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Variations in pathways and resource use in follow-up after abnormal mammography screening: A nationwide register-based study.

Susanne Fogh Jørgensen,[a,b*](ORCID: 0000-0003-4534-0351) Berit Andersen,[a,b] (ORCID: 0000-0003-4074-6504) Anders Lernevall,[a] Matejka Rebolj,[cα] (ORCID: 0000-0001-9597-645X) Sisse Helle Njor[a,bα] (ORCID: 0000-0003-0429-4176)

[a] University Research Clinic for Cancer Screening, Department of Public Health Programmes, Randers Regional Hospital

[b] Department of Clinical Medicine, Aarhus University, Aarhus, DK

[c] Cancer Prevention Group, School of Cancer & Pharmaceutical Sciences, Faculty of Life Sciences & Medicine, King's College London, London, UK

* Corresponding author. Email address: susanne.fogh@rm.dk. Full postal address: Randers Regional Hospital, Department of Public Health Programs, Skovlyvej 15, 8930 Randers NØ, Denmark

[α] Contributed equally

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Abstract

Purpose: Mammography screening reduces breast cancer mortality, but a successful screening programme depends on both high participation and a sufficient follow-up of abnormalities. This study investigated patterns of follow-up after abnormal screening mammography in Denmark, and whether the variation was associated with health care resource use.

Methods: We included 19,458 women aged 50-69 years with an abnormal screening mammography during a 3-year period of 2014-2016. Women were followed until the end of 2018. Their follow-up pathway was categorized in terms of the timeliness, appropriateness (i.e., whether all recommended diagnostic tests were utilised), and the ratio of benign vs. malignant surgeries. Further, we estimated health care resource use including post-diagnostic imaging and surgery procedures.

Results: Ninety-seven percent of women had a diagnostic follow-up test within 6 months and 94% of those had diagnostic procedures in accordance with the recommendations. The proportion with timely follow-up (i.e., within 1 month) was 83%, but varied significantly between administrative regions ($p<0.001$), and also between women with a screen-detected cancer and those with a false-positive mammogram (87% vs. 81%, $p<0.001$). The ratio between having a benign vs. a malignant surgery was 1:8, but it varied depending on which tests were used for diagnosis. The average number of procedures was, generally, in accordance with the recommendations.

Conclusion: In most cases, follow-up after abnormal screening mammography followed national recommendations. We nevertheless found that this was not always the case in certain subgroups and administrative regions.

Keywords: screening, screening mammography, breast cancer, diagnostic resolution, follow-up time, guideline adherence

List of abbreviations:

BI-RADS – Breast Imaging Reporting and Data System

CIS – Carcinoma in situ

DBCG – Danish Breast Cancer Cooperative Group

DCIS – Ductal carcinoma in situ

DKMS – The Danish Quality Database for Breast Cancer Screening

PLCIS – Pleomorphic lobular carcinoma in situ

UL – Ultrasound

MRI – Magnetic Resonance Imaging

Introduction

Breast cancer is the most common female cancer.[1] Participation in mammography screening reduces breast cancer mortality,[2, 3] however, sufficient and timely follow-up of screen-detected abnormalities is crucial in avoiding the worsening of the cancer prognosis.[4, 5] Follow-up pathways to investigate these abnormalities usually require multiple diagnostic procedures to be undertaken at predetermined times. Detailed information on guideline adherence is limited and while several studies have evaluated the follow-up adherence, they have primarily focused on the proportion of women with at least one diagnostic appointment and whether the timing of that appointment was as recommended.[6-10] Few studies differentiated between the types of diagnostic procedures that were utilised.[8-10] To our knowledge, no study has evaluated whether the recommended follow-up processes were followed in their entirety and with the correct timing, and also not how that affected the health care resource use. Such data would greatly benefit when, for example, assessing the extent of the screening programme and the related activities within a health care setting, and in informing cost-effectiveness analyses.

We studied patterns of adherence to the recommended clinical follow-up after an abnormal screening mammography in Denmark, and how that variation was associated with the performance of the diagnostic process and health care resource use.

Methods

Setting

In Denmark, women aged 50-69 years are invited to participate in biennial mammography screening, which started being rolled out nationwide in 2007, although a few counties had implemented it earlier.[3] National coverage was achieved by 2011.[11] The programme is organized within the 5 administrative regions that govern health care services provided by primary and secondary health care providers.[12]

National clinical guidelines for follow-up after an abnormal screening mammography were published by the Danish Breast Cancer Cooperative Group (DBCG).[13] All women with screen-detected abnormalities are recommended to have a supplemental mammography (which can also be done as magnetic resonance imaging [MRI] or tomosynthesis), ultrasound, and a clinical examination, preferably in a single appointment. If relevant, women should also have a breast biopsy from any suspicious area. These elements together are referred to as the "diagnostic mammography". Screening and follow-up procedures are free of charge for all women.

