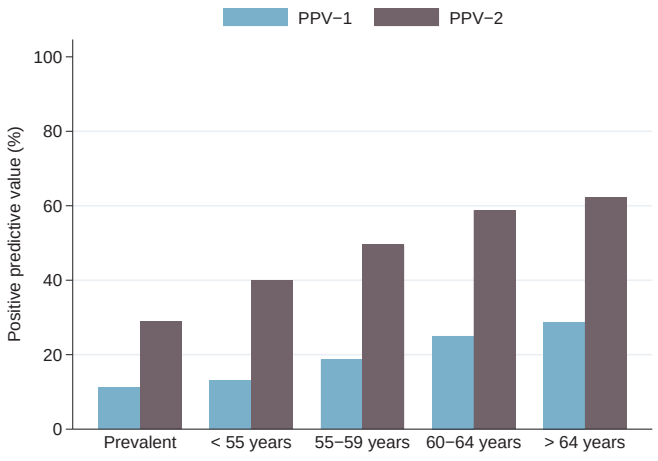


Figure 4.13: Proportion of breast cancer cases diagnosed as a result of a recall due to abnormal mammographic findings (PPV-1; 1996-2016) and as a result of an invasive procedure (PPV-2; 1996-2015), by age group

Table 4.13: Proportion of breast cancers among women recalled due to abnormal mammographic findings (PPV-1) by screening area and year, 1996-2016

Screening area	Screening year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	18 %	22 %	20 %	23 %	25 %	21 %
Hordaland	16 %	21 %	21 %	17 %	14 %	19 %
Oslo	18 %	20 %	14 %	25 %	13 %	19 %
Akershus	13 %	12 %	12 %			12 %
Telemark	18 %	18 %	19 %	32 %	38 %	22 %
Agder	15 %	18 %	20 %	23 %	24 %	20 %
Troms og Finnmark	21 %	17 %	21 %	33 %	16 %	22 %
Østfold		8 %	17 %	16 %	25 %	13 %
Nordland		24 %	18 %	23 %	21 %	21 %
Buskerud		13 %	14 %			13 %
Trøndelag		15 %	18 %	19 %	19 %	18 %
Oppland		19 %	20 %	22 %	19 %	21 %
Møre og Romsdal		18 %	19 %	17 %	18 %	18 %
Sogn og Fjordane		15 %	16 %	9 %	10 %	12 %
Vestfold		19 %	21 %	19 %	22 %	20 %
Hedmark		14 %	12 %	15 %	14 %	14 %
Akershus Øst			15 %	19 %	16 %	17 %
Akershus Vest			10 %			10 %
Vestre Viken				20 %	13 %	18 %
Total	16 %	16 %	17 %	20 %	17 %	18 %

Table 4.14: Proportion of breast cancer cases among women recalled due to abnormal mammographic findings (PPV-1) for prevalent and subsequent screening by screening area and year, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub
Rogaland	15 %	21 %	14 %	26 %	12 %	23 %	14 %	29 %	8 %	34 %	14 %	25 %
Hordaland	15 %	19 %	13 %	25 %	11 %	25 %	9 %	21 %	8 %	17 %	12 %	22 %
Oslo	17 %	22 %	12 %	22 %	10 %	16 %	13 %	32 %	7 %	19 %	13 %	23 %
Akershus	12 %	14 %	7 %	15 %	8 %	14 %					10 %	14 %
Telemark	18 %		14 %	21 %	4 %	24 %	14 %	39 %	5 %	45 %	13 %	28 %
Agder	15 %		12 %	23 %	7 %	26 %	10 %	30 %	11 %	29 %	11 %	27 %
Troms og Finnmark	21 %		15 %	20 %	15 %	24 %	16 %	39 %	9 %	19 %	15 %	27 %
Østfold			7 %	13 %	11 %	19 %	8 %	19 %	15 %	31 %	8 %	18 %
Nordland			24 %	27 %	10 %	22 %	10 %	30 %	6 %	28 %	15 %	26 %
Buskerud			13 %	13 %	6 %	19 %					10 %	17 %
Trøndelag			15 %	16 %	7 %	24 %	8 %	24 %	7 %	25 %	11 %	23 %
Oppland			18 %	20 %	12 %	23 %	14 %	26 %	9 %	28 %	15 %	24 %
Møre og Romsdal			17 %	20 %	9 %	24 %	8 %	22 %	8 %	22 %	11 %	22 %
Sogn og Fjordane			13 %	26 %	6 %	22 %	3 %	13 %	2 %	14 %	7 %	16 %
Vestfold			19 %	18 %	11 %	29 %	7 %	26 %	11 %	28 %	13 %	27 %
Hedmark			13 %	16 %	6 %	15 %	8 %	18 %	6 %	18 %	9 %	17 %
Akershus Øst					8 %	21 %	7 %	30 %	8 %	23 %	7 %	25 %
Akershus Vest					7 %	12 %					7 %	12 %
Vestre Viken							8 %	27 %	8 %	16 %	8 %	24 %
Total	15 %	19 %	13 %	19 %	9 %	21 %	9 %	26 %	8 %	23 %	11 %	22 %

Table 4.15: Proportion of breast cancers among women recalled for any reason (PPV-1) by screening area and year, 1996-2016

Screening area	Screening year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	14 %	18 %	18 %	22 %	24 %	18 %
Hordaland	12 %	15 %	18 %	16 %	13 %	15 %
Oslo	14 %	17 %	13 %	22 %	12 %	16 %
Akershus	11 %	10 %	10 %			10 %
Telemark	14 %	15 %	16 %	29 %	34 %	19 %
Agder	12 %	15 %	16 %	21 %	22 %	17 %
Troms og Finnmark	12 %	12 %	19 %	31 %	14 %	18 %
Østfold		7 %	14 %	14 %	22 %	11 %
Nordland		21 %	14 %	21 %	20 %	18 %
Buskerud		11 %	11 %			11 %
Trøndelag		13 %	14 %	18 %	18 %	15 %
Oppland		16 %	16 %	19 %	16 %	17 %
Møre og Romsdal		12 %	14 %	15 %	16 %	14 %
Sogn og Fjordane		12 %	14 %	9 %	9 %	11 %
Vestfold		16 %	19 %	17 %	20 %	18 %
Hedmark		11 %	10 %	13 %	13 %	11 %
Akershus Øst			15 %	18 %	15 %	16 %
Akershus Vest			8 %			8 %
Vestre Viken				17 %	11 %	16 %
Total	12 %	13 %	14 %	18 %	16 %	15 %

"One in five women recalled due to abnormal mammographic findings were diagnosed with breast cancer. One in two women who underwent a needle biopsy were diagnosed with breast cancer"

Table 4.16: Proportion of breast cancer cases diagnosed as a result of an invasive procedure (PPV-2) by screening area and year, 1996-2015

Screening area	Screening year				
	1996-2000	2001-2005	2006-2010	2011-2015	Total
Rogaland	43 %	53 %	53 %	56 %	51 %
Hordaland	43 %	52 %	43 %	40 %	43 %
Oslo	47 %	52 %	47 %	57 %	51 %
Akershus	23 %	29 %	29 %		26 %
Telemark	50 %	43 %	42 %	68 %	49 %
Agder	39 %	52 %	55 %	58 %	54 %
Troms og Finnmark	81 %	36 %	47 %	61 %	48 %
Østfold		26 %	44 %	49 %	38 %
Nordland		57 %	50 %	54 %	53 %
Buskerud		37 %	42 %		40 %
Trøndelag		50 %	58 %	45 %	50 %
Oppland		55 %	60 %	59 %	58 %
Møre og Romsdal		39 %	40 %	39 %	39 %
Sogn og Fjordane		35 %	45 %	37 %	39 %
Vestfold		39 %	53 %	47 %	47 %
Hedmark		33 %	38 %	40 %	38 %
Akershus Øst			37 %	32 %	34 %
Akershus Vest			25 %		25 %
Vestre Viken				49 %	49 %
Total	37 %	41 %	45 %	48 %	44 %

Table 4.17: Proportion of breast cancer cases diagnosed as a result of an invasive procedure (PPV-2) for prevalent and subsequent screening by screening area and year, 1996-2015

Screening area	Screening year									
	1996-2000		2001-2005		2006-2010		2011-2015		Total	
	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub	Prev	Sub
Rogaland	37 %	55 %	37 %	58 %	34 %	60 %	34 %	66 %	36 %	61 %
Hordaland	37 %	60 %	33 %	58 %	21 %	53 %	17 %	50 %	28 %	54 %
Oslo	42 %	54 %	34 %	58 %	36 %	52 %	34 %	68 %	38 %	59 %
Akershus	20 %	27 %	15 %	35 %	17 %	35 %			18 %	33 %
Telemark	50 %		36 %	48 %	10 %	54 %	37 %	79 %	34 %	59 %
Agder	39 %		35 %	69 %	23 %	69 %	29 %	69 %	32 %	69 %
Troms og Finnmark	81 %		32 %	41 %	36 %	51 %	30 %	71 %	35 %	56 %
Østfold			21 %	41 %	31 %	50 %	25 %	61 %	23 %	52 %
Nordland			50 %	76 %	28 %	61 %	29 %	66 %	38 %	65 %
Buskerud			35 %	44 %	20 %	55 %			30 %	51 %
Trøndelag			46 %	59 %	28 %	70 %	20 %	56 %	34 %	61 %
Oppland			52 %	64 %	33 %	69 %	39 %	67 %	44 %	67 %
Møre og Romsdal			37 %	46 %	18 %	49 %	16 %	52 %	25 %	50 %
Sogn og Fjordane			32 %	54 %	21 %	56 %	13 %	48 %	25 %	52 %
Vestfold			39 %	50 %	30 %	66 %	18 %	59 %	31 %	62 %
Hedmark			31 %	50 %	20 %	48 %	20 %	50 %	25 %	49 %
Akershus Øst					19 %	49 %	12 %	49 %	14 %	49 %
Akershus Vest					17 %	29 %			17 %	29 %
Vestre Viken							23 %	61 %	23 %	61 %
Total	33 %	45 %	33 %	50 %	25 %	54 %	23 %	60 %	29 %	55 %

Tumour histopathology

This report includes only women's first screen-detected or interval breast cancer diagnosed as a result of participating in the screening program. Women diagnosed with breast cancer before their first invitation, metastatic breast cancer, breast cancer recurrence, or other types of cancer localised in the breast were excluded. This section presents results about tumour histologic type, size, grade, lymph node involvement, and hormone receptor status, and focuses on invasive breast cancers.

Histologic type

Of all screen-detected breast cancers, 17% were DCIS, 70% were invasive carcinoma of no special type (previously called invasive ductal carcinoma), and 8% were invasive lobular carcinoma (Figure 4.14). The remaining 5% were "other invasive breast cancer". The proportions of DCIS and invasive lobular carcinoma among interval breast cancers were 6% and 12%, respectively.

Histopathologic type varied between screening areas. The proportion of DCIS varied from 12% to 21% for screen-detected and from 3% to 12% for interval breast cancers (Tables 4.18 and 4.19). The proportion of DCIS was generally higher among the youngest women. However, there was variation between age groups over time (Figure 4.15). The overall rate of DCIS has been relatively stable over time, however, the number of DCIS cases in each age group is small and the results should be interpreted with caution. Additionally, the lower percentage of DCIS in some screening areas compared to earlier years may be due to incomplete reporting, coding, or data extraction (see page S48).

DCIS accounted for 5% of all breast cancer cases registered before the start of organised screening in 1996 (66). There was no systematic registration of DCIS before the screening program started, and the rate of DCIS increased after the start of the organised screening program (66). It is expected that DCIS makes up a lower proportion of interval than screen-detected breast cancers as studies show that less than 5% of DCIS cases are symptomatic (67). However, this study was performed 40 years ago and the incidence of DCIS has likely increased the past decades due to increased awareness of this disease, and more precise histopathologic diagnostic methods.

