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METHODOLOGY

Existing data sources for clinical epidemiology: the Danish Quality Database of Mammography Screening

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Abstract: The Danish Quality Database of Mammography Screening (DKMS) was established in 2007, when screening was implemented on a nationwide basis and offered biennially to all Danish women aged 50–69 years. The primary aims of the database are to monitor and evaluate the quality of the screening program and – after years of follow-up – to evaluate the effect of nationwide screening on breast cancer-specific mortality. Here, we describe the database and present results for quality assurance from the first round of national screening. The steering committee for the DKMS defined eleven organizational and clinical quality indicators and standards to monitor the Danish breast cancer screening program. We calculated the relevant proportions and ratios with 95% confidence intervals for each quality indicator. All indicators were assessed on a national and regional level. Of 670,039 women invited for mammography, 518,823 (77.4%) participated. Seventy-one percent of the women received the result of their mammography examination within 10 days of screening, and 3% of the participants were recalled for further investigation. Among all detected cancers, 86% were invasive cancers, and the proportion of women with node negative cancer was 67%. There were 36% women with small cancers, and the ratio of surgery for benign lesions to malignant lesions was 1:6.3. A total of 80% of women with invasive cancers were treated with breast conserving therapy. Screening interval and interval cancers were not relevant in the first round, and data regarding radiation dose were not available at the time of evaluation. Overall, the quality indicators showed satisfactory quality in the first round of national breast cancer screening in Denmark. The DKMS is a potentially valuable tool for improving quality and conducting research in the field of breast cancer screening.

Keywords: screening, breast cancer, quality indicators

Introduction

Breast cancer is the most common female cancer in Denmark, with approximately 4500 women diagnosed each year.[1] In 2006–2010, breast cancer accounted for 28% of all incident cancers and 16% of all cancer deaths among Danish women.[2]

Mammography screening of asymptomatic women has the potential to detect breast cancer at an early stage and improve prognosis. An overview of the randomized trials in Sweden showed that, after a follow-up period of 5 to 13 years, breast cancer mortality was reduced 29% among women aged 50–69 years who were invited for breast cancer screening.[3] Numerous studies from different countries have concluded that organized mammography screening reduces breast cancer mortality,[4–6] though the extent of the reduction has been debated.[7,8]

In Denmark, organized population-based breast cancer screening with mammography began in Copenhagen in 1991, in the county of Funen in 1993, and in

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the municipality of Frederiksberg in 1994.[9] These three programs covered approximately 20% of the Danish female population aged 50–69 years.[9] Mammography screening was introduced in Bornholm in 2001 and in 2004 in the county of West Zealand. By law, breast cancer screening was implemented on a nationwide basis at the end of 2007 and offered free of charge every 2 years to all Danish women aged 50–69 years.[10]

The overall goal of a breast cancer screening program is to reduce breast cancer-specific mortality and morbidity with as few negative side effects as possible. To achieve this goal, high clinical and organizational standards are necessary in the screening program, as well as in the ensuing diagnostic and treatment processes.[9] The effect of screening on mortality cannot be evaluated until several years after the implementation of the program. Thus, continuous monitoring of the quality of all aspects of the screening program is essential for securing a high standard. Here, we describe the Danish Quality Database of Mammography Screening (DKMS) and present the results for quality assurance from the first round of national screening.

DKMS

In 2007, the Danish Regions appointed a steering committee for the DKMS to collect data and manage quality assurance. The committee has developed guidelines concerning organizational requirements for the Danish screening program[9] and defined eleven quality indicators and associated standards based on the fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis.[11] The screening program and establishment of the quality database are financed by the Danish health care system. The primary aims of the quality database are to monitor and evaluate the quality of the screening program and evaluate, after years of follow-up, the effect of nationwide screening on breast cancer-specific mortality.