Study design

We included women aged 50-69 years who were invited for mammography screening between 1 January 2014 and 31 December 2016 and had an abnormal screening mammography. In Denmark, screening mammograms referred to further diagnostics, are solely registered with a code for 'normal' or 'abnormal´ even though the Breast Imaging-Reporting and Data System (BI-RADS) or a modified version thereof may be used by breast radiologists internally [14, 15], When a woman had more than one abnormal mammography in the study period, only the first was included. Women with a previous diagnosis of breast cancer were excluded because they might still be in post-treatment follow-up. We additionally excluded women who died or emigrated within 30 days of screening. Women who died later than 30 days after screening were included to avoid underestimating the resource use in women with cancer.

A screening episode was defined as the period from the abnormal screening mammography until the subsequent screening mammography after approximately two years, diagnostic resolution, or 31 December 2018, whichever came first. Diagnostic resolution was defined as either a diagnosis of invasive breast cancer or carcinoma in situ (CIS), the last test before a return to regular screening,

or no more tests in 1.5 year. Episodes included also post-diagnostic procedures for women with screen-detected cancer.
We included all follow-up mammograms, breast-tomosyntheses, ultrasounds, breast MRIs and other imaging procedures such as galactography, coil-placement, breast-cystography and needle-marking. Furthermore, we included biopsies (stereotactic or guided by ultrasound), surgeries and other excisional procedures where the topography in the pathology register was breast. To avoid counting diagnostic procedures because of emerging symptoms, the first follow-up visit had to be within 6 months after screening.

Women were categorized into follow-up pathway groups depending on the tests they received before diagnostic resolution. These groups were: 1) no follow-up within 6 months, 2) mammography, ultrasound and biopsy (fine needle or core), 3) mammography and ultrasound only, 4) biopsy only, 5) mammography and biopsy only, 6) ultrasound and biopsy only, and 7) ultrasound only or mammography only. Groups 2 and 3 were in accordance with the national guidelines.[13]

Cancer diagnoses were considered screen-detected if made within 6 months of screening, and interval cancers if diagnosed later than 6 months after screening but before the next screen. CIS diagnoses included ductal carcinoma in situ (DCIS) and pleomorphic lobular carcinoma in situ (PLCIS). Women without a screen-detected cancer or CIS were considered to have a false-positive mammogram.

Surgeries among women with a screen-detected cancer diagnosis were considered malignant surgeries, whereas surgeries without a breast cancer diagnosis were considered benign. To compare the diagnostic work-up between the different pathways, we calculated the benign/malignant surgery ratio for each pathway.

Information on screening invitations during the study period was retrieved from the Danish Quality Database for Mammography Screening (DKMS).[11] Information of screening outcomes and diagnostic procedures was retrieved from the Danish National Patient Register.[16] All cytological and histological diagnoses resulting from biopsies and surgeries were retrieved from the National Pathology Register.[17, 18] Information on cancer diagnoses was retrieved from the Danish Cancer Register.[19] Screening data were linked with birth dates, and vital and emigration status from the

Civil Registration System[20] using the unique personal identification numbers that are mandatory for all Danish residents.

As a legal requirement, women should be offered a first diagnostic procedure no later than 14 days after consensus has been reached by two radiologists regarding the suspicious screening mammography.[13] Date of consensus is though only registered in local patient systems and is not available for research. It is, furthermore, recommended that women receive the result of the screening mammography within 10 working days (approximately 14 days) of screening. The first follow-up test should therefore be within 28 days of screening. We defined timely follow-up as the first diagnostic procedure taking place within 1 month of screening.

The total time to resolution was defined as the difference between the date of screening and the date of diagnostic resolution. For women with screen-detected cancer, we also calculated the time spent in the post-diagnostic pathway.

The total volume of diagnostic and treatment resources utilised during follow-up, for each pathway separately, were determined for imaging procedures, surgeries, and needle and excisional biopsies. We did not include clinical examinations, as they could not be differentiated from clinical examinations for other conditions.

Statistical analysis

The time to the first follow-up test and the total time to resolution were presented as medians and interquartile ranges (IQR). The variation in timely follow-up between administrative regions was tested using the chi-squared test. Exact binomial 95% confidence intervals were calculated for proportions and ratios. Resources used in the different pathways were presented as means and ranges between the 5th and the 95th percentiles (p5-p95). Following the national data protection restrictions, the absolute numbers were not reported when counts were smaller than 5.

Results

Study population

We identified 20,057 abnormal screening mammograms during the study period, resulting in a referral rate of 2.4% (Figure 1). After exclusions explained above, 19,458 women were included in the analyses.

Diagnostic follow-up pathways

The frequency of the seven diagnostic pathways are presented by 5-year age group and administrative region in Table 1. A total of 18,867 women (97.0%) had at least one follow-up procedure within 6 months of screening. Of those, 17,652 (93.6%) had diagnostic procedures as recommended by the guidelines, i.e. in groups 2 (diagnostic mammography, ultrasound and biopsy) or 3 (diagnostic mammography and ultrasound only). Older women more often had a biopsy in their diagnostic pathway, probably due to the higher cancer risk. Furthermore, some regional variation in biopsy use could be observed. The proportions of women undergoing other pathways tended to be very small and varied between administrative regions. This was predominantly the case for group 7 (where women underwent only an ultrasound or only a mammography examination), suggesting different practices throughout the country. For example, when supplemental mammograms show that the area of interest is only overlying tissue, no further diagnostics is done in some regions. The majority of women in group 7, however, underwent an ultrasound examination (data not shown).