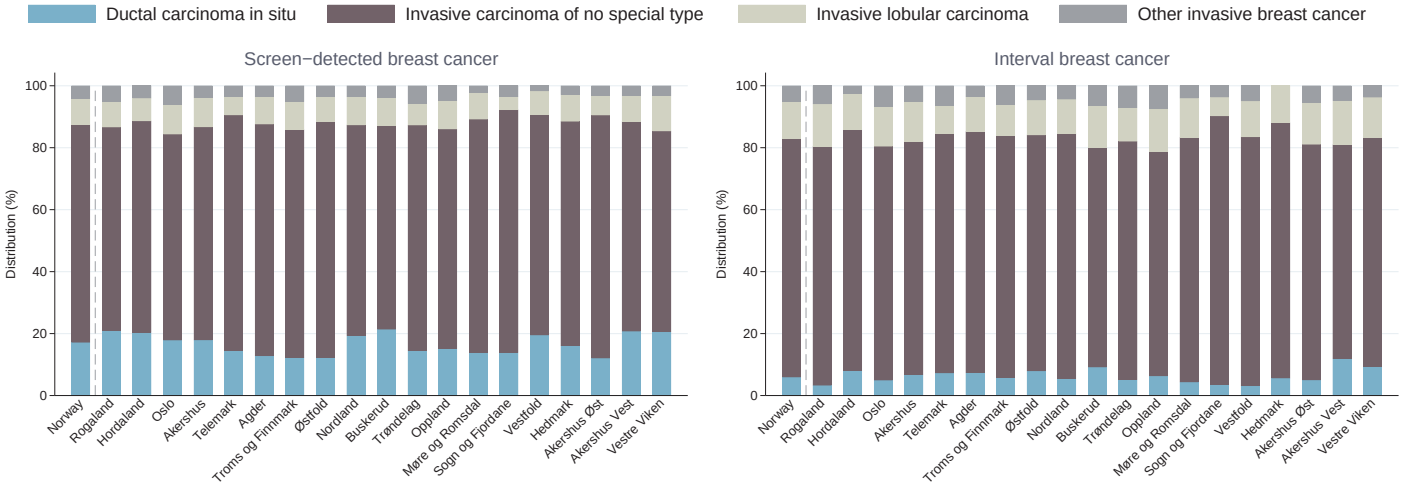


Figure 4.14: Histopathologic type of screen-detected (left, 1996-2016) and interval (right, 1996-2014) breast cancers by screening area

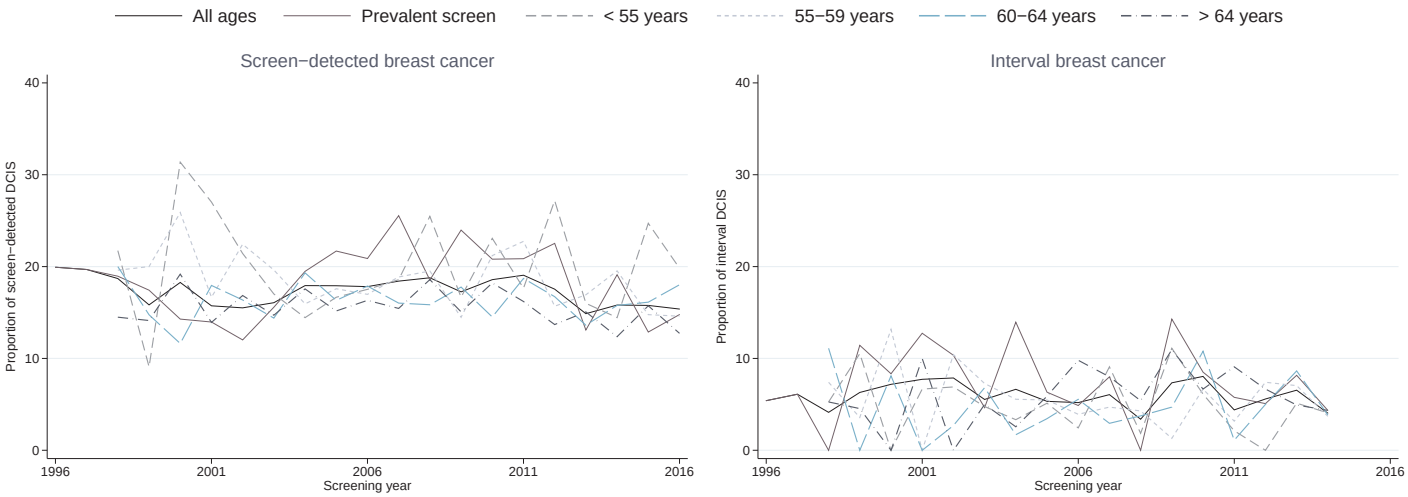


Figure 4.15: Percent of Ductal carcinoma *in situ* (DCIS) cases among all screen-detected (left, 1996-2016) and interval (right, 1996-2014) breast cancers by screening area

Table 4.18: Proportion (%) of DCIS among screen-detected breast cancers by screening area and year, 1996-2016

Screening area	Screening year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	23.2 %	18.2 %	22.7 %	20.0 %	19.8 %	21.0 %
Hordaland	22.0 %	18.2 %	24.3 %	19.2 %	12.3 %	20.5 %
Oslo	14.7 %	20.6 %	21.3 %	16.5 %	14.6 %	17.9 %
Akershus	15.5 %	19.2 %	19.4 %			17.9 %
Telemark	15.6 %	16.7 %	14.7 %	14.0 %	6.5 %	14.6 %
Agder	12.5 %	14.5 %	9.8 %	13.8 %	12.8 %	12.8 %
Troms og Finnmark	7.4 %	8.5 %	12.2 %	14.7 %	15.6 %	12.2 %
Østfold		11.2 %	13.5 %	12.2 %	9.6 %	12.2 %
Nordland		15.9 %	18.8 %	22.0 %	24.5 %	19.4 %
Buskerud		20.5 %	22.3 %			21.4 %
Trøndelag		12.6 %	16.1 %	15.0 %	11.9 %	14.5 %
Oppland		9.6 %	18.4 %	15.2 %	19.6 %	15.2 %
Møre og Romsdal		12.7 %	11.8 %	16.5 %	12.5 %	13.9 %
Sogn og Fjordane		18.6 %	12.0 %	11.7 %	18.5 %	14.0 %
Vestfold		24.6 %	18.4 %	18.6 %	17.9 %	19.5 %
Hedmark		17.1 %	16.4 %	14.9 %	17.5 %	16.1 %
Akershus Øst			16.0 %	10.0 %	10.5 %	12.1 %
Akershus Vest			20.8 %			20.8 %
Vestre Viken				20.1 %	22.6 %	20.6 %
Total	18.5 %	16.7 %	18.2 %	16.6 %	15.4 %	17.2 %

Table 4.19: Proportion (%) of DCIS among interval breast cancers by screening area and year, 1996-2014

Screening area	Screening year				
	1996-2000	2001-2005	2006-2010	2011-2014	Total
Rogaland	3.2 %	5.3 %	1.9 %	3.6 %	3.4 %
Hordaland	8.1 %	7.9 %	8.8 %	8.3 %	8.3 %
Oslo	4.4 %	4.0 %	6.4 %	5.5 %	5.0 %
Akershus	7.4 %	6.9 %	4.6 %		6.8 %
Telemark	9.1 %	8.5 %	7.6 %	4.4 %	7.3 %
Agder	5.0 %	12.2 %	4.4 %	6.5 %	7.4 %
Troms og Finnmark	<0.1 %	3.9 %	1.6 %	9.8 %	5.5 %
Østfold		7.8 %	11.4 %	1.5 %	7.3 %
Nordland		5.8 %	5.6 %	1.6 %	4.6 %
Buskerud		10.3 %	8.5 %		9.2 %
Trøndelag		5.5 %	5.3 %	4.1 %	5.0 %
Oppland		8.3 %	4.5 %	5.1 %	5.6 %
Møre og Romsdal		6.6 %	5.4 %	2.5 %	4.7 %
Sogn og Fjordane		< 0.1 %	6.5 %	3.3 %	3.9 %
Vestfold		4.9 %	4.2 %	<0.1 %	2.8 %
Hedmark		< 0.1 %	8.5 %	4.5 %	5.3 %
Akershus Øst			5.1 %	5.5 %	5.4 %
Akershus Vest			11.9 %		11.9 %
Vestre Viken				9.3 %	9.3 %
Total	6.0 %	6.5 %	6.0 %	5.2 %	5.9 %

Tumour size - invasive breast cancer

Between 1996 and 2016, the mean and median tumour size for invasive screen-detected breast cancers was 15 mm and 13 mm, respectively (Table 4.20). On average, the largest screen-detected tumours were reported in Sogn og Fjordane (mean 18 mm, median 14 mm), and the smallest were reported in Akershus Vest (mean 12 mm, median 10 mm).

Overall, reported tumour size was stable throughout the reporting period, although small variations were detected between and within screening areas over time (Table 4.20). Nearly half of reported screen-detected tumours (45%) were 11-20 mm, while less than 1% of cases were greater than 50 mm (Figure 4.17). Tumour size reports for screen-detected breast cancer decreased with increasing age (Figure 4.16). The mean (median) tumour size was 16 mm (14 mm) for prevalently and 15 mm (12 mm) for subsequently screened women.

For interval breast cancers, the mean and median tumour size was 21 mm and 18 mm, respectively (Table 4.21). On average, the largest interval breast cancers were reported in Rogaland (mean 24 mm, median 21 mm), while the smallest were reported in Møre og Romsdal (mean 19 mm, median 16 mm). Nearly half (42%) of all interval breast cancers were between 11-20 mm. A substantially lower proportion of interval breast cancers were <11 mm (16.9%) compared with screen-detected cancers (36.5%). Tumour size did not differ substantially across age groups, time, or screening areas (Figures 4.16 and 4.17, and Table 4.21). Prior analysis of tumour characteristics have demonstrated that tumour size was the only difference between interval breast cancer detected in the first versus the second year following a screening examination (*61*).

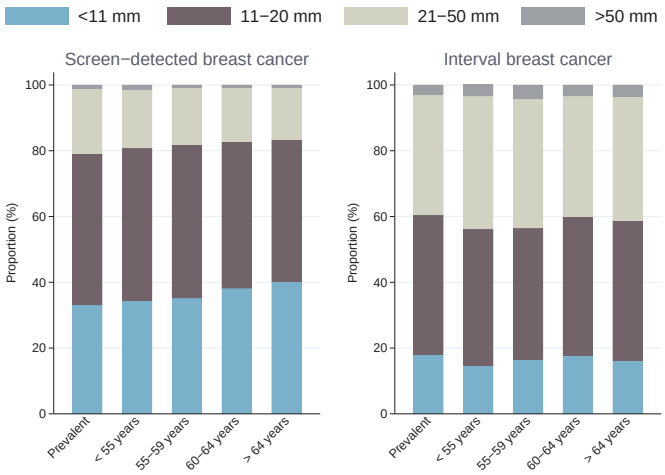


Figure 4.16: Largest reported tumour diameter (<11 mm, 11-20 mm, 21-50 mm, >50 mm) for screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014), by age group

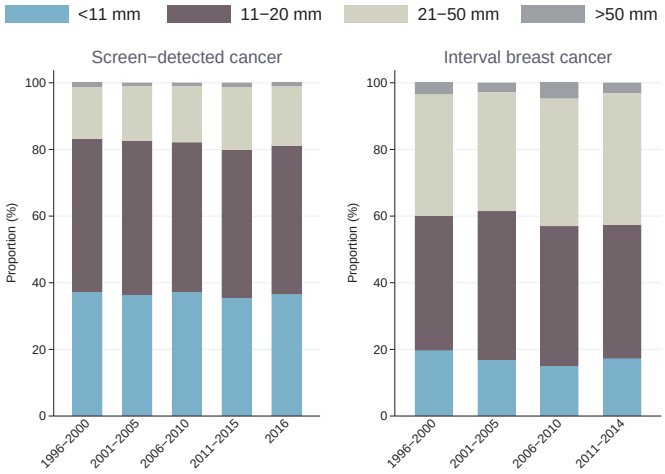


Figure 4.17: Largest reported tumour diameter (<11 mm, 11-20 mm, 21-50 mm, >50 mm) for screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014), by screening year

Table 4.20: Mean and median reported tumour diameter (mm) of screen-detected breast cancers by screening area, 1996-2016

Screening area	Screening year											
	1996-2000		2001-2005		2006-2010		2011-2015		2016		Total	
	Mean	Median	Mean	Median	Mean	Median	Mean	Median	Mean	Median	Mean	Median
Rogaland	14	12	15	13	14	12	16	13	17	15	15	13
Hordaland	16	13	14	12	16	14	16	14	17	15	16	13
Oslo	15	13	15	13	14	12	14	12	12	11	14	12
Akershus	15	13	14	12	14	12					14	12
Telemark	13	12	15	13	15	13	13	12	14	12	14	12
Agder	17	13	15	13	16	13	14	12	13	12	15	13
Troms og Finnmark	17	14	15	12	15	13	15	12	14	15	15	12
Østfold			14	12	13	11	16	12	15	14	15	12
Nordland			15	14	15	13	16	14	17	15	15	14
Buskerud			15	12	14	12					15	12
Trøndelag			14	12	14	12	16	13	14	13	15	13
Oppland			16	13	15	13	15	12	11	10	15	13
Møre og Romsdal			15	14	15	13	14	12	14	12	15	13
Sogn og Fjordane			16	13	19	15	18	15	18	13	18	14
Vestfold			16	14	14	13	15	13	14	12	15	13
Hedmark			16	15	14	13	15	12	13	11	15	12
Akershus Øst					15	13	17	15	15	12	16	13
Akershus Vest					12	10					12	10
Vestre Viken							16	13	15	14	15	13
Total	15	13	15	13	15	12	15	13	15	13	15	13

Table 4.21: Mean and median reported tumour diameter (mm) of interval breast cancers by screening area, 1996-2014

Screening area	Screening year									
	1996-2000		2001-2005		2006-2010		2011-2014		Total	
	Mean	Median	Mean	Median	Mean	Median	Mean	Median	Mean	Median
Rogaland	25	19	23	21	26	21	23	22	24	21
Hordaland	20	20	20	18	23	20	24	21	22	20
Oslo	20	18	19	16	22	18	21	16	20	17
Akershus	21	19	18	17	19	16			19	18
Telemark	18	18	21	20	22	20	21	19	21	19
Agder	24	22	23	20	23	20	18	16	22	20
Troms og Finnmark	20	18	21	18	24	20	20	17	21	18
Østfold			19	15	22	19	22	19	21	18
Nordland			24	20	20	18	21	18	22	19
Buskerud			24	20	20	19			22	20
Trøndelag			18	16	22	18	20	18	20	18
Oppland			20	16	18	17	23	19	20	17
Møre og Romsdal			19	18	19	16	19	16	19	16
Sogn og Fjordane			19	20	23	20	25	20	24	20
Vestfold			15	15	22	18	21	18	21	17
Hedmark			22	20	21	19	18	17	20	18
Akershus Øst					22	18	24	20	23	19
Akershus Vest					21	20			21	20
Vestre Viken							20	20	20	20
Total	21	19	20	18	22	19	21	19	21	18

Histologic grade – invasive breast cancer

Grade was reported for invasive cancers using the Nottingham histologic score system (Elston-Ellis modification of the Scarff-Bloom-Richardson grading system) (*68*).