Organization of the screening program

Every 2 years, all Danish women aged 50–69 years receive a letter with an invitation for a mammography. The five regions in Denmark, which all perform mammography screening, each have their own booking systems and send personal invitations to the women, based on updated population data from the Civil Registration System.[12] The women can decline participation or rejoin the screening program at any time. The invitation includes a suggested time for an appointment as well as an information leaflet about mammography screening. A questionnaire concerning issues, such as treatment with estrogen replacement therapy, previous breast surgery, and self-detected breast abnormalities, is enclosed with the invitation or presented at the time of screening. This information is forwarded electronically to the radiologists who evaluate the mammogram images. Two images are taken of each breast at each screening session. The images are read independently by two radiologists, at least one of whom is an experienced screening radiologist.[9] Any suspicious abnormalities detected by screening lead to further diagnostic investigation. Clinical examination, imaging, needle biopsy, and/or surgery are central to the diagnostic process. The diagnostic investigations of any abnormalities detected by screening adhere to the Danish Breast Cancer Cooperative Group's guidelines concerning diagnosis.[13]

Population in the first screening round

The first nationwide round of screening in Denmark covered the five regions over slightly different time periods. The first women were invited in mid-2007, and the last women were screened in December 2010.[14] Women who specifically requested not to participate in earlier local breast cancer screening programs conducted in some areas of Copenhagen, Zealand, and Southern Denmark were not invited to join the nationwide screening program. In the Capital Region of Denmark, women who had been operated on for breast cancer within the last 18 months were not invited. A total of 670,039 women were invited during the first round of screening, and 518,823 (77.4%) participated in the screening. Women who were invited more than once because they moved to another region during the study period were only counted once (n = 1289).[14]

Table 1 presents the proportion of invited women, according to age, who participated in the first round of the Danish screening program. Women aged 65–69 years were the least likely to participate in the screening. The same pattern was seen in each region except for the North Denmark Region (data not shown), where women aged 50–54 years were the least likely to participate (participation: 58.7%, 95% confidence interval 58.0–59.3). In all regions, the mean age of the women who participated in screening was 59 years old (data not shown).

Data and data linkage

Data from the booking system (civil registration number, screening round, date of invitation, date of screening, and date of sending the screening result to the woman) in each of

Table 1 Proportion of invited women who participated in the first round of nationwide mammography screening

Age group (years)	Number of screened women	Number of invited women	Proportion (95% CI)
<50[a]	12	36	33.3 (18.6–51.0)
50–54	140,558	182,212	77.1 (76.9–77.3)
55–59	133,167	167,713	79.4 (79.2–77.3)
60–64	140,113	178,345	78.6 (78.4–78.8)
65–69	103,084	138,890	74.2 (74.0–74.4)
>69[a]	1889	2843	66.4 (64.7–68.2)
Total	518,823	670,039	77.4 (77.3–77.5)

Note: [a]The table includes women who turned 50 or 70 years during the year of invitation to screening.
Abbreviation: CI, confidence interval.

the five Danish regions are transferred electronically to the DKMS. The data are registered and validated by the DKMS in an ongoing process, and the completeness of data in the DKMS is almost 100%.[14]

Data regarding biopsies are reported online to the Danish National Pathology Registry (DNPR), which contains detailed records of all cytological and histological specimens analyzed in Denmark since 1997.[15] Reporting to the DNPR is based on national guidelines for uniform registration. Data are updated on a daily basis and are of high quality and completeness.[15] From this registry, the DKMS retrieves primary outcome data [breast cancer, ductal carcinoma in situ (DCIS) lesions, tumor size, and node negative cancers] for all women in the cohort.

Information on the results of mammography screening (normal/abnormal), surgery for malignant and benign lesions, and the number of women with breast cancer treated with breast conserving therapy is retrieved from the National Registry of Patients. This registry contains detailed information, including the civil registration number, date of admission and discharge, and up to 20 discharge diagnoses and procedures for all patients admitted to a somatic hospital in Denmark since 1977, including all outpatient contacts since 1995.[16] To calculate the number of interval cancers as a proportion of the underlying expected breast cancer incidence rate in the absence of nationwide screening, information about the incidence of breast cancer in the background population in 2006 is ascertained from the Danish Cancer Registry.[17]

Data from all sources are linked using the civil registration number, a unique ten digit personal identification number assigned to each Danish resident. The Civil Registration System is continuously updated with information on all Danish residents regarding vital status, change of address, and emigration.[12]

Quality indicators

The eleven organizational and clinical quality indicators and standards defined by the DKMS steering committee to monitor the Danish breast cancer screening program are participation, screening interval, time to result, radiation dose, recall, interval cancers, invasive tumors, node negative cancers, small cancers, breast conserving therapy, and ratio of surgery for benign to malignant lesions.