Cancer diagnoses

Among women with a screen-detected breast cancer, 90.5% had a diagnostic work-up that included all three recommended tests (group 2 in Table 2). However, also in groups 4-6, where women received only some of the recommended diagnostic procedures but had a biopsy, high proportions had a diagnosis of breast cancer. In groups 3 and 7, where women did not undergo a biopsy, few or no screen-detected cancers were diagnosed.

The total number of interval cancers was small compared to the number of screen-detected cancers (the ratio was >60 screen-detected cancers per 1 interval cancer) (Tables 2&3). The majority was diagnosed in pathways that were in accordance with the recommendations (groups 2 and 3). In group 2 (mammography, ultrasound, biopsy), where 56.0% of women had a screen-detected cancer, approximately 1.0% of those with a false-positive mammogram developed an interval cancer (Table

3). Among these interval cancers, about a quarter were CIS. In group 3 (mammography, ultrasound), 0.1% of women had a screen-detected cancer and 0.4% had an interval cancer, predominantly of invasive type.

Description of the diagnostic follow-up pathways

The overall benign:malignant surgery ratio was 1:7.8 (95% CI: 1:7.2-1:8.5) (Table 2). The variation was, however, substantial in pathways 4-7 where the follow-up deviated from the guidelines. In group 5 (mammography plus biopsy), the ratio was 1:2.5 (95% CI: 1:1.4-1:5.0) but the group represented 0.4% of all women with an abnormal mammography (Table 1).

The median time to the first follow-up examination was 17 days (Table 2), although this varied between the pathways. Significant variation in the proportion of women who received timely follow-up was present by administrative region both for women with screen-detected cancer ($p<0.001$) and those without ($p<0.001$) (Figures 2&3).

The median time to the final resolution was 20 days. Three quarters of women reached resolution in up to 33 days. Again, this varied between the pathways, administrative regions, and between women with screen-detected cancer (99% had a diagnosis within 3 months) and those without (90% were resolved within 3 months; Figures 2&3). Differences by age were not observed in any of the data breakdowns. After a cancer diagnosis, women remained in follow-up for about a year longer (Table 2).

Health care resource use

The use of ultrasound and mammography examinations was broadly in line with the expectations (Table 4). On average, 1.14 (recommended: 1) ultrasounds and 1.09 (recommended: 1) mammograms were used per woman without screen-detected cancer. Among women with screen-detected breast cancer, this was 2.22 ultrasounds and 2.12 mammograms, respectively, ranging up to 4, which included diagnostic, pre-, and post-surgical images. In addition, approximately one-third of the women had tomosynthesis and a smaller proportion had MRI. This varied between administrative regions (data not shown). Women without screen-detected cancer had on average 0.38 core and/or fine needle biopsies, whereas women with screen-detected cancer had 2.33, including both pre- and post-diagnostic biopsies. This difference is expected, since a biopsy most

often precedes a diagnosis, but also due to post-diagnostic lymph-node biopsies performed during surgery.

Loss to follow-up

Some information was available for the 591 (3.0%) women who had no follow-up examination within 6 months of screening. Of these, 17 (2.9%) died within two years. Another 24 (4.1%) had at least one breast-related diagnostic procedure later than 6 months after screening, whereas 427 (72.3%) attended the next screening round. In total, 123 (20.8%) had no breast-related investigations until the end of follow-up on 31 December 2018. Fewer than 5 were diagnosed with interval cancer.

Discussion

Main findings

In Denmark, 97% of women with abnormal screening mammograms had at least one diagnostic follow-up procedure. In 94% of those, the national recommendations were followed in full. The ratio between surgeries with benign vs. malignant outcomes was generally low. Overall, 83% of women were examined within 30 days as recommended, but the variation between administrative regions was notable. Regional differences were also observed for the total length of the diagnostic process. The resource use was, generally, as recommended by the guidelines.

Strengths and limitations

Using high-quality Danish health registers with individual-level data enabled us to evaluate follow-up pathways for virtually all women with abnormal screening mammograms. We could map the follow-up in detail and show the variability in diagnostic processes performed in real-life settings, even for women who did not undergo any follow-up.

Nevertheless, this study still has some limitations. In Denmark, women with abnormal mammography can seek diagnostic follow-up in private hospitals, even though it is recommended that this is to be performed in the public National Breast Centres.[14] Public hospitals might also refer women to a private hospital or specialist if the expected waiting time is higher than recommended. Although the Danish National Patient Registry is a highly complete data source for

procedures undertaken in public hospitals, data from private hospitals are known to be less complete.[16] Hence, it is likely that the proportion of women with no follow-up was overestimated due to incomplete registration of private hospital data, particularly in some regions. A small proportion of women who only appeared to have had biopsies in their diagnostic pathway might also have had diagnostic imaging done in private hospitals, which would cause misclassification between the studied pathways.