Nearly half of invasive screen-detected breast cancer cases were classified as histologic grade II (48%), while 19% were classified as grade III (Table 4.22) during the last 20 years. There were substantial variations in the distribution of histologic grade between screening areas (Table 4.22). The proportion of grade III tumours increased from 9% in 1996 to 24% in 2016 (Figure 4.19).

The proportion of grade III tumours varied between 17% and 23% for both prevalently and subsequently screened women (Figure 4.18). Variations in histologic grade by age-group were not clinically significant.

For interval breast cancer, 46% of invasive breast cancer tumours were diagnosed as grade II, while 37% were classified as grade III (Table 4.23). The proportion of grade I and II tumours increased with age (Figure 4.18).

Similar to screen-detected breast cancers, among interval breast cancers the proportion of grade III tumours increased over time (Table 4.23). Overall, grade II and III tumours made up roughly 80% of interval breast cancer cases in most screening areas, however this proportion varied substantially between some screening areas. Variation in the distribution of tumour grade between and across screening areas could be due to inter- and intra-rater variation among pathologists. The clinical significance of these differences is unclear and needs to be investigated.

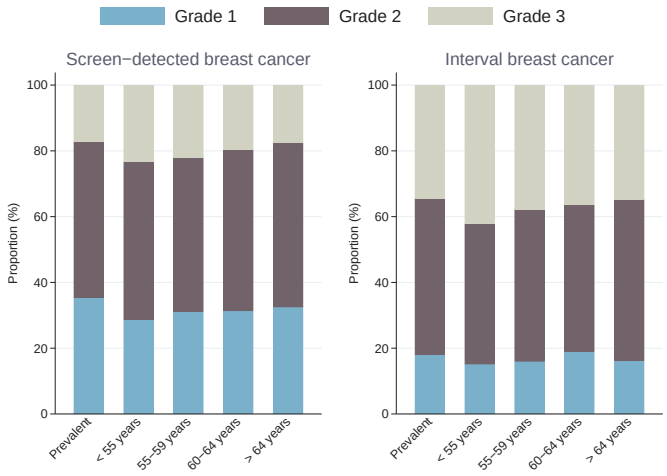


Figure 4.18: Distribution of histologic grade for invasive screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014) by age group

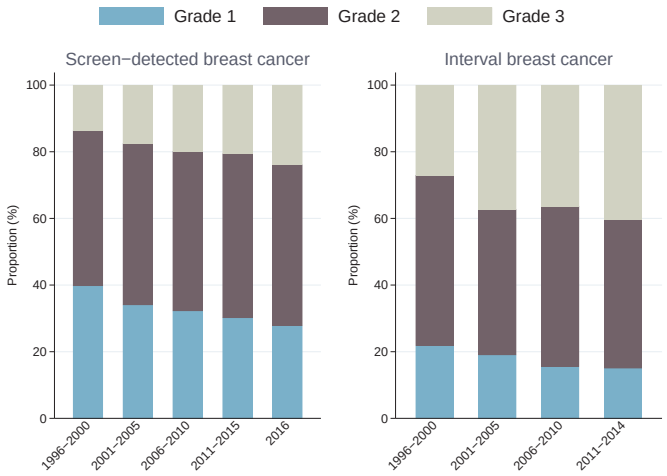


Figure 4.19: Distribution of histologic grade for invasive screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014) by screening year

"The distribution of histologic grade varied substantially across screening areas. Whether these differences are real or due to individual pathologist variation remains unclear and needs to be investigated"

Table 4.22: Distribution of histologic grade for invasive screen-detected breast cancers by screening year, 1996-2016

Screening area	Screening year																	
	1996-2000			2001-2005			2006-2010			2011-2015			2016			Total		
	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III
Rogaland	44 %	40 %	16 %	29 %	51 %	20 %	33 %	46 %	21 %	29 %	43 %	28 %	24 %	38 %	39 %	33 %	45 %	23 %
Hordaland	43 %	42 %	15 %	43 %	44 %	13 %	37 %	45 %	19 %	35 %	46 %	19 %	28 %	47 %	26 %	38 %	45 %	17 %
Oslo	36 %	51 %	13 %	34 %	52 %	14 %	35 %	43 %	21 %	36 %	48 %	16 %	21 %	52 %	27 %	35 %	49 %	17 %
Akershus	35 %	54 %	11 %	27 %	56 %	17 %	28 %	58 %	14 %							30 %	56 %	14 %
Telemark	39 %	47 %	14 %	34 %	46 %	20 %	26 %	55 %	20 %	34 %	43 %	23 %	40 %	38 %	21 %	33 %	47 %	20 %
Agder	47 %	47 %	7 %	45 %	40 %	15 %	36 %	49 %	15 %	34 %	55 %	11 %	39 %	48 %	13 %	39 %	48 %	13 %
Troms og Finnmark	46 %	33 %	21 %	35 %	47 %	18 %	38 %	44 %	18 %	44 %	39 %	17 %	30 %	41 %	30 %	39 %	42 %	19 %
Østfold				29 %	48 %	23 %	28 %	58 %	14 %	19 %	62 %	18 %	20 %	60 %	20 %	25 %	57 %	18 %
Nordland				39 %	40 %	22 %	29 %	41 %	30 %	23 %	47 %	30 %	28 %	47 %	25 %	30 %	43 %	27 %
Buskerud				41 %	44 %	15 %	40 %	37 %	23 %							41 %	41 %	19 %
Trøndelag				29 %	50 %	21 %	25 %	51 %	24 %	26 %	49 %	26 %	28 %	50 %	22 %	26 %	50 %	24 %
Oppland				30 %	56 %	14 %	39 %	49 %	12 %	32 %	54 %	14 %	41 %	32 %	27 %	34 %	52 %	14 %
Møre og Romsdal				34 %	43 %	23 %	34 %	41 %	24 %	43 %	38 %	18 %	29 %	45 %	27 %	37 %	41 %	22 %
Sogn og Fjordane				47 %	32 %	21 %	22 %	51 %	27 %	12 %	56 %	31 %	14 %	62 %	24 %	24 %	49 %	27 %
Vestfold				28 %	48 %	24 %	27 %	55 %	19 %	27 %	55 %	18 %	28 %	57 %	15 %	27 %	54 %	19 %
Hedmark				29 %	61 %	10 %	29 %	57 %	14 %	28 %	56 %	17 %	17 %	64 %	19 %	27 %	58 %	15 %
Akershus Øst							31 %	44 %	25 %	21 %	49 %	30 %	31 %	47 %	22 %	26 %	47 %	27 %
Akershus Vest							42 %	44 %	14 %							42 %	44 %	14 %
Vestre Viken										28 %	53 %	20 %	29 %	48 %	22 %	28 %	52 %	20 %
Total	40 %	47 %	14 %	34 %	48 %	18 %	32 %	48 %	20 %	30 %	49 %	21 %	28 %	48 %	24 %	32 %	48 %	19 %

Table 4.23: Distribution of histologic grade for interval breast cancers by screening year, 1996-2014

Screening area	Screening year														
	1996-2000			2001-2005			2006-2010			2011-2014			Total		
	I	II	III	I	II	III	I	II	III	I	II	III	I	II	III
Rogaland	31 %	34 %	35 %	18 %	34 %	48 %	11 %	50 %	39 %	15 %	44 %	41 %	18 %	41 %	41 %
Hordaland	24 %	50 %	26 %	22 %	42 %	36 %	14 %	45 %	40 %	19 %	30 %	51 %	20 %	42 %	38 %
Oslo	25 %	52 %	23 %	27 %	42 %	31 %	17 %	44 %	40 %	12 %	51 %	37 %	20 %	47 %	32 %
Akershus	11 %	61 %	28 %	14 %	53 %	33 %	16 %	49 %	34 %				13 %	56 %	31 %
Telemark	44 %	44 %	11 %	15 %	48 %	37 %	21 %	34 %	44 %	14 %	52 %	34 %	20 %	44 %	36 %
Agder	< 1 %	63 %	37 %	23 %	37 %	40 %	17 %	55 %	27 %	24 %	52 %	23 %	20 %	50 %	30 %
Troms og Finnmark	29 %	43 %	29 %	21 %	49 %	31 %	20 %	44 %	36 %	21 %	36 %	43 %	21 %	43 %	36 %
Østfold				18 %	50 %	32 %	15 %	55 %	30 %	11 %	55 %	35 %	14 %	54 %	32 %
Nordland				21 %	43 %	36 %	14 %	46 %	40 %	11 %	43 %	46 %	16 %	44 %	40 %
Buskerud				9 %	43 %	48 %	20 %	47 %	33 %				16 %	45 %	39 %
Trøndelag				16 %	44 %	40 %	15 %	43 %	43 %	14 %	44 %	42 %	15 %	43 %	41 %
Oppland				31 %	41 %	28 %	19 %	53 %	27 %	11 %	59 %	30 %	18 %	53 %	29 %
Møre og Romsdal				19 %	42 %	39 %	24 %	35 %	41 %	25 %	34 %	41 %	23 %	36 %	40 %
Sogn og Fjordane				14 %	43 %	43 %	7 %	59 %	33 %	4 %	54 %	42 %	7 %	54 %	39 %
Vestfold				16 %	34 %	50 %	7 %	62 %	31 %	19 %	49 %	32 %	13 %	52 %	35 %
Hedmark				7 %	60 %	33 %	15 %	57 %	28 %	16 %	53 %	30 %	13 %	57 %	30 %
Akershus Øst							15 %	45 %	40 %	11 %	39 %	50 %	12 %	41 %	46 %
Akershus Vest							8 %	53 %	39 %				8 %	53 %	39 %
Vestre Viken										10 %	42 %	48 %	10 %	42 %	48 %
Total	22 %	51 %	27 %	19 %	44 %	37 %	16 %	48 %	36 %	15 %	45 %	40 %	17 %	46 %	37 %

Lymph node involvement

The rate of lymph node involvement among women with screen-detected breast cancer was relatively stable over time. Rates ranged from 29% in 1998 and 2007 to 18% in 2016 (Figure 4.20). The 2016 rate may be effected by incomplete reporting or data registration/extraction (Figure 4.26) and will be monitored.

Overall, roughly a quarter (23%) of women diagnosed with screen-detected breast cancer between 1996-2016 had lymph node involvement (Table 4.24). This proportion varied between screening areas from 16% (Akershus Vest) to 30% (Møre og Romsdal). As with histologic grade, some of this variability may be due to differences between individual pathologists.

Among women with lymph node positive screen-detected breast cancer, 1-3 lymph nodes were involved in over 78% of cases, while 4-9 lymph nodes were involved in 16% of cases (Figure 4.22). In the remaining 6% of cases, 10 or more lymph nodes were involved. Overall, the proportion of women diagnosed with any lymph node involvement decreased with increasing age (Figure 4.21).

The rate of lymph node involvement among women with interval breast cancer peaked in 2006 (48%) but reached a low in 2014 (31%, Figure 4.20). Overall, 40% of women diagnosed between 1996-2014 had lymph node involvement, ranging from 36% in Vestfold and Trøndelag to 47% in Nordland (Table 4.25). This rate decreased slightly with increasing age (Figure 4.21). 1-3 lymph nodes were involved in the majority (66%) of interval breast cancer cases with lymph node involvement (Figure 4.22). However, 4-9 lymph nodes were involved in a larger proportion (23%) of interval breast cancer cases than screen-detected cases and the proportion with >9 lymph nodes involved was 11%.

Changes in the rates of lymph node positive tumours over time could be due to the introduction of the sentinel node technique in the late 1990s. The sentinel node is the first lymph node into which a breast cancer tumour spreads. If this lymph node contains cancer cells, this indicates spreading to lymph nodes in the axilla (armpit) and that these must be removed. The absence of cancer cells in the sentinel node indicates that cancer has not spread to the lymphatic system and that surgery to remove axillary lymph nodes is not required.