Organizational quality indicators

Participation

For screening to achieve an effect on breast cancer morbidity and mortality, high participation is important. The proportion of invited women who participate in mammography screening, excluding women who have resigned from the program, has a standard value of >75%. In contrast, the proportion of all women aged 50–69 years who reside in Denmark at the start of the screening round and participate in the screening has no set standard.

Screening interval

Monitoring the screening interval is an important quality control factor for increasing the detection of tumors at an early stage. In Denmark, the interval between screens has been set to 24 months (±3 months), which is in accordance with the majority of other population-based screening programs.[9] The interval is a measure of the number of women who are re-invited to screening within 24 months (±3 months) compared to all women re-invited to screening. The standard value for this indicator is ≥98%.

Time from screening to result

Waiting for results may induce unnecessary anxiety. The number of women who received their screening result ≤ 10 working days after screening compared to the total number of women who were screened has a standard value of >95%. Women without a registered date for their results in the first screening round were excluded from the present analysis.

Clinical quality indicators

Radiation dose

Technical quality control will ensure that the radiologist obtains the best possible images using the lowest possible radiation dose.[11] Data are reported as the mean glandular dose, which is the radiation dose measured on a 45 mm polymethylmethacrylate test phantom corresponding to a 53 mm standard breast.[14] The radiation dose should be measured once a week on all technical equipment used

for mammography screening.[14] The standard value for this indicator is <2.0 mGy.

Recall

Any suspicious abnormalities detected on mammogram led to a recall for additional diagnostic investigation. To reduce cost and minimize anxiety, the number of recalled women without cancer (false positives) should be kept as low as possible with due respect to the detection rate. The proportion of all screened women recalled for further examination (including true and false positives) has a standard value of <5% in the first screening round (prevalent and incident cases) and <3% in subsequent screening rounds (incident cases).

Interval cancers

A screening program cannot identify all malignant tumors at a given time.[9] This indicator describes the number of over-looked, fast growing, or radiologically undetectable invasive malignant tumors at the time of screening and reports the number of women diagnosed with invasive malignant tumors in the 2 year interval after the women tested negative at screening, compared to the occurrence of breast cancer in the background population in the absence of screening (in 2006). The standard value for this indicator is <30% (≤12 months after screening) and <50% 12–24 months months after screening).

Invasive breast tumors

A potential negative effect of breast cancer screening is over-diagnosis, which is defined as the identification of cancers that would not have been found during the lifetime of the woman in the absence of screening.[9] To minimize the risk of over-diagnosis and over-treatment, the relative number of DCIS cases identified in a screening program should not exceed 20%, and it should not be less than 10%; 30%–50% of DCIS lesions are estimated to progress to invasive cancer.[9] The number of women with invasive cancers compared to the total number of women diagnosed with cancer (including DCIS) due to the organized screening program has a standard value of 80%–90%.

Node negative cancers

Node status is a prognostic factor for breast cancer survival. Detecting cancer at an early stage increases the likelihood of negative axillary status. The number of women with invasive node negative cancers compared to the total number of women operated on for invasive breast cancer due to the organized screening program has a standard value of >70% during the first screening round (prevalent and incident cases) and >75% during subsequent screening rounds (incident cases).

Small cancers

Tumor size is a prognostic factor, and the percentage of small cancers is a principal radiological quality indicator. The number of women with an invasive cancer ≤ 1 cm compared to the total number of women operated on for invasive cancer due to the organized screening program has a standard value of ≥25% during the first screening round (prevalent and incident cases) and ≥30% during subsequent screening rounds (incident cases).