Further, we could not verify that the registration of the screening result in the National Patient Register was correct. This might explain the higher-than-expected proportion of women with no follow-up (around 3%) and their very low rate of interval cancers. From a clinical perspective, it is very rare that women are not seen for further diagnostics. If they do not seek follow-up, they are in some regions contacted directly.

Comparison with the literature and clinical implications

Our finding that 97% of the women referred for further assessment after an abnormal screening mammography received follow-up was slightly lower than the proportions from other organized, population-based breast screening programmes where the estimates reached 98-99%.[21, 22] For almost all women, the timing of the procedures closely followed the national guidelines. Time from screening to diagnosis is an important factor in ensuring a better prognosis for breast cancer, although the negative effect of delays only appears to become significant when these are longer than 3-6 months.[4, 5, 23] In Denmark, high proportions of women whose screening abnormality was resolved within a month suggests that most abnormalities were resolved during the first follow-up visit. Further, only 1% of women with screen-detected abnormalities had to wait for the cancer diagnosis longer than 3 months. Longer resolution times may affect the women's wellbeing because the waiting time and false-positive screening mammograms are known to increase anxiety and stress.[24, 25] In our study, 90% of women with false-positive screening mammograms were resolved within 3 months, but 3% still remained in prolonged follow-up after 1 year. The observed regional differences in how long it took to investigate the abnormalities might reflect different organizational cultures or differently streamlined diagnostic processes, fine-tuning of the service, or the available capacity volume. Sharing operational knowledge or even resources across administrative regions could help improve follow-up in regions with weaker performance.

Approximately 10 out of 11 women with an abnormal mammography underwent the diagnostic procedures recommended by the national clinical management guidelines. Of the remaining, approximately two-thirds were followed-up but received only some of the recommended procedures. Possibly, these decisions were based on clinical judgement (information on which is not available for research). Among women in group 4, who only had a diagnostic biopsy, 70% had a screen-detected cancer, indicating that further imaging procedures might have been considered redundant if the biopsy results were significantly malignant. Group 7 had no biopsy procedures registered and as a result had no screen-detected cancers, but if diagnostic images were convincingly benign, this may have been an acceptable choice from a clinical perspective. None of the women in either of these two groups had an interval cancer. This could indicate that in certain cases, utilising diagnostic resources in line with clinical judgement does not result in missed cancers. Sometimes, however, deviation from the guidelines was associated with a high benign:malignant surgery ratio such as that observed in group 5, where women had a mammography and a biopsy but did not have an ultrasound examination. Whether or not using ultrasound is crucial in preventing surgeries for benign lesions remains to be studied. In group 5, 24 out of 72 women underwent a stereotactic biopsy, possibly because of micro-calcifications suspected on the screening mammogram. This could help explain why an ultrasound examination was not the first diagnostic choice. However, 6 out of 15 benign surgeries were also preceded by a stereotactic biopsy, suggesting that there may have been other reasons for the high benign:malignant ratio in this small group of screened women. Further analysis on this small group revealed no differences in terms of previous screening, biopsies performed or result of the biopsy compared to the 19 women with no surgery for their benign condition. However, 80% of the benign surgeries were performed in one administrative region, at the same hospital, which could indicate that different local practices could be an explanation for the high benign:malignant surgery ratio. Another reason for a high rate of benign surgeries might be women’s request due to distress. Our findings should motivate clinicians with access to medical journals to do further research to obtain more complete explanations of reasons for deviations. Overall in our study, however, the benign:malignant surgery ratio was substantially below 1:4 recommended by the European breast cancer screening guidelines.[15]

Only a small number of women ultimately had an interval cancer diagnosis after they had ended their diagnostic follow-up process without a screen-detected breast cancer diagnosis. This included women with CIS. CIS is, however, very rarely associated with symptoms.[26, 27] It is likely that the interval CIS, observed primarily in group 2, may have been diagnosed as part of early recalls based on inconclusive diagnostic processes.

Deviations from the recommended follow-up may affect health care resource use. However, our study showed that these were few and those may to a large extent be due to an assessment of individual patient needs, with a limited implication on the overall resource use. We cannot fully determine the reason for the regional variation in the use of supplemental imaging procedures, such as tomosynthesis and MRI. However, not all facilities had access to e.g. tomosynthesis during this period.

Conclusion

In Denmark, the diagnostic follow-up after abnormal mammography screening was generally performed in accordance with the national clinical guidelines. There were a few exceptions, however, and we also observed some variation between administrative regions. This suggests a role of organizational factors to further improve the follow-up and secure that women with abnormal screening mammography receive the same quality of service throughout the country.

DECLARATIONS

FUNDING

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CONFLICTS OF INTEREST

Financial interests: Matejka Rebolj's employer received a speaker fee on her behalf from Hologic. She has attended meetings with manufacturers of various cervical cancer screening technologies. Susanne Fogh Jørgensen, Berit Andersen, Anders Lernevall and Sisse Helle Njor reports no financial interests.