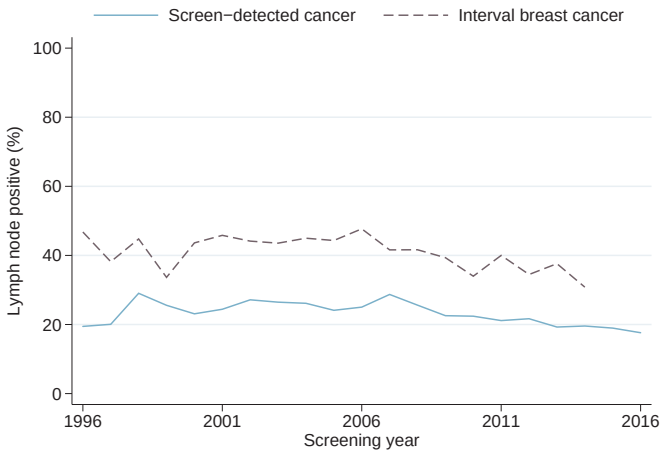


Figure 4.20: Proportion of screen-detected (1996-2016) and interval breast cancers (1996-2014) with lymph node involvement by screening year

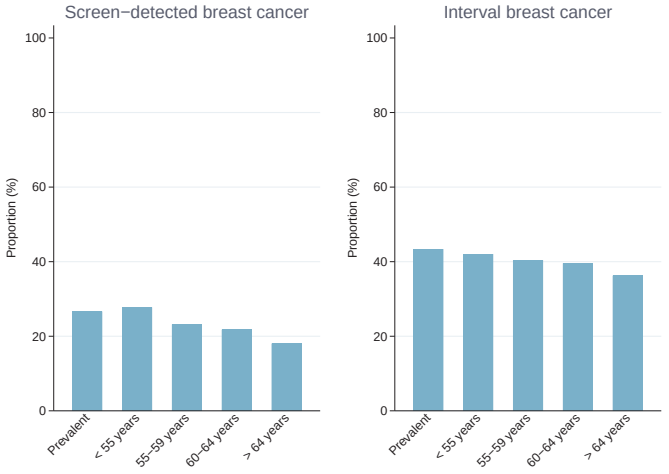


Figure 4.21: Proportion of screen-detected (left, 1996-2016) and interval breast cancers (right, 1996-2014) with lymph node involvement by age group

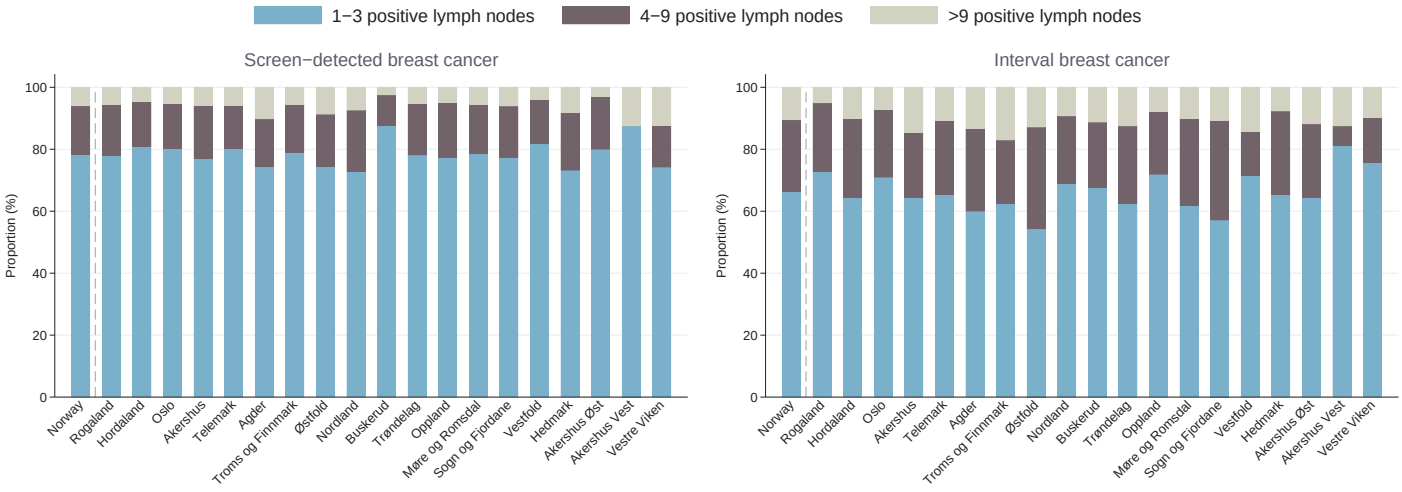


Figure 4.22: Distribution of lymph node involvement among women with positive lymph nodes diagnosed with screen-detected (left, 1996-2016) and interval breast cancers (right, 1996-2014) by screening area

Table 4.24: Proportion screen-detected breast cancers with lymph node involvement by screening area and year, 1996-2016

Screening area	Screening year					
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total
Rogaland	18 %	28 %	26 %	18 %	26 %	22 %
Hordaland	23 %	26 %	22 %	15 %	11 %	20 %
Oslo	27 %	24 %	21 %	18 %	16 %	21 %
Akershus	24 %	25 %	32 %			26 %
Telemark	28 %	26 %	28 %	17 %	22 %	24 %
Agder	35 %	19 %	21 %	23 %	15 %	21 %
Troms og Finnmark	20 %	23 %	25 %	20 %	16 %	22 %
Østfold		27 %	21 %	24 %	27 %	24 %
Nordland		24 %	31 %	22 %	29 %	26 %
Buskerud		24 %	23 %			24 %
Trøndelag		22 %	28 %	23 %	17 %	24 %
Oppland		35 %	25 %	22 %	16 %	26 %
Møre og Romsdal		36 %	35 %	23 %	17 %	30 %
Sogn og Fjordane		23 %	26 %	31 %	20 %	27 %
Vestfold		35 %	23 %	19 %	12 %	23 %
Hedmark		30 %	24 %	22 %	14 %	23 %
Akershus Øst			21 %	19 %	16 %	19 %
Akershus Vest			16 %			16 %
Vestre Viken				18 %	15 %	17 %
Total	23 %	26 %	25 %	20 %	18 %	23 %

Table 4.25: Proportion interval breast cancers with lymph node involvement by screening area and year, 1996-2014

Screening area	Screening year				
	1996-2000	2001-2005	2006-2010	2011-2014	Total
Rogaland	45 %	46 %	41 %	36 %	42 %
Hordaland	37 %	47 %	50 %	31 %	41 %
Oslo	38 %	40 %	38 %	29 %	37 %
Akershus	45 %	43 %	42 %		44 %
Telemark	35 %	54 %	41 %	43 %	45 %
Agder	50 %	44 %	39 %	25 %	37 %
Troms og Finnmark	43 %	44 %	33 %	44 %	41 %
Østfold		32 %	36 %	42 %	37 %
Nordland		55 %	50 %	33 %	47 %
Buskerud		52 %	41 %		45 %
Trøndelag		42 %	35 %	31 %	36 %
Oppland		42 %	42 %	50 %	45 %
Møre og Romsdal		46 %	37 %	43 %	42 %
Sogn og Fjordane		27 %	46 %	41 %	41 %
Vestfold		40 %	39 %	30 %	36 %
Hedmark		48 %	43 %	39 %	43 %
Akershus Øst			42 %	36 %	38 %
Akershus Vest			46 %		46 %
Vestre Viken				37 %	37 %
Total	41 %	44 %	41 %	36 %	40 %

Hormone receptor status

The Cancer Registry collects information about oestrogen receptor, progesterone receptor, and human epidermal growth factor receptor 2 (Her2) status, as well as Ki-67 expression. Information about oestrogen and progesterone receptor status has been systematically collected and registered since 1996. Information has been collected and registered about Her2 receptor status since 2005, while other tumour characteristics, such as Ki-67 expression, have been registered since 2010.

Oestrogen receptor status

Nearly nine of ten women with screen-detected cancer and seven of ten women with interval breast cancer had oestrogen receptor positive tumours (Figure 4.25). There were small variations in the proportion of women with oestrogen receptor positive tumours over time and across screening areas (Table 4.26).

The proportion of prevalently screened women with oestrogen receptor positive tumours was 90% and was 89% for subsequently screened women. These proportions were lower for women with interval breast cancer. The proportion of oestrogen receptor positive tumours was similar across all age groups for women with screen-detected breast cancer and increased slightly with age among women with interval breast cancer (Figure 4.23).

Progesterone receptor status

Seven of ten women with screen-detected breast cancer and six of ten women with interval breast cancer had progesterone receptor positive tumours (Figure 4.25 and Table 4.27). This proportion ranged from 62% in Østfold to 81% in Vestre Viken for screen-detected cancers, and for interval breast cancers ranged from 46% in Østfold to 55% in Vestre Viken.

The proportion of prevalently screened women with progesterone receptor positive tumours was 73%. For subsequently screened women it was 70%. These proportions were lower for women with interval breast cancer (Figure 4.24). The proportion of progesterone receptor positive tumours increased with age among subsequently screened women with interval breast cancer.

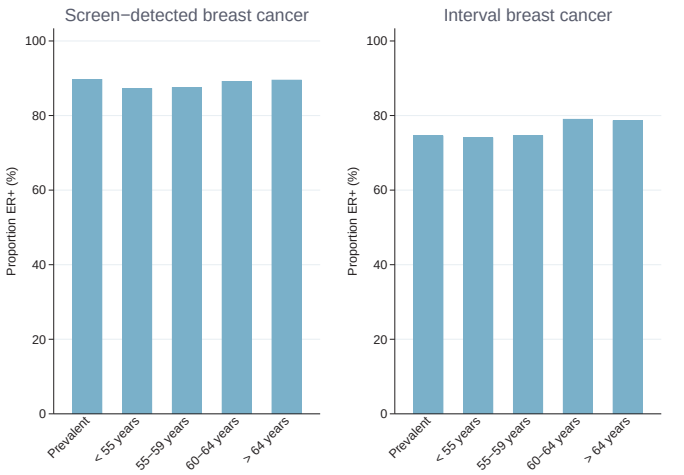


Figure 4.23: Proportion of oestrogen receptor positive (ER+) screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014) by screening year

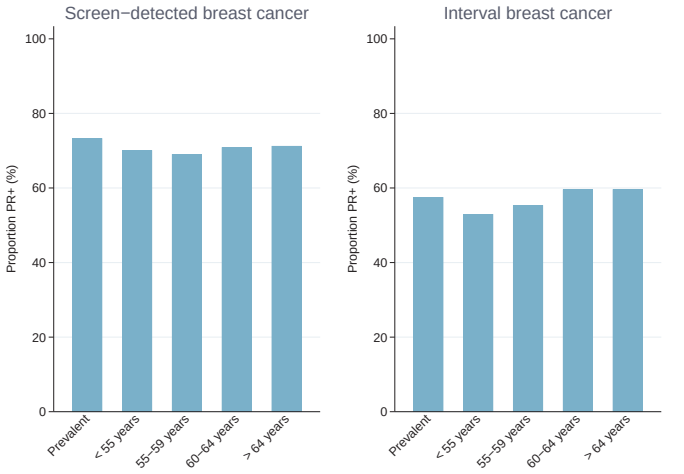


Figure 4.24: Proportion of progesterone receptor positive (PR+) screen-detected breast cancers (left, 1996-2016) and interval breast cancers (right, 1996-2014) by screening year

Figure 4.25: Proportion of oestrogen (ER+, left) and progesterone (PR+, right) receptor positive screen-detected breast cancers (1996-2016) and interval breast cancers (1996-2014) by screening year

Table 4.26: Proportion (%) of women with positive oestrogen receptor status (ER+) screen-detected (1996-2016) and interval (1996-2014) breast cancer by screening area and year

Screening area	Screening Year										
	Screen-detected breast cancer						Interval breast cancer				
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total	1996-2000	2001-2005	2006-2010	2011-2014	Total
Rogaland	86 %	92 %	90 %	90 %	92 %	90 %	72 %	72 %	71 %	84 %	75 %
Hordaland	91 %	89 %	87 %	89 %	94 %	89 %	72 %	78 %	73 %	76 %	75 %
Oslo	76 %	85 %	89 %	93 %	92 %	87 %	71 %	75 %	76 %	76 %	75 %
Akershus	87 %	88 %	92 %			88 %	76 %	76 %	87 %		78 %
Telemark	88 %	90 %	85 %	89 %	90 %	88 %	72 %	78 %	78 %	75 %	76 %
Agder	89 %	89 %	92 %	91 %	90 %	90 %	64 %	80 %	71 %	77 %	75 %
Troms og Finnmark	92 %	85 %	88 %	90 %	89 %	88 %	71 %	70 %	70 %	74 %	72 %
Østfold		87 %	90 %	90 %	94 %	90 %		83 %	79 %	85 %	82 %
Nordland		84 %	85 %	93 %	88 %	87 %		64 %	73 %	67 %	68 %
Buskerud		91 %	91 %			91 %		75 %	80 %		78 %
Trøndelag		89 %	87 %	88 %	91 %	88 %		74 %	79 %	81 %	78 %
Oppland		94 %	87 %	87 %	95 %	89 %		75 %	77 %	84 %	79 %
Møre og Romsdal		89 %	85 %	90 %	93 %	88 %		75 %	75 %	78 %	76 %
Sogn og Fjordane		91 %	84 %	96 %	86 %	90 %		87 %	73 %	76 %	77 %
Vestfold		91 %	91 %	90 %	94 %	91 %		69 %	86 %	84 %	82 %
Hedmark		89 %	89 %	88 %	91 %	89 %		66 %	81 %	79 %	77 %
Akershus Øst			86 %	87 %	91 %	88 %			88 %	75 %	79 %
Akershus Vest			91 %			91 %			72 %		72 %
Vestre Viken				93 %	93 %	93 %				81 %	81 %
Total	85 %	89 %	88 %	90 %	92 %	89 %	73 %	75 %	77 %	78 %	76 %

Table 4.27: Proportion (%) of women with positive progesterone receptor status (PR+) screen-detected (1996-2016) and interval (1996-2014) breast cancer by screening area and year

Screening area	Screening Year										
	Screen-detected breast cancer						Interval breast cancer				
	1996-2000	2001-2005	2006-2010	2011-2015	2016	Total	1996-2000	2001-2005	2006-2010	2011-2014	Total
Rogaland	60%	62%	81%	68%	80%	69%	35%	57%	66%	57%	56%
Hordaland	73%	76%	67%	75%	85%	74%	55%	60%	53%	65%	58%
Oslo	59%	66%	72%	75%	71%	70%	48%	56%	58%	59%	55%
Akershus	70%	70%	71%			70%	63%	63%	60%		62%
Telemark	71%	68%	61%	68%	69%	67%	56%	58%	57%	48%	55%
Agder	80%	63%	75%	66%	70%	69%	36%	57%	61%	54%	56%
Troms og Finnmark	42%	60%	73%	77%	73%	69%	14%	37%	66%	59%	52%
Østfold		54%	53%	72%	79%	62%		40%	42%	55%	46%
Nordland		78%	71%	80%	75%	76%		45%	52%	61%	52%
Buskerud		76%	81%			79%		75%	64%		68%
Trøndelag		71%	70%	71%	76%	71%		56%	55%	61%	57%
Oppland		81%	73%	71%	76%	74%		61%	58%	55%	58%
Møre og Romsdal		72%	57%	64%	75%	64%		58%	55%	56%	56%
Sogn og Fjordane		72%	71%	81%	82%	76%		67%	54%	66%	61%
Vestfold		60%	77%	80%	79%	76%		59%	68%	66%	66%
Hedmark		77%	75%	74%	79%	75%		52%	62%	65%	61%
Akershus Øst			71%	70%	76%	71%			67%	53%	57%
Akershus Vest			78%			78%			61%		61%
Vestre Viken				82%	77%	81%				65%	65%
Total	66%	69%	71%	73%	77%	71%	51%	56%	59%	59%	57%

Unavailable tumour characteristic data

The systems and processes for data collection and registration have changed since the start-up of the screening program (see page S8). These changes present challenges to longitudinal interpretation of prognostic and predictive breast tumours characteristics. Moreover, information about tumour size can be unavailable for women with locally advanced disease and for those who undergo neoadjuvant therapy prior to surgery.