Surgery for benign versus malignant lesions

The ratio of the number of surgeries for benign lesions to the number of surgeries for malignant lesions is an indicator of the combined quality of the diagnostic team consisting of radiologists, surgeons, and pathologists.[9] The number of women with benign lesions who are referred to surgery should be kept as low as possible without compromising the detection of malignant lesions. The ratio of the number of women with benign lesions who are referred to surgery and the number of women with malignant lesions (including DCIS) who are referred to surgery has a standard value of ≤1:4.

Breast conserving therapy

Mammography screening leads to the detection of cancer at an early stage, increasing the potential for breast conserving therapy. The number of women diagnosed with invasive cancer and treated with breast conserving therapy compared to the total number of women operated on for invasive breast cancer due to the organized screening program has a standard value of >50% during the first screening round (prevalent and incident cases) and >60% during subsequent screening rounds (incident cases).

Data analysis

To evaluate whether the screening program performed as desired, we calculated the relevant values and 95% confidence intervals for each quality indicator in accordance with the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis.[11] All indicators were assessed on a national and regional level.

First results

Tables 2 and 3 present the organizational and clinical quality indicators based on the first screening round in Denmark,

Table 2 Organizational quality indicators based on the first round of nationwide mammography screening in Denmark

Organizational quality indicators	Number of women	Proportion (95% CI)	Standard[a]
Proportion of invited women who participated in the screening program			
Screened women/all women invited			>75%
Capital Region of Denmark	139,987/191,279	73.2% (73.0–73.4)	
Region Zealand	91,113/111,522	81.7% (81.5–81.9)	
North Denmark Region	48,980/75,260	65.1% (64.7–65.4)	
Central Denmark Region	115,717/149,817	77.2% (77.0–77.5)	
Region of Southern Denmark	123,026/142,161	86.5% (86.4–86.7)	
Total	518,823/670,039	77.4% (77.3–77.5)	
Proportion of women in the target population who participated in screening			
Screened women/women living in the region, aged 50–69 years, January 1, 2010			Not defined
Capital Region of Denmark	139,987/195,013	71.8% (71.6–72.0)	
Region Zealand	91,113/112,249	81.2% (80.9–81.4)	
North Denmark Region	48,980/73,861	66.3% (66.0–66.7)	
Central Denmark Region	115,717/149,266	77.5% (77.3–77.7)	
Region of Southern Denmark	123,026/152,057	80.9% (80.7–81.1)	
Total	518,823/682,446	76.0% (75.9–76.1)	
Time from screening to result			
Women who received their result ≤10 days after screening/all women screened[b]			>95%
Capital Region of Denmark	30,345/139,841	21.7% (21.5–21.9)	
Region Zealand	71,778/90,931	78.9% (78.7–79.2)	
North Denmark Region	27,373/40,996	66.8% (66.3–67.2)	
Central Denmark Region	111,911/115,708	96.7% (96.6–96.8)	
Region of Southern Denmark	121,700/123,006	98.9% (98.9–99.0)	
Total	363,107/510,482	71.1% (71.0–71.3)	

Notes: [a]Standards are defined by the steering committee for the Danish Quality Database of Mammography Screening (DKMS) based on the fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis;[11] [b]8341 women were excluded because the date of result was undisclosed.
Abbreviation: CI, confidence interval.

excluding screening interval, interval cancers, and radiation dose. The screening interval and interval cancers were not relevant to the first round, and data regarding radiation dose were not available at the time of evaluation. An effort is currently being made to ensure that radiation dose is measured on a weekly basis and reported to the DKMS.

Regional differences were found in the proportion of women who participated in the screening (Table 2) but, with the exception of the Danish Capital Region (73%) and the North Denmark Region (65%), participation in all regions met the standard of >75%. Only 71% of the women received the result of their mammography examination within 10 days of screening, and the regional differences were large. The long time for a response reflects the fact that the screening program was undergoing implementation and that only screening radiologists read the mammogram images in order to achieve high quality. Time to response is expected to be reduced when the program is fully implemented.