Non-financial interests: none

AVAILABILITY OF DATA

The data that support the findings of this study are available from The Danish Health Data Authority. Restrictions apply to the availability of these data, which were used under license for this study. Data may be available upon reasonable request to The Danish Health Data Authority with permission.

AUTHOR CONTRIBUTIONS

Conceptualization: Sisse Helle Njor, Matejka Rebolj; **Methodology:** Susanne Fogh Jørgensen, Berit Andersen, Anders Lernevall, Matejka Rebolj & Sisse Helle Njor; **Data curation, formal analysis and investigation:** Susanne Fogh Jørgensen, Sisse Helle Njor; **Writing - original draft preparation:** Susanne Fogh Jørgensen; **Writing - review and editing:** Susanne Fogh Jørgensen, Berit Andersen, Anders Lernevall, Matejka Rebolj & Sisse Helle Njor; **Funding acquisition:** Sisse Helle Njor & Matejka Rebolj; **Resources:** Berit Andersen; **Supervision:** Sisse Helle Njor

COMPLIANCE WITH ETHICAL STANDARDS

According to EU's General Data Protection Regulation (article 30), the project was listed at the record of processing activities for research projects in Central Denmark Region (J. No.: 1-16-02-301-18).

According to the Consolidation Act on Research Ethics Review of Health Research Projects, Consolidation Act number 1083 of 15 September 2017 section 14, notification of registry-based studies is only required if the project involves human biological material. Therefore, this study did not need an approval from the Ethics Committees.

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Fig. 1 Flowchart of the study population

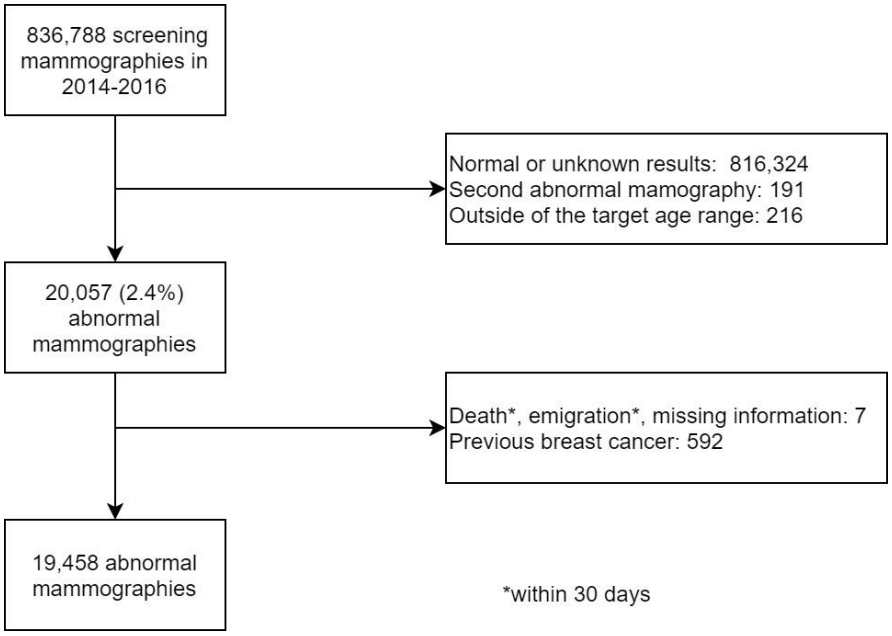

Fig. 2 Cumulative proportions of women with screen-detected breast cancer, by time to the first diagnostic test and time to diagnosis, administrative region, and age at screening