Overall, complete histopathology information about screen-detected breast cancer was available for over 95% of cases with respect to tumour size, grade, or lymph node involvement (Table 4.28).

Complete information about oestrogen and progesterone receptor status was available for 95% of screen-detected and interval breast cancer cases (Tables 4.28 and 4.29). Reporting and coding of hormonal status information were implemented as a part of the screening program. Rates of missing hormone receptor status were highest when the screening program started (Figure 4.26). This may be associated with a lack of procedures and reminders for this information to be sent to the Cancer Registry in the initial years of the program. However, data completeness reached an acceptable level within a short time.

Information for interval breast cancer was generally missing at a higher rate than that for screen-detected breast cancers (Table 4.29). However, with the exception of tumour size, the proportion of not available information for interval breast cancer decreased over time (Figure 4.26). Complete information about tumour size was available for 89% of cases. Because a higher proportion of women undergo neoadjuvant therapy prior to surgery following a diagnosis of interval breast cancer than for screen-detected breast cancer, this was not an unexpected finding. The rate of missing data about tumour size for interval breast cancers generally grew with the screening program and peaked in 2006. It is difficult to determine how much of this increase was attributable to growing pains as various screening areas joined the program, and how much was attributable to a change in database software around this time.

Other reasons that histopathology data were not available for some women are: omissions in reporting, failures to send a reminder upon no receipt of expected histopathology information, failures in coding and registration, and failures in the extraction of data from the databases.

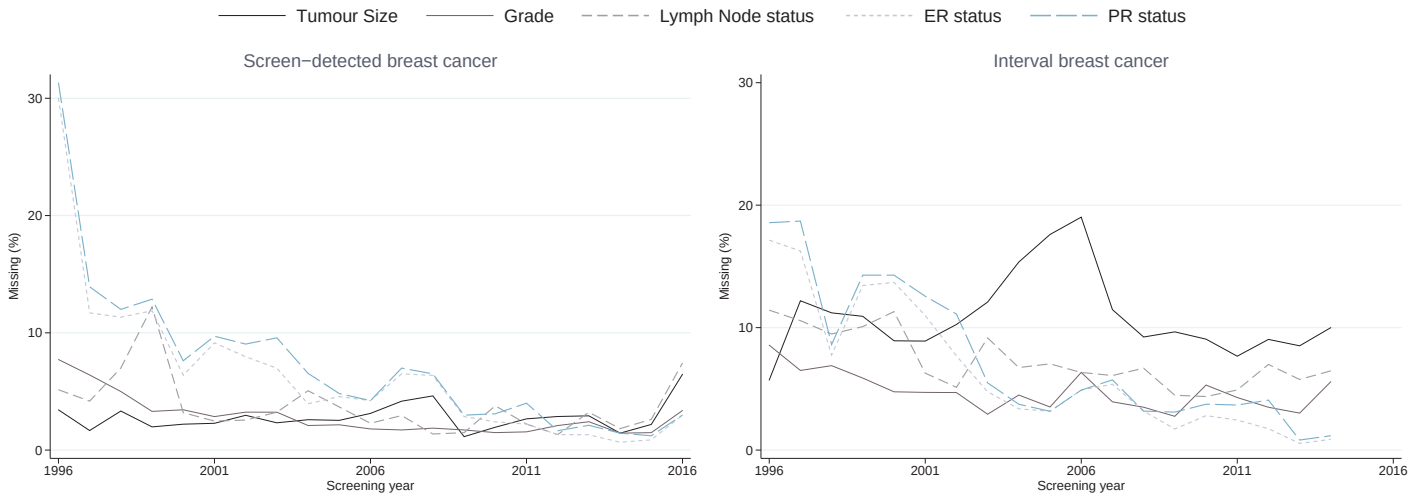


Figure 4.26: Proportion of missing data for histopathologic tumour characteristics of screen-detected (left, 1996-2016) and interval breast cancers (right, 1996-2014)

Table 4.28: Proportion (%) of missing information about histopathologic tumour size (mm), grade, lymph node involvement, and oestrogen receptor (ER) and progesterone receptor (PR) status among women diagnosed with screen-detected breast cancer by screening area, 1996-2016

Screening area	Tumour size	Histologic grade	Lymph node involvement	ER status	PR status
Rogaland	1.5 %	2.3 %	2.6 %	6.3 %	9.2 %
Hordaland	4.0 %	3.6 %	5.6 %	4.4 %	4.5 %
Oslo	2.6 %	2.2 %	5.8 %	5.0 %	5.8 %
Akershus	3.6 %	4.4 %	2.8 %	11.7 %	11.9 %
Telemark	3.1 %	1.0 %	1.4 %	3.1 %	3.1 %
Agder	2.5 %	2.6 %	2.6 %	2.4 %	3.3 %
Troms og Finnmark	2.7 %	1.8 %	2.4 %	6.6 %	12.8 %
Østfold	2.7 %	2.2 %	3.3 %	3.5 %	4.3 %
Nordland	2.7 %	5.0 %	2.5 %	3.0 %	3.0 %
Buskerud	3.6 %	1.7 %	1.9 %	7.7 %	8.1 %
Trøndelag	3.6 %	3.1 %	2.3 %	4.6 %	4.6 %
Oppland	2.9 %	1.3 %	2.7 %	4.5 %	4.6 %
Møre og Romsdal	2.2 %	2.1 %	3.4 %	2.1 %	2.4 %
Sogn og Fjordane	3.0 %	2.6 %	6.8 %	1.5 %	1.5 %
Vestfold	3.0 %	2.2 %	2.7 %	3.0 %	3.1 %
Hedmark	1.3 %	0.2 %	1.5 %	3.8 %	3.8 %
Akershus Øst	3.5 %	0.9 %	3.7 %	1.5 %	1.5 %
Akershus Vest	6.8 %	1.0 %	1.0 %	3.9 %	2.9 %
Vestre Viken	2.1 %	0.4 %	2.1 %	0.5 %	0.5 %
Total	2.9 %	2.4 %	3.3 %	4.6 %	5.5 %

Table 4.29: Proportion (%) of missing information about histopathologic tumour size (mm), grade, lymph node involvement, and oestrogen receptor (ER) and progesterone receptor (PR) status among women diagnosed with interval breast cancer by screening area, 1996-2014

Screening area	Tumour size	Histologic grade	Lymph node involvement	ER status	PR status
Rogaland	9.3 %	5.7 %	6.3 %	5.1 %	8.1 %
Hordaland	12.7 %	5.6 %	10.7 %	2.1 %	1.9 %
Oslo	9.9 %	5.4 %	8.0 %	8.2 %	8.8 %
Akershus	10.8 %	3.8 %	3.5 %	9.4 %	10.2 %
Telemark	11.2 %	1.1 %	6.7 %	5.0 %	5.0 %
Agder	9.9 %	5.3 %	6.3 %	4.6 %	5.6 %
Troms og Finnmark	13.8 %	2.7 %	4.9 %	9.8 %	17.4 %
Østfold	14.6 %	4.4 %	7.3 %	2.4 %	2.0 %
Nordland	13.2 %	7.5 %	9.7 %	1.8 %	1.8 %
Buskerud	17.9 %	3.0 %	6.6 %	2.4 %	2.4 %
Trøndelag	12.0 %	6.8 %	5.2 %	4.3 %	4.9 %
Oppland	15.0 %	3.9 %	6.5 %	5.9 %	5.9 %
Møre og Romsdal	6.7 %	1.8 %	4.9 %	1.3 %	1.3 %
Sogn og Fjordane	9.5 %	9.5 %	8.1 %	5.4 %	5.4 %
Vestfold	10.1 %	2.9 %	5.8 %	1.9 %	1.9 %
Hedmark	7.9 %	<0.1 %	4.7 %	1.6 %	1.6 %
Akershus Øst	7.9 %	1.9 %	6.5 %	2.3 %	2.3 %
Akershus Vest	10.8 %	2.7 %	5.4 %	2.7 %	2.7 %
Vestre Viken	11.1 %	2.6 %	5.1 %	2.6 %	3.4 %
Total	11.1 %	4.5 %	6.7 %	4.7 %	5.6 %

Mobile versus stationary units

Early performance measures typically combine results from stationary and mobile screening units. However, because the mammography equipment on mobile units requires frequent technical adjustments/technical quality controls, and because mobile units service a largely rural population, it might be useful to also evaluate early performance measures for stationary and mobile units separately. Moreover, the picture archiving and communication systems (PACS), and workstations differ between the mobile and stationary units, which might affect the display of images for interpreting radiologists.

Approximately 17% of all screening examinations were performed at mobile units. The majority of these women typically live in rural areas a long distance from stationary units. Mobile units were most commonly used in Nordland, Troms og Finnmark, Hedmark, and Hordaland (Table 4.30). Women invited to screening at a mobile unit had a higher attendance rate than women invited to stationary screening units: 80% and 75%, respectively.

For most of the past 20 years, recall rates due to abnormal mammographic findings at mobile units have been slightly lower than at stationary units (Figure 4.28). Moreover, women screened at mobile units had lower cancer detection rates than women screened at stationary units (Figure 4.29). These differences were seen across all age groups, for prevalently and subsequently screened women, and for screen-detected and interval breast cancer. Differences in urban versus rural lifestyles, and distributions of sociodemographic factors associated with breast cancer may partially explain why recall and cancer detection rates were lower among women screened at mobile versus stationary units.

The positive predictive values of mammography (PPV-1) and of biopsy (PPV-2) were similar for mobile and stationary units. This indicates that the quality of care offered at mobile units was comparable to that offered at stationary units (Figure 4.30).

Figure 4.27: Radiographers Astri Brown and Berit Moen on mobile screening unit Frøya, stationed in Jevnaker (2016). Photo by Grete Lier, Oppland breast centre

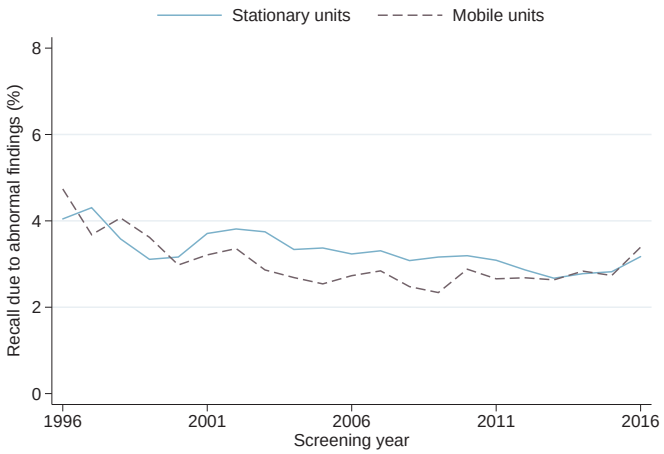


Figure 4.28: Recall rates due to abnormal mammographic findings (%) at stationary and mobile units by screening area and year, 1996-2016

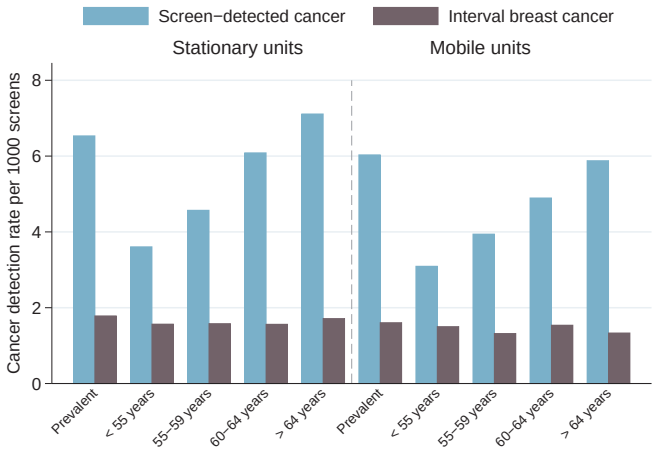


Figure 4.29: Screen-detected and interval breast cancer detection rates at stationary and mobile units per 1000 screening examinations by screening area and year, 1996-2016