Only 3% of the participants were recalled for further investigation, and all regions fulfilled the standard (Table 3). Among all detected cancers (including DCIS), 86% were invasive cancers and, with the exception of the North Denmark Region (92.2%), all regions complied with the standard. The proportion of women with node negative cancer was 67%, which did not meet the standard of >70% based on the European Guidelines. However, these guidelines were written before the implementation of the sentinel lymph node technique, which facilitates the identification of lymph node metastases. A previous study found that the introduction of sentinel lymph node dissection in Denmark resulted in a stage migration of 4% due to the identification of more micrometastases.[18]

All regions fulfilled the standard for the proportion of small cancers. However, information on tumor size was missing for 835 women (21.3%), who were excluded from the analysis. Initiatives have been launched to increase the registration of tumor size, which is a new variable in the DNPR.

The ratio of surgery for benign lesions to malignant lesions was fulfilled by all regions except the North Denmark Region (ratio 1:3.6). In addition, a total of 80% of women with invasive cancers were treated with breast conserving therapy, which means that the standard of >50% was

Table 3 Clinical quality indicators based on the first round of nationwide mammography screening in Denmark

Clinical quality indicators	Number of women	Proportion or ratio (95% CI)	Standard[a]
Recall			
Recalled women/all women screened			<5%
Capital Region Denmark	3982/139,987	2.8% (2.8–2.9)	
Region Zealand	2477/91,113	2.7% (2.6–2.8)	
North Denmark Region	2351/48,980	4.8% (4.6–5.0)	
Central Denmark Region	3456/115,717	3.0% (2.9–3.1)	
Region of Southern Denmark	3165/123,026	2.6% (2.5–2.7)	
Total	15,431/518,823	3.0% (2.9–3.0)	
Invasive breast tumors			
Women with invasive cancers[b]/all women with cancer (including DCIS)			≥80% and ≤90%
Capital Region of Denmark	1059/1235	85.7% (83.7–87.7)	
Region Zealand	753/882	85.4% (82.9–87.6)	
North Denmark Region	400/434	92.2% (89.2–94.5)	
Central Denmark Region	963/1096	87.9% (85.8–89.7)	
Region of Southern Denmark	933/1110	84.1% (81.8–86.2)	
Total	4108/4757	86.4% (85.3–87.3)	
Node negative cancers			
Women with node negative invasive carcinomas/women operated on for invasive carcinomas[c]			>70%
Capital Region of Denmark	682/1008	67.7% (64.7–70.5)	
Region Zealand	500/717	69.7% (66.2–73.1)	
North Denmark Region	237/385	61.6% (56.5–66.4)	
Central Denmark Region	590/876	67.4% (64.1–70.5)	
Region of Southern Denmark	605/892	67.8% (64.6–70.9)	
Total	2614/3878	67.4% (65,9–68,9)	
Small cancers			
Women with invasive carcinomas ≤1 cm/women operated on for invasive carcinomas[d]			≥25%
Capital Region of Denmark	279/718	38.9% (35.3–42.5)	
Region Zealand	274/717	38.2% (34.6–41.9)	
North Denmark Region	66/228	28.9% (23.2–35.3)	
Central Denmark Region	196/591	33.2% (29.4–37.1)	
Region of Southern Denmark	312/840	37.1% (33.9–40.5)	
Total	1127/3094	36.4% (34.7–38.1)	
Ratio of surgery for benign versus malignant lesions[e]			
Women operated on for benign lesions/women operated on for malignant lesions (incl DCIS)[f]			Ratio: ≤1:4
Capital Region of Denmark	131/1196	1:9.1	
Region Zealand	119/857	1:7.2	
North Denmark Region	119/430	1:3.6	
Central Denmark Region	178/1033	1:5.8	
Region of Southern Denmark	198/1147	1:5.8	
Total	745/4663	1:6.3	
Breast conserving therapy			
Women with invasive carcinomas treated with breast conserving therapy/women operated on for invasive carcinomas			>50%
Capital Region of Denmark	811/1022	79.4% (76.7–81.8)	
Region Zealand	628/726	86.5% (83.8–88.9)	
North Denmark Region	271/389	69.7% (64.8–74.2)	
Central Denmark Region	670/887	75.5% (72.6–78.3)	
Region of Southern Denmark	770/905	85.1% (82.6–87.3)	
Total	3150/3929	80.2% (78.9–81.4)	