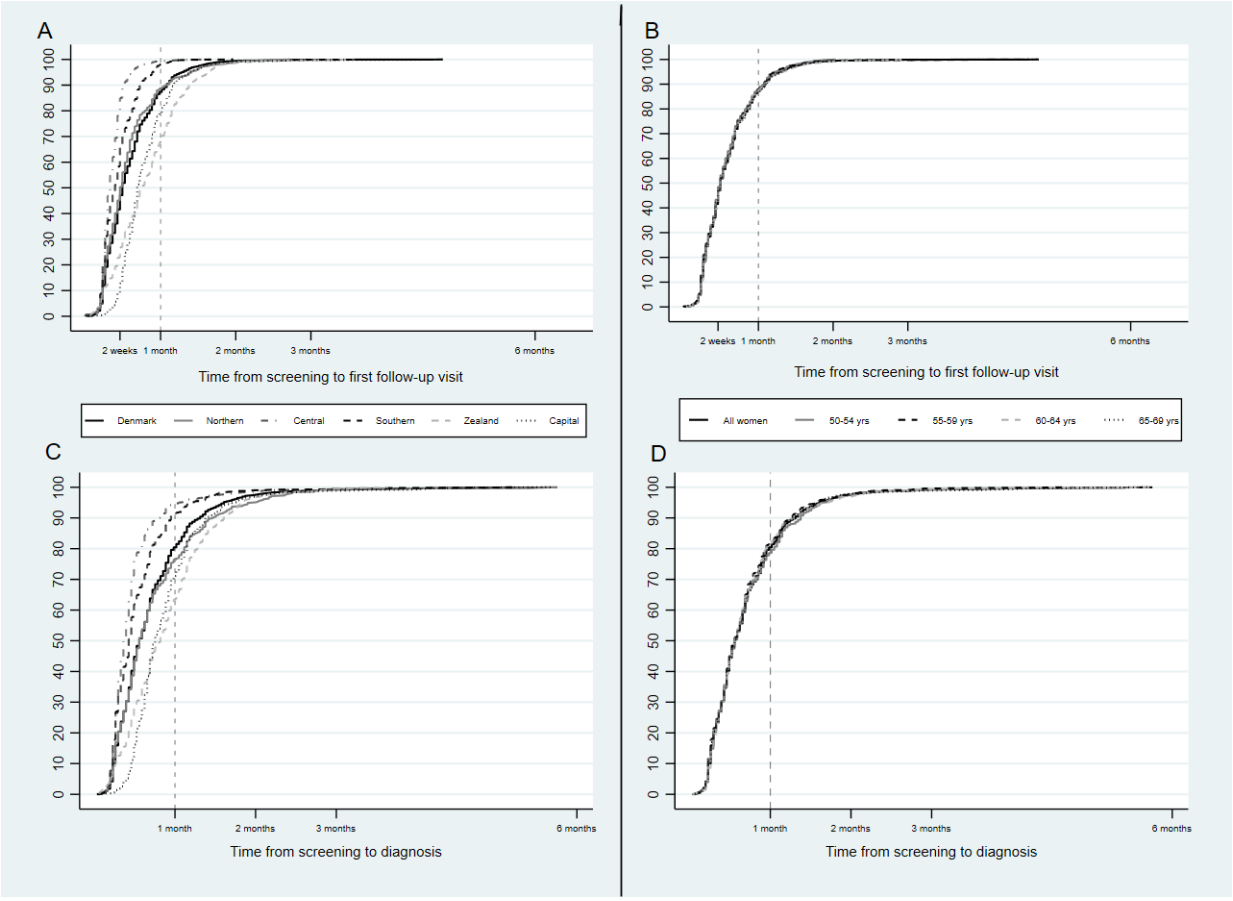

Fig. 3 Cumulative proportions of false-positive women, by time to the first diagnostic test and time to final resolution, administrative region, and age at screening