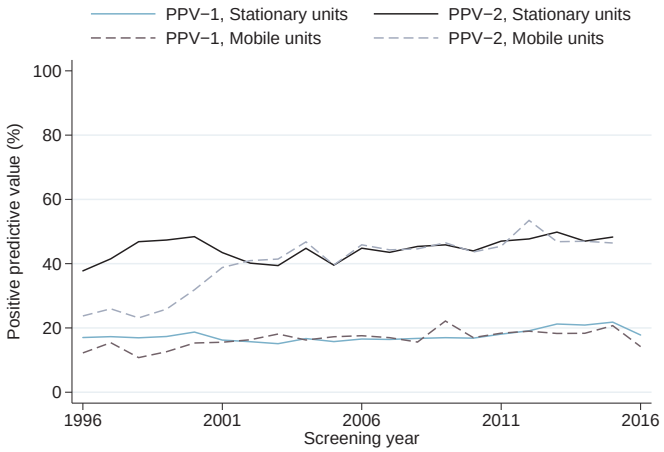


Figure 4.30: Positive predictive values of mammography (PPV-1) and biopsy (PPV-2) at stationary and mobile units by screening area and year, 1996-2016

Table 4.30: Percent (%) screening exminations performed at a mobile unit by screening area and year, 1996-2014

Screening area	Screening year					
	1996-2000	2001-2005	2006-2010	2011-2016	2016	Total
Rogaland	0 %	0 %	0 %	0 %	0 %	0 %
Hordaland	41 %	41 %	37 %	34 %	15 %	37 %
Oslo	0 %	0 %	0 %	0 %	0 %	0 %
Akershus	99 %	23 %	1 %			51 %
Telemark	0 %	0 %	0 %	0 %	0 %	0 %
Agder	4 %	2 %	1 %	2 %	0 %	2 %
Troms og Finnmark	83 %	70 %	68 %	49 %	63 %	62 %
Østfold		0 %	0 %	0 %	0 %	0 %
Nordland		72 %	69 %	65 %	63 %	68 %
Buskerud		28 %	18 %	43 %		24 %
Trøndelag		4 %	3 %	4 %	4 %	4 %
Oppland		6 %	9 %	17 %	16 %	12 %
Møre og Romsdal		3 %	5 %	7 %	6 %	5 %
Sogn og Fjordane		0 %	0 %	0 %	0 %	0 %
Vestfold		0 %	0 %	0 %	0 %	0 %
Hedmark		55 %	33 %	43 %	47 %	42 %
Akershus Øst			0 %	0 %	0 %	0 %
Akershus Vest			0 %	0 %		0 %
Vestre Viken				13 %	12 %	13 %
Total	36 %	19 %	14 %	14 %	12 %	17 %

"The attendance rate among women invited to mobile units is 5 percentage points higher than at stationary units: 80% versus 75% on average"

Surgical treatment

Roughly 62% of women diagnosed with screen-detected or interval breast cancer were treated with breast conserving surgery between 1996 and 2016. The proportion of women who received this treatment increased from 27% in 1996 to 79% in 2016 (Figure 4.31). The proportion of women in 2016 who received breast conserving surgery following a diagnosis of screen-detected DCIS was 80%, screen-detected invasive breast cancer was 80%, and of invasive interval breast cancer was 59%.

The proportion of women who underwent breast conserving surgery varied between screening areas (Figure 4.32). Of those areas that are currently active, the highest proportion of breast conserving surgery was performed in Telemark and the lowest in Hordaland, for both screen-detected and interval breast cancers. This variation has been observed in prior reports as well (*62*, *69*, *70*).

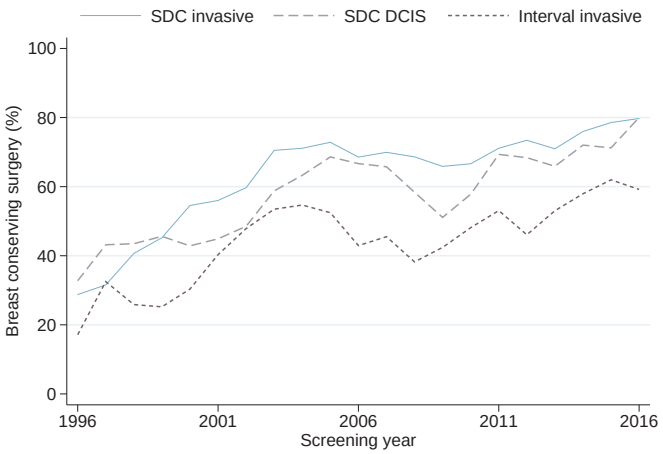


Figure 4.31: Proportion of women with invasive screen-detected breast cancer (SDC) or ductal carcinoma *in situ* (DCIS) (1996-2016) and with invasive interval breast cancer (1996-2014) who had breast conserving surgery by screening year

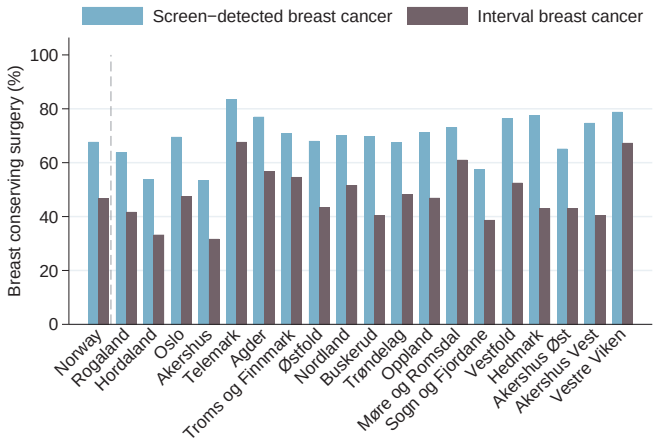


Figure 4.32: Proportion of women with screen-detected (1996-2016) or interval invasive breast cancer (1996-2014) who had breast conserving surgery by screening area

"Eight in ten women with screen-detected DCIS or invasive breast cancer received breast conserving surgery in 2016"

Summary

The evaluation of early performance measures helps to ensure that women are offered high quality health care. This section summaries a number of such measures over the past 20 years.

Roughly 75% of women attended screening following a personal invitation or reminder. Attendance rates varied by age: older women had higher attendance rates than younger women. Moreover, women who were subsequently invited to screening had higher attendance rates than prevalently invited women.

The overall recall rate decreased from 6.1% to 3.6% from 1996 to 2016. Recalls due to abnormal mammographic findings were 5.5% for prevalent screening examinations and 2.6% for subsequent examinations. Recall rates varied across screening areas.

Rates of screen-detected and interval breast cancer have been relatively stable since the start of the program (5.3-5.9/1000 screening examinations, and 1.7-1.9/1000 screening examinations, respectively). Interval breast cancers accounted for approximately 24% of all breast cancers detected among screened women, and the majority were diagnosed over a year after screening.

PPV-1 increased by roughly two percentage points from 1996 to 2016. Among screening examinations resulting in assessment because of abnormal mammographic findings, approximately 1 in 10 resulted in a diagnosis of screen-detected breast cancer among prevalently screened women. This rate was roughly twice as high for subsequently screened women (2 in 10). PPV-2 increased by roughly 15 percentage points from 1996 to 2016. Among those who underwent an invasive procedure, nearly 30% of prevalently screened women and over 50% of subsequently screened were diagnosed with screen-detected breast cancer.

Invasive carcinoma of no special type (previously referred to as invasive ductal carcinoma) was the most common breast cancer diagnosis for both screen-detected and interval breast cancers (70% and 77%, respectively). Moreover, approximately 17% of screen-detected and 6% of interval breast cancers were DCIS.

The size of interval breast cancers was slightly larger than screen-detected breast cancers (mean 21 mm, median 18 mm versus mean 15 mm, median 13 mm, respectively). Tumour size decreased with increasing age among women diagnosed with screen-detected breast cancer, but no such relationship was observed among women with interval breast cancer.

The increase in grade III tumours over time is striking (14% from 1996-2000 to 24% in 2016 among screen-detected cancers and 27% from 1996-2000 to 40% from 2011-2014 for interval breast cancers.) However, there are local variations in the distribution of grade, which may have clinical implications. This issue requires further investigation.

Roughly 25% of screen-detected breast cancers were lymph node positive, while this rate was about 40% for interval breast cancer. The increase in lymph node positive cancers over time may be associated with the introduction of the sentinel node technique. Differences in rates across screening areas is likely due to differences in local procedures and individual pathologists. The clinical implications of this variability need to be investigated.

The majority of women diagnosed with screen-detected breast cancer had oestrogen or progesterone receptor positive tumours (89% and 71%, respectively). Roughly 76% and 57% of women diagnosed with interval breast cancer had oestrogen or progesterone receptor positive tumours. There were small variations in hormone receptor status over time and between screening areas. It is difficult to determine how much variability in hormone receptor status is due to true geographical variation of breast cancer across screening areas, and how much is due to local pathologists.

Mobile screening is typically offered in more rural areas. Recall rates due to abnormal mammographic findings were higher at stationary versus mobile units from 2000 to 2013, as were screen-detected breast cancer rates. However, PPV-1 and PPV-2 did not differ for stationary and mobile units.

Nearly 70% of women with screen-detected invasive breast cancer had breast conserving surgery. A lower proportion of women diagnosed with DCIS or invasive interval breast cancer had this type of surgery. The proportion of breast conserving surgery varied between screening areas, with the lowest rate in Hordaland and the highest in Telemark.

Figure 4.33: Radiographers Gunvor Waade and Line Camilla Westermann evaluate the image quality of mammograms during "amabassador week" (2017). Photo by Anne Kathrin Ertzaas, Cancer Registry of Norway

5. Breast cancer mortality and early detection

Breast cancer mortality

The main aim of the Norwegian Breast Cancer Screening Program is to reduce breast cancer mortality by detecting cancer in an early stage. Substantial follow-up time and the availability of individual data are prerequisites to estimate this effect. Mortality reductions can be calculated among those invited (intention to treat) or among those who have ever attended the program (per protocol) (*71*). Not screened women are a heterogeneous group that includes both those who do not want to participate and those who undergo mammography at private clinics. Reductions in mortality are expected to be lower among invited women than screened women due to the inclusion of both screened and not screened women in the invited group.

The first study using data from the Norwegian Breast Cancer Screening Program to estimate breast cancer mortality was published in the New England Journal of Medicine in 2010 (*72*). Kalager et al. concluded that the screening program resulted in a 10% reduction in breast cancer mortality among invited women. This publication received a lot of attention and is frequently cited. However, the results have been discussed due to short follow-up time. Further, the inclusion of the first years of screening in the nominally exposed and non-exposed groups has been questioned because it counteracts the effect of prevalently screened women who have a higher incidence of breast cancer.

Two studies on breast cancer mortality were part of the external evaluation of the program (see page S56 for more details). Comparing breast cancer mortality among invited versus not invited women, Olsen et al. estimated that the screening program reduced mortality by roughly 10%, while Weedon-Fekjær et al. estimated the reduction to be 28% (*73*, *74*). The latter study had substantially longer follow-up time, and studied the effect on the entire Norwegian population, not only those in the pilot project.

In 2013, Hofvind et al. estimated that breast cancer mortality was 43% lower among screened versus not screened women (*75*). This study had 15 years of follow up, the longest of any Norwegian study so far. The decision to estimate the mortality reduction among screened women (per protocol) was discussed due to the potential for selection bias in favour of participation. However, the fact that the study was based on ever versus never screened might have underestimated the true effect of participation.

Information about screening outside the program has not been available for any of the aforementioned studies. This may have affected the observed effect in reducing breast cancer mortality. For this report we present the cumulative risk of breast cancer mortality among screened versus not screened women in the program since its start-up (Figure 5.1). The cumulative risk of breast cancer death among never screened women increased slowly from that of ever screened women after the start-up of the program in 1996. By the time the program was nationwide in 2005, the cumulative mortality was substantially higher among women who had never been screened. This difference increased over time and confirms that the reduction in breast cancer mortality among women screened in the program continues. However, more studies using both an intention to treat and per protocol design are needed to ensure the program continues to achieve its main goal.