Notes: [a]Standards for each quality indicator are defined by the steering committee for the Danish Quality Database of Mammography Screening (DKMS) based on the fourth edition of the European Guidelines for Quality Assurance in Breast Cancer Screening and Diagnosis;[11] [b]includes women diagnosed with invasive carcinomas, sarcomas, or malignant lymphomas. Data extracted from the DNPR; [c]51 women were excluded due to missing information on axillary status. Data extracted from the DNPR; [d]835 women were excluded due to missing information on tumor size. Data extracted from the DNPR; [e]assessed as a proportion (women operated on for benign lesions/all women operated on for breast tumors) and with a standard of ≤20%, the proportions (95% CI) were: 9.9% (8.3–11.6), 12.2% (10.2–14.4), 21.7% (18.3–25.4), 14.7% (12.8–16.8), 14.7% (12.9–16.7), and 13.8% (12.9–14.7) for Capital Region of Denmark, Region Zealand, North Denmark Region, Central Denmark Region, Region of Southern Denmark, and all of Denmark, respectively; [f]data on women operated on for a malignant lesion were extracted from the NRP. The number is not equal to the number of invasive carcinomas registered in the DNPR.

Abbreviations: CI, confidence interval; DCIS, ductal carcinoma in situ; DNPR, Danish National Pathology Registry; NRP, National Registry of Patients.

met easily. The high incidence of breast conserving therapy can be explained by changes in surgical practice.

Conclusion

Overall, the quality indicators showed satisfactory quality in the first round of national breast cancer screening in Denmark. The DKMS is a potentially valuable tool for improving quality and conducting research in the field of breast cancer screening. However, the data have some limitations. Data from the first screening round did not include information on the screening interval or interval cancers due to the short follow-up time. The fact that local screening programs were conducted in some areas of Denmark before the nationwide screening program was implemented is a limitation for comparisons between regions, as the screening program will detect more prevalent cases in some regions than in others. Comparing results from the first screening round to results from the second round, where predominantly incident cases are detected, may also be difficult.

The strengths of the DKMS include a large sample size that increases every year and detailed registration of the quality indicators with regular quality assessment. Breast cancer screening is free of charge and all Danish women between 50 and 69 years of age are invited to participate, which reduces potential selection bias. In addition, we are able to obtain nearly complete follow-up for the main outcomes: invasive breast tumors, node negative cancers, small cancers, breast conserving therapy, and mortality from nationwide registries. Thus, women who decline participation in the screening program or drop out after a few screening rounds can be compared to women who stay in the program in regards to breast cancer-specific morbidity and mortality.

In this baseline study, we did not adjust for potential confounders, such as the age and socioeconomic background of the participants, which may differ between regions. However, we found no differences in the mean age of screening participants in the five regions. Thus, we assume no confounding occurred due to age. In future studies based on the DKMS, data on different exposures, such as comorbidity, demographic variables, and socioeconomic status, can be retrieved from other Danish registries and enable the researchers to control for several potential confounders in multivariable analyses.

Access for other researchers

The data are held by the DKMS at Competence Center North, Department of Clinical Epidemiology, Aarhus University Hospital. The DKMS home page can be accessed on the web via: http://kea.au.dk/kliniskkvalitet/kliniskedatabaser/danskkvalitetsdatabaseformammografiscreening/. We encourage interested parties to contact the chairman of DKMS, senior consultant Jens Peter Garne at jpg@rn.dk or senior researcher Ellen M Mikkelsen at em@dce.au.dk.

Disclosure

The authors report no conflicts of interest in this work.

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