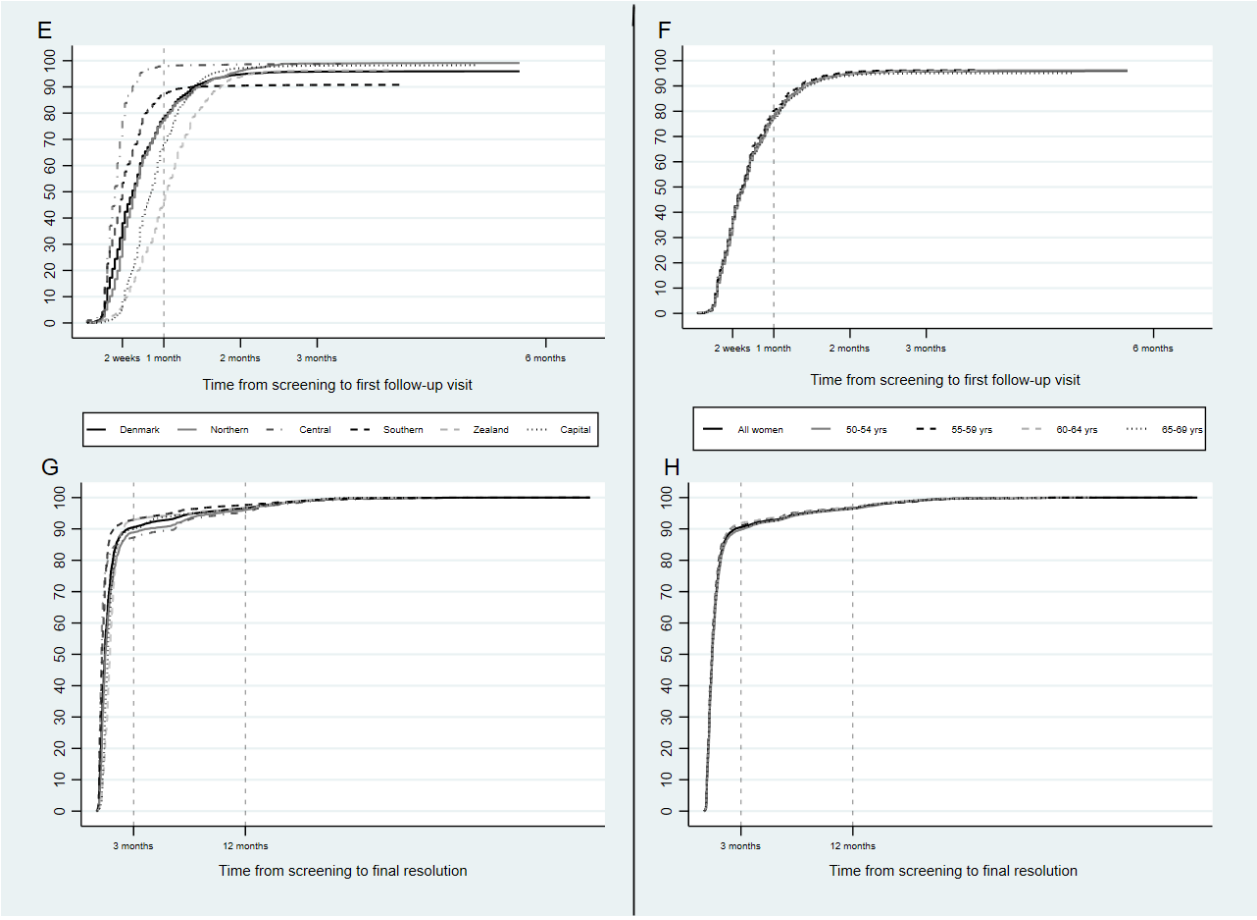

Table 1 Frequency of diagnostic follow-up patterns, by age at screening and administrative region

	Group 1: No follow-up	Group 2: Mammography, ultrasound and biopsy	Group 3: Mammography and ultrasound	Group 4: Only biopsy	Group 5: Mammography and biopsy	Group 6: Ultrasound and biopsy	Group 7: Either ultrasound or mammography	Total
Age at screening								
50-54	245 (3.3%)	2617 (34.7%)	4290 (56.9%)	107 (1.4%)	25 (0.3%)	79 (1.1%)	173 (2.3%)	7536 (100%)
55-59	106 (2.8%)	1424 (38.0%)	1973 (52.7%)	68 (1.8%)	14 (0.4%)	60 (1.6%)	98 (2.6%)	3743 (100%)
60-64	106 (2.8%)	1718 (45.0%)	1739 (45.5%)	62 (1.6%)	15 (0.4%)	62 (1.6%)	118 (3.1%)	3820 (100%)
65-69	134 (3.1%)	2071 (47.5%)	1820 (41.8%)	117 (2.7%)	18 (0.4%)	79 (1.8%)	120 (2.7%)	4359 (100%)
Administrative region								
Capital	61 (1.2%)	2311 (46.0%)	2591 (51.5%)	66 (1.3%)[a]				5029 (100%)
Central	31 (0.9%)	1619 (44.6%)	1498 (41.3%)	30 (0.8%)	5 (0.1%)	157 (4.3%)	290 (8.0%)	3630 (100%)
Northern	19 (0.7%)	940 (34.8%)	1698 (62.8%)	46 (1.7%)[a]				2703 (100%)
Zealand	62 (2.6%)	1143 (47.0%)	1140 (46.9%)	88 (3.6%)[a]				2433 (100%)
Southern	418 (7.4%)	1817 (32.1%)	2895 (51.1%)	198 (3.5%)	50 (0.9%)	113 (2.0%)	172 (3.0%)	5663 (100%)
Total	591 (3.0%)	7830 (40.2%)	9822 (50.5%)	354 (1.8%)	72 (0.4%)	280 (1.4%)	509 (2.6%)	19,458 (100%)

[a] Numbers cannot be shown for each pathway separately because some of the cells included fewer than 5 observations.

Table 2 Description of the diagnostic follow-up pathways

Diagnostic work-up pathway after an abnormal screening mammography	**N (%)**	**Screen-detected breast cancers (N, %)**	**Of which invasive breast cancers (N, %)**	**Number of women undergoing a surgery[a] (N, %)**	**Benign: malignant surgery ratio[b] (95% CI)**	**Time to first follow-up procedure (median, IQR)**	**Time to resolution (median, IQR)**	**Time spent in follow-up after a cancer diagnosis (median, IQR)**
Group 2: Mammography, ultrasound and biopsy[c]	7830	4385 (56.0%)	3766 (85.9%)	4865 (62.1%)	1:8.4 (1:7.7-1:9.2)	16 (11-26)	21 (13-36)	322 (21-552)
Group 3: Mammography and ultrasound	9822	9 (0.1%)	<5	68 (0.7%)	n/a	18 (12-28)	20 (13-31)	268 (31-508)
Group 4: Only biopsy	354	248 (70.1%)	218 (87.9%)	251 (70.9%)	1:34.8 (1:16.7-1:87.7)	14 (9-22)	15 (10-25)	409 (21-558)
Group 5: Biopsy and mammography	72	38 (52.8%)	33 (86.8%)	53 (73.6%)	1:2.5 (1:1.4-1:5.0)	15 (10-25)	28 (14-42)	405 (87-547)
Group 6: Biopsy and ultrasound	280	167 (59.6%)	148 (88.6%)	175 (62.5%)	1:14.9 (1:8.1-1:30.5)	11 (8-14)	12 (9-18)	366 (10-549)
Group 7: Either mammography or ultrasound	509	0	n/a	<5	n/a	11 (8-15)	12 (8-16)	n/a
Total	18,867	4847 (25.7%)	~86%[d]	~29%[d]	1:7.8 (1:7.2 -1:8.5)	17 (11-26)	20 (13-33)	332 (21-552)

Abbreviations. IQR=interquartile range.