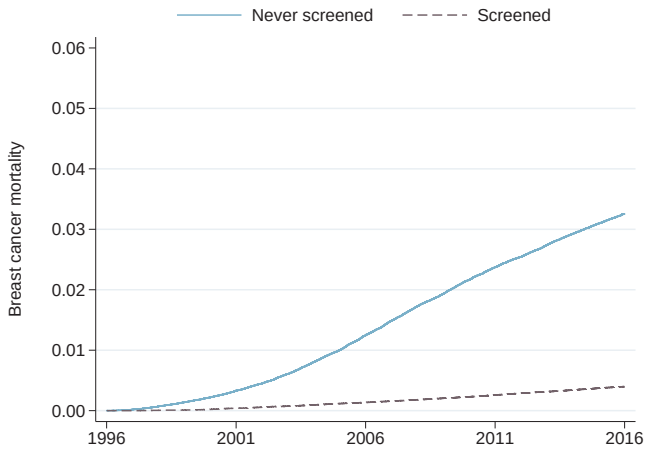


Figure 5.1: Cumulative breast cancer mortality among never screened and screened women in the Norwegian Breast Cancer Screening Program, 1996-2016

Table 5.1: Studies performed on breast cancer mortality among women invited to the Norwegian Breast Cancer Screening Program

Study	Study groups	Effect measure	Estimated effect
Kalager et al. 2010 (*72*)	Invited vs non-invited	Rate ratio difference	10 (95% CI -4 to 24)
Olsen et al. 2013 (*73*)	Invited vs non-invited	Rate ratio	0.93 (95% CI 0.77 to 1.12)
Weedon-Fekjær et al. 2014 (*74*)	Invited vs non-invited	Rate ratio	0.72 (95% CI 0.64 to 0.79)
Hofvind et al. 2013 (*75*)	Screened vs non-screened	Rate ratio	0.57 (95% CI 0.51 to 0.64)

Early detection and overdiagnosis

Detecting breast cancer in an early, asymptomatic stage is essential for successful screening and to reduce breast cancer mortality. However, during the past decades, the benefit of detecting early stage breast cancer has been questioned. Currently there is no method to identify which breast cancers will develop into aggressive disease, and which will never become life-threatening. All women diagnosed with *in situ* or invasive breast cancer are therefore offered treatment.

Detection of cancers that would have never been found were it not for screening is referred to as overdetection or overdiagnosis (*76*). Overdiagnosis occurs because some early stage breast cancers might be dormant or so slow growing that they never progress to become symptomatic in the absence of screening. Some women with breast cancer might therefore be overtreated or die from another cause before their cancer becomes evident (symptomatic). Overdiagnosis is only an epidemiologic term because whether a particular woman has an overdiagnosed cancer cannot be clinically verified.

The period between detecting an asymptomatic breast cancer at screening and its symptomatic stage, lead-time, is an inevitable part of screening. Due to the adoption of improved, digital screening tools, lead-time is assumed to be longer than it was using analogue mammography. This may have influenced the risk of detecting dormant or slow growing breast cancers.

Several papers show favourable tumour characteristics and prognoses among women with screen-detected versus interval breast cancer or breast cancer detected outside the screening program (*4*, *77*, *78*). In the first years following the start-up of the screening program in Norway, the majority of advanced breast cancer cases (stage ≥ 2) were detected at screening. However, the cumulative incidence of advanced breast cancer among women aged 50-69 diverged substantially between those who were and were not screened after the program became nationwide in 2005 (Figure 5.2).

Similar to estimating changes in breast cancer mortality as a result of organised breast cancer screening, estimation of overdiagnosis requires individual data, and substantial follow up time (*79*). The Independent UK Panel on Breast Cancer Screening presented four different measures of overdiagnosis based on whether estimates were based on invited or screened women, and follow up time (*12*). It is critical to be aware of the different approaches when communicating and comparing results from different studies (*80*).

There are several studies estimating overdiagnosis in the Norwegian Breast Cancer Screening Program. A summary of the results from four studies based on individual data and from three studies using ecologic data are presented in Table 5.2. These studies represent a mix of the four measures described by the Independent UK Panel and investigated invasive breast cancer alone and in combination with DCIS. The results highlight the inherent challenges in estimating overdiagnosis.

Because of the lack of consensus on optimal methods and resulting variability in methods used in the studies published to date, it is difficult to determine an accurate rate of overdiagnosis in the Norwegian screening program. The Research Council of Norway also underlined the large uncertainty in the estimation of overdiagnosis in their report (*13*).

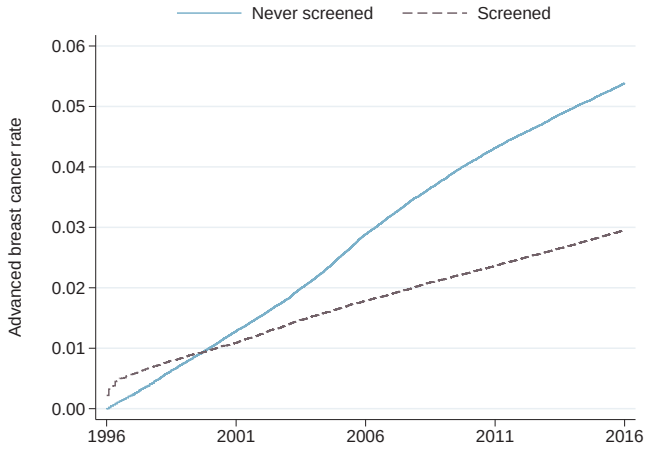


Figure 5.2: Cumulative rate of advanced breast cancer (stage ≥ 2) among women screened and never screened in the Norwegian Breast Cancer Screening Program, 1996-2016

Table 5.2: Studies evaluating overdiagnosis in the Nowegian Breast Cancer Screening Program. Note that various methods were used to calculate overdiagnosis and estimated rates may therefore not be diectly comparable

Study	Data	Comparison groups	Estimated rate of ovediagnosis
Zahl et al. 2004 (*81*)	Ecologic	Target vs non-target group	50%
Jorgensen et al. 2009 (*82*)	Ecologic	Target vs non-target group	37 to 52 %
Kalager et al. 2012 (*83*)	Ecologic	Target vs non-target group	18 to 25 %
Falk et al. 2013 (*84*)	Individual	Invited vs not invited Screened vs not screened	11 to 16 % 13 to 19 %
Lund et al. 2013 (*85*)	Individual	Screened vs not screened	7 to 18 %
Michalopoulos and Duffy 2016 (*86*)	Individual	Screened vs not screened	0 to 17%
van Luijt et al. 2016 (*87*)	Simulated (Individual)	Invited vs not invited	2 to 11%

6. Program evaluation and research

Ongoing quality assurance, program evaluation, and research activities contribute to the high quality of the Norwegian Breast Cancer Screening Program. Because of the personal identification number assigned to all residents in Norway and nationwide implementation, the screening program is in a unique position to perform truly population-based analyses. This section summarises the external evaluation performed by the Research Council of Norway in 2015 and describes what is known about the cost-effectiveness of the program. Further, past and present research conducted within the screening program is summarised. A full list of publications associated with the program is included at the end of this report (page S66).

External evaluation

From 2007 to 2015, the Research Council of Norway spearheaded an independent external evaluation of the Norwegian Breast Cancer Screening Program on behalf of the Ministry of Health and Care Services. The evaluation was conducted to determine whether the screening program had "fulfilled its intentions and purpose, and to establish a scientific basis for potential expansion of the screening program to include other age groups" (*13*). A particular focus of the evaluation was to determine whether the screening program had achieved a 30% reduction in breast cancer specific mortality among invited women.

To this end, an international call for research proposals was put forward in 2008. Projects were to evaluate the impact of the screening program on incidence (i.e. overdiagnosis), stage at diagnosis, interval breast cancer rates, breast cancer mortality, women's perspectives on the program, or costs associated with screening. Eight Norwegian and three international project proposals were submitted. Seven projects were funded: five lead by Norwegian investigators and two lead by international investigators.

The steering committee for the external evaluation stated that individual level data from a single database should be used for all projects. This way, any variation between study results could be attributed to differences in methodology. One set of quality assured data from the Cancer Registry was used to conduct all evaluation activities. However, the database at the Cancer Registry is designed for administrative purposes. Therefore, before the research teams could access any data, a research-friendly project database had to be established. This was completed in 2009.

Due to challenges related to changes in the informed consent model (see page S17), updated data from the Cancer Registry were available to research teams in 2012. Linked data from other registries were available in 2014.

The funded projects were completed by 2015 and results from observational studies suggested that the screening program reduced breast cancer mortality by approximately 20-30%. However, the effect of the screening program could not be completely disentangled from that associated with advances in diagnosis and treatment. Overall, the evaluation concluded that the program was cost effective on a societal level but that individual women need to make an informed decision whether to attend screening based on their own values. A recommendation was made for future research as well as for continued evaluation and monitoring of the screening program. The final report is available online (*13*).

Cost effectiveness

From a societal perspective, the balance between the benefits and costs associated with a national screening program must be within the accepted limits for health care services.

The cost-effectiveness of the program's first screening round was published in 2001 (*88*). The cost of screening was estimated to be 29,475 NOK per life-year gained, and 676,314 NOK per life saved. In 2015, the external evaluation published results about the economic effectiveness of the program. The direct and indirect costs associated with the organisation and operation of the program, including screening, recall examinations, treatments, and expenses incurred by women were assessed, and a cost-benefit analysis of the program was performed (*13*).

It was estimated that, in 2012, the cost per screening round was roughly 1400 NOK per woman screened (574 million NOK in total). This included costs associated with recall examinations, and women's time and travel expenses, but excluded costs associated with program administration. The average cost per screening round excluding recall examinations was 1300 NOK per woman screened: 64% of this was health service costs, 15% travel-related expenses, and the remaining 21% was associated with loss of productivity. The average cost of screening per recalled woman was estimated to be roughly 3700 NOK (*89*).

For women aged 50-69 diagnosed with breast cancer, the estimated cost of 10 years of treatment and follow up for breast cancer at a hospital was 356,000 NOK (based on 2008/09 data) (*90*). The costs of breast cancer treatment for women diagnosed within the screening program were roughly 60,000 NOK lower than for women diagnosed outside of the program.

In terms of quality of life, the cost per quality-adjusted life year (QALY) gained through mammographic screening was between 190,000-480,000 NOK, which was within the recommended threshold from the WHO (1.9 million NOK per QALY) (*13*).

Evaluation of the cost effectiveness of the screening program is dependent on accurate estimates of costs associated with screening. Researchers have indicated that there are a number of uncertainties in their calculations, but that overall the cost of the screening program is within what Norwegian health authorities define as acceptable for health services (*13*).

Research projects performed as a part of the screening program

The Oslo I and Oslo II studies

The Oslo I and Oslo II studies compared early performance measures and breast cancer detection rates from screen film and full-field digital mammography in the screening program. The principal investigator for both studies was professor emeritus Per Skaane.

In the Oslo I study, all participating women were screened using both screen film and digital mammography during a single visit between January and June 2000 in Oslo (*46*). Independent double reading with consensus was used. Meetings were held separately for screen film and digital mammograms. Images were interpreted without prior films for comparison. The study included a two-year follow-up to record cases of interval breast cancer and screen-detected cancer in the subsequent screening round. The study found no statistically significant difference in breast cancer detection rates between screen film and digital mammography (*26*). Moreover, cancer conspicuity was similar for both modalities.

In the Oslo II study, all women attending screening in Oslo between November 2000 and December 2001 were randomised to undergo either screen film or digital mammography (*47*). The process for image interpretation was the same as in Oslo I except separate consensus meetings were not held for screen film and digital mammograms. The study found that digital mammography was associated with a higher cancer detection rate than screen film mammography, and concluded that digital mammography with soft-copy reading was suitable for population-based mammography screening programs (*27*).

The Oslo tomosynthesis trial (OTST)

The aim of the Oslo tomosynthesis trial was to investigate early performance measures from full-field digital mammography and digital breast tomosynthesis (including synthetic mammography) combined in the Norwegian Breast Cancer Screening Program. The study was performed in Oslo from 2011 to 2012. Image interpretation was divided into four arms: digital mammography alone, digital mammography with computer aided detection, digital mammography with tomosynthesis, and tomosynthesis with synthetic mammography.

Interim analyses showed that screening with digital mammography and tomosynthesis led to a significantly higher cancer detection rate, increased the detection of invasive breast cancers in screening, and led to a decrease in false-positive recalls (*28*, *91*). Final results, including screen-detected cancer and interval breast cancer rates, are in progress.

The Oslo tomosynthesis trial was headed by professor emeritus Per Skaane. This trial is considered a pioneering study in the field of screening tomosynthesis, and provides a basis for the evaluation of implementing digital breast tomosynthesis in organised mammographic screening.

Ongoing research studies performed as a part of the screening program

The Tomosynthesis trial in Bergen (TOBE)

Digital breast tomosynthesis is claimed to be a better screening tool than the current standard (full-field digital mammography) based on studies showing lower recall rate and a higher rate of screen-detected breast cancer when screening with tomosynthesis compared to digital mammography (*59*, *60*). However, there is insufficient evidence to support the introduction of tomosynthesis as a tool for breast cancer screening in Norway (*92*). The Bergin tomosynthesis trail titled "Digital breast tomosynthesis – the future screening tool for breast cancer?" is an ongoing randomised controlled trial funded by the Research Council of Norway. The goal is to measure the effect of screening with tomosynthesis versus digital mammography by comparing results of early performance measures including radiation dose, tumour characteristics, and cost-effectiveness. The study started in 2015 and will be run for one screening round with two years' follow up to record cases of interval breast cancer. Professor Solveig Hofvind is the principal investigator for this study.

Oslo, Vestfold, and Vestre Viken study (OVVV)

Most studies investigating the effect of screening with digital breast tomosynthesis have used tomosynthesis in combination with full-field digital mammography. This almost doubles the radiation dose compared with digital mammography alone (*93*, *94*). Vendors now offer synthetic two-dimensional mammography generated from the raw tomosynthesis data in combination with tomosynthesis. The objective of the Oslo, Vestfold, and Vestre Viken study (OVVV) is to evaluate whether tomosynthesis is a modality suitable for screening when used independently of digital mammography. Women screened with synthetic mammography and tomosynthesis in Oslo will be compared to women screened with digital mammography in Vestfold and Vestre Viken, with a focus on early performance measures (recall rate, cancer detection rate, positive predictive values, and tumour characteristics). Women will be followed up until January 2018 to record cases of interval breast cancer. This study is considered a quality improvement study as part of the Norwegian Breast Cancer Screening Program.

Reviewing screening mammograms

During 2016 and 2017, radiologists from the screening program conducted an informed review of screening mammograms from 75 screen-detected and 75 interval breast cancer cases that were randomly selected from each breast centre in Norway. Consensus assessments from a panel of five radiologists were used to classify cases into one of five radiological classifications (missed, minimal sign actionable, minimal sign not actionable, true, or occult) based on the prior screening and diagnostic mammograms. A consensus assessment was also assigned for mammographic features, including mammographic density. This study will assess the mammographic features and histopathology associated with differing radiological classifications, stratified by mode of detection. This is a quality assurance/quality improvement study headed by the Cancer Registry of Norway. Funding for a PhD student has been applied for.

Figure 6.1: (L-R) Kaitlyn Tsuruda, Marie Lilleborge, Gunvor G. Wåde, Solveig Hofvind, Tone Hovda, Åsne S. Holen, Nataliia Moshina, and Sameer Bhargava, all presenters at the European Congress of Radiology, Vienna, Austria (March 2017)

Screening among immigrants

Mammographic screening and breast cancer among immigrant women has been investigated in many countries with organised screening, but never in Norway. The purpose of this study is to gain knowledge about immigrants and mammographic screening in Norway. This project will compare attendance rates among immigrant and non-immigrant women and study how attendance is associated with sociodemographic circumstances. Immigrant women's rationales for attendance and non-attendance in the screening program will be investigated. Lastly, this project will explore the relationships between screening parameters, tumour histopathology, and survival among immigrant and non-immigrant women diagnosed with breast cancer. This project is part of a PhD project performed by Sameer Bhargava. The primary investigator of the project is professor Solveig Hofvind.

Compression in mammography

Compression force is used in mammography to reduce breast thickness and thereby improve image quality and lower the radiation dose. The screening program's quality assurance manual states that the compression force for images acquired using digital mammography should be within 11 to 18 kg; however, there are no evidence-based recommendations for optimal compression force. The purpose of this study is to analyse breast compression parameters (such as compression force, pressure, and compressed breast thickness) and radiation dose in the screening program, as a first step toward establishing evidence-based recommendations for optimal breast compression. This study is a part of Gunvor Wåde's PhD project performed at Oslo and Akershus University College of Applied Sciences. Her main supervisor is Solveig Hofvind.

Pain and discomfort during screening

Compression during mammography may cause some women to experience pain or discomfort. Because of this, some women choose to not participate in organised mammographic screening. The purpose of this study is to examine the association between breast compression and women's expected and experienced pain and discomfort during mammography. This study started in 2017 and is a quality improvement study in the Norwegian Breast Cancer Screening Program.

Mammographic density

High mammographic density may result in delayed breast cancer diagnosis or missed cancers due to masking, and is independently associated with an increased risk of breast cancer. However, there is a lack of evidence about how mammographic density affects the performance of organised mammographic screening. The objective of this study was to investigate the association between mammographic density and early performance measures in organised screening. Early performance measures of interest were positive predictive values of recall and needle biopsy, and the number of women needed to be recalled or undergo a biopsy to detect breast cancer. Results from this study demonstrated that high mammographic density was lower positive predictive values, and the number of women needed to be recalled or biopsied increased with increasing density (*95*). Another study concluded that that high mammographic density is associated with less favourable histopathologic tumour characteristics in organised screening (*96*). This study was performed as a part of Nataliia Moshina's PhD project and is headed by professor Solveig Hofvind. Further studies will be performed on this topic.

Progression of premalignant lesions

A small proportion of women attending the screening program undergo a needle biopsy and are diagnosed not with invasive

breast cancer but a benign finding. Such findings can range from normal cells to atypical cells of an *in situ* (premalignant) lesion. Women diagnosed with a premalignant lesion are at an increased risk for developing invasive breast cancer in the future. In this project, women's screening histories are being used to estimate their long term risk of invasive breast cancer. Further goals are to identify epidemiological risk factors and mammographic features that can predict the progression of premalignant lesions. This is a part of a post doc project conducted by Marie Lilleborge. The study is a part of a larger ongoing multidisciplinary study about tumour progression.

PhD projects

The following PhD projects have been conducted using data from the screening program:

- Moshina, N. Understanding the role of mammographic density in a population based breast cancer screening program: a step towards stratified screening for breast cancer in Norway? Oslo: Faculty of Medicine, University of Oslo, 2017.
- Suhrke, P. The incidence and treatment of breast cancer in Norway over three decades. The relationship between mammography, hormone therapy use and overdiagnosis. Oslo: Faculty of Medicine, University of Oslo, 2017.
- Hoff, SR. Radiological and epidemiological aspects of mammographic screening. Trondheim: Faculty of Medicine, Norwegian University of Science and Technology, 2013.
- Falk, RS. Epidemiological studies of early-stage breast cancer in the Norwegian breast cancer screening program. Oslo: Faculty of Medicine, University of Oslo, 2013.
- Kalager, M. The Norwegian Breast Cancer Screening Program: effects on incidence, prognosis and mortality of breast cancer. Oslo: Faculty of Medicine, University of Oslo, 2012.
- Solbjør, M. Women's experiences of mammography screening: decision making, participation and recall. Trondheim: Faculty of Social and Educational Sciences, Norwegian University of Science and Technology, 2008.
- Weedon-Fekjær, H. Modelling breast cancer incidence, progression and screening test sensitivity using screening data. Oslo: Faculty of Medicine, University of Oslo, 2008.
- Hofvind, S. The Norwegian Breast Cancer Screening Program: selected process indicators and their utilization in epidemiological research. Oslo: Faculty of Medicine, University of Oslo, 2005.
- Wang, H. Epidemiological studies of breast cancer in Norway: with focus on implementation of organized mammography screening. Oslo: Faculty of Medicine, University of Oslo, 2002.

7. The future of breast cancer screening

Medical imaging has developed substantially since the first mammographic screening trial in 1963. The ever earlier detection of breast cancers is controversial because of the potential for the detection of dormant and slow growing tumours and subsequent overtreatment. There is a continuous need to generate new evidence about factors influencing breast cancer progression and detection, and how to use this information to improve organised screening and thus increase its benefits for individual women and society. Due to the complexity, uncertainty, and rapid changes in knowledge, the task of conveying information represents a continual challenge.

The use of personalised letters stating a time and place for screening examination was a major factor contributing to the success of the Norwegian Breast Cancer Screening Program when it started in 1995. Over twenty years later it is still just as important to the program's continued success. However, today an increasing amount of information is shared digitally with women: roughly 40% of women are invited through a secure digital mailbox. In the future, we aim to offer women online booking services, and make women's screening histories available online to them and their general practitioners. We believe that general practitioners will play an increasingly important role in breast screening and aim to support their role in informing women about breast care and the screening program in particular.

Mammographic imaging technology is steadily improving. Between 2000 and 2011, digital mammography replaced analogue mammography as a screening tool in the Norwegian screening program. Now tomosynthesis is being considered as an additional tool or a replacement for digital mammography (*5*, *92*). Tomosynthesis is commonly used for clinical mammography, but the evidence about the effectiveness of this technique as a screening tool is limited and still being generated. The transition from screen-film to digital mammography required substantial, expensive changes to the infrastructure used to acquire, interpret, and store mammography images. While the infrastructure needed for tomosynthesis is nearly identical to that for digital mammography, tomosynthesis will increase financial costs, mostly due to increased reading time and data storage (*5*, *92*). The financial cost of screening with tomosynthesis is not currently known for programs run based on the current European guidelines.

While mammographic x-ray tube positioning, detectors, positioning (views), and vendor-specific projection angles were tested, evaluated, and improved for digital breast tomosynthesis, contrast enhanced spectral mammography, hand-held and automated breast ultrasound, and MRI were adapted for screening and/or clinical mammography (*97*–*100*). Multimodality screening has come knocking on our door.

With all these improvements in imaging technology, women and society should benefit from an increase in program sensitivity. This improvement would ideally maintain the current rate of screen-detected breast cancer, as to not increase overdiagnosis, and reduce the rate of interval breast cancer. We hypothesise that in the future we will be able to identify dormant or slow growing breast cancers, and treat these cancers accordingly. We also hypothesise that multimodality screening will help us detect "missed" cancers and thereby reduce the rate of interval breast cancer. Reducing this rate will presumably be favourable for future disease specific mortality since interval breast cancers are usually detected in a later stage than screen-detected breast cancers.

Age and a number of other personal traits affect a woman's risk of breast cancer. There is a wide variation in the distribution of risk factors among women and therefore the lifetime risk of breast cancer. The target group of organised screening has been continuously discussed since the start-up of our program. Recently, the European Commission Initiative on Breast Cancer released recommendations for breast cancer screening (*5*). Their recommendation was based on strong evidence for organised screening of women aged 50-69 while the recommendations for age groups 45-49 and 70-74 were based on conditional evidence. We assume that a future discussion and subsequent investigation about expanding the target group of the Norwegian Breast Cancer Program will take place.

Like women, breast tumours are heterogeneous and can appear differently in different women. Some tumours may be clearly visible in mammographic fatty and dense breasts, while others may hide in dense parenchyma or not be visible on mammograms at all. A "one-size fits all" approach may thus not be ideal for individual women. As a result, risk-factor based stratification has been highly discussed during the past decade as a method to improve the sensitivity of screening programs. A number of strategies have been proposed (*101*–*104*). In particular, a survey of women's risk factors has been suggested before individual plans for breast screening schedules are established. This will result in different screening schedules for individual women: some women may receive annual multimodality screening, while others may receive mammographic screening every three years. Regular reviews will be needed due to changes in risk factors over time, such as the use of hormonal treatment and mammographic density. However, the practical aspects of such stratified screening need to be identified and standardised before they can be feasible. There are substantial organisational and practical challenges left to be resolved before organised biennial mammographic screening can change course. Moreover, extensive evidence is needed to guarantee that stratified screening is ethically justifiable, that is, that women are offered similar or better quality screening using a stratified model versus the current "traditional" model.

Many radiologists are involved in the interpretation of screening mammograms in an organised program. Computer aided detection (CAD) has been used as a method to improve the performance of screening mammography for decades (*105*). CAD is intended to reduce the rate of false negative findings but possibly at the cost of increased false positive findings (*106*, *107*). This might be

a reason why European screening programs generally have used double reading with consensus instead of using CAD.

Although traditional CAD is not widely used in European screening programs, machine learning methods, such as deep learning, offer new opportunities to make screening more effective, and appear to be taking off in this era of digital imaging. Organised mammographic screening generates large data sets due to the massive number of images acquired daily and the amount of information available for each image. Repeated examinations of the same women are performed at regular intervals and the availability of results for each screening examination provide ideal building blocks to develop evidence-based solutions for breast screening based on population-based data. Because of this, medical image analysis groups across the world are now quickly entering the field of radiology, and specifically breast imaging, to apply rapidly improving methodologies to a wide variety of applications. Results to date have been promising in the field of mammographic imaging (*108*). We think that machine learning methods will be able to reduce the workload of breast radiologists in screening, freeing up time to dedicate to clinical mammography, which will probably include a broader spectrum of diagnostic techniques in the future.

Non-imaging based solutions are also being investigated for their utility in early detection and ability to forecast breast cancer prognosis. Enzymes and proteins expressing abnormal cells might be strong markers for changes in the breast. Saliva and/or blood samples may one day have the potential to replace digital mammography or tomosynthesis as screening tools. Several breast centres have taken and/or take part in studies aimed at investigating blood as a marker to predict or identify cancer cells. Further studies using saliva are in progress. If we and our international colleges identify this marker, traditional imaging techniques may in turn be offered to women whose biological samples test positive for breast cancer. Similar to current practice, further assessment could include ultrasound, MRI, contrast enhanced spectral mammography or positron emission tomography/computed tomography.

Future developments in "-omics" (for example genomics, proteomics, metabolomics, and epigenomics) will certainly pave the way for understanding more about tumour characteristics, including biology, progression rates, and risk. This knowledge may help us identify more individualised treatments that are unique for specific tumours. The hope is that, as a result, overdiagnosis and overtreatment will be minimised, as will the side effects of treatment that women experience, and that breast cancer mortality will be diminished. However, years of experience tell us that we are a long way from taking these promising results from basic research to making changes in clinical practice. Currently, there are still huge knowledge gaps that need to be filled before this is a reality.

The "-omics" and other aspects of screening are challenging to understand. They are also challenging to communicate. Additionally, there is now an increased focus on personal privacy and data protection, which requires focused attention in order to satisfy the evolving privacy legislation. All these factors present a challenge with respect to providing women with information to make an informed choice about participation.

One of the goals of the Norwegian Breast Cancer Screening Program is to be among the best screening programs in the world. There are currently challenges related to data access and funding for quality improvement and research studies, particularly for a screening program that is administered and run very well. Until the future is here, we have many years ahead of us to work to increase the benefits and decrease the harms associated with breast cancer screening. We are dedicated and hope that the maintenance and further development of the screening program will be given political priority and financing.

Figure 7.1: The future of breast cancer screening is bright. Oslo breast centre, 2017. Photo by Wenche Melby, Cancer Registry of Norway

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