[a] Both among women with a screen-detected cancer and women with false-positive mammograms.

[b] Calculated by dividing the number of surgeries performed among women with no breast cancer (benign) with the number of surgeries performed among women with a breast cancer diagnosis (malignant).

[c] Either fine needle or core biopsy.

[d] Absolute numbers cannot be reported because some of the counts in the column were <5.

Table 3 Interval cancers, by type and time to diagnosis

	Group 2: Mammography, ultrasound and biopsy	**Group 3: Mammography and ultrasound**	**Groups 1 or 4-7: Fewer procedures than recommended**
Total	33 (1.0%)[b]	39 (0.4%)[b]	<5
Type			
Invasive cancer	24 (73%)	NR[a]	<5 (100%)
DCIS or PLCIS	9 (27%)	<5	0
Time of diagnosis			
6-12 months after screening	18 (55%)	16 (41%)	-
12-24 months after screening	15 (45%)	23 (59%)	<5 (100%)

Abbreviations. DCIS=ductal carcinoma in situ. PLCIS=pleomorphic lobular carcinoma in situ.

[a] Numbers could not be reported because the number of DCIS and PLCIS were <5.

[b] The proportion was calculated per 100 women without a screen-detected cancer (see Table 2).

Table 4 Numbers of ~~D~~diagnostic and treatment procedures performed throughout the entire screening episode, including the period after surgery among women with screen-detected cancer and women with false-positive mammograms, by diagnostic follow-up group

		Group 2: Mammography, ultrasound and biopsy	Group 3: Mammography and ultrasound	Group 4: Only biopsy	Group 5: Biopsy and mammography	Group 6: Biopsy and ultrasound	Group 7: Only mammograhy or only ultrasound	Total
Type of diagnostic procedure	Screen-detected diagnosis	Mean (range p5-p95)	Mean (range p5-p95)	Mean (range p5-p95)	Mean (range p5-p95)	Mean (range p5-p95)	Mean (range p5-p95)	Mean (range p5-p95)
Mammography	Breast cancer	2.22 (1-4)	2.30 (1-3)	1.15 (0-3)	2.24 (1-4)	1.02 (0-3)	n/a	2.12 (1-4)
	FP mammogram	1.37 (1-3)	1.06 (1-2)	n/a	1.12 (0-3)	n/a	0.15 (0-1)	1.09 (1-2)
Tomosynthesis	Breast cancer	0.36 (0-1)	< 5	n/a	0.37 (0-1)	< 5	n/a	0.33 (0-1)
	FP mammogram	0.33 (0-1)	0.42 (0-1)	n/a	< 5	n/a	0.09 (0-1)	0.37 (0-1)
MRI	Breast cancer	0.16 (0-1)	0.56 (0-3)	0.12 (0-1)	0.24 (0-2)	0.07 (0-1)	n/a	0.16 (0-1)
	FP mammogram	0.08 (0-1)	0.03 (0-0)	n/a	0.24 (0-2)	n/a	0.01 (0-0)	0.04 (0-0)
Ultrasound	Breast cancer	2.30 (1-4)	2.11 (1-4)	1.03 (0-3)	1.05 (0-3)	2.35 (1-4)	n/a	2.22 (1-4)
	FP mammogram	1.40 (1-3)	1.07 (1-2)	n/a	n/a	1.11 (1-2)	0.86 (0-1)	1.14 (1-2)
Other imaging procedures[a]	Breast cancer	0.70 (0-2)	0.89 (0-2)	0.54 (0-1)	0.71 (0-2)	0.56 (0-2)	n/a	0.69 (0-2)
	FP mammogram	0.26 (0-1)	<0.01 (0-0)	< 5	0.53 (0-2)	0.13 (0-1)	< 5	0.07 (0-1)
Fine needle biopsy	Breast cancer	0.37 (0-1)	< 5	0.52 (0-2)	0.61 (0-2)	0.22 (0-1)	n/a	0.37 (0-1)
	FP mammogram	0.48 (0-1)	n/a	0.43 (0-1)	0.79 (0-2)	0.57 (0-1)	n/a	0.13 (0-1)
Core biopsy	Breast cancer	1.95 (1-3)	< 5	1.89 (1-3)	1.95 (1-4)	2.16 (1-3)	n/a	1.96 (1-3)
	FP mammogram	0.95 (0-2)	n/a	0.76 (0-2)	0.91 (0-2)	0.72 (0-2)	n/a	0.25 (0-1)
Excisional biopsy or other not defined excisions.	Breast cancer	0.15 (0-1)	1.22 (0-3)	0.06 (0-1)	< 5	0.10 (0-1)	n/a	0.15 (0-1)
	FP mammogram	0.06 (0-1)	<0.01 (0-0)	< 5	< 5	< 5	< 5	0.02 (0-0)
Mastectomy	Breast cancer	0.19 (0-1)	0.56 (0-1)	0.21 (0-1)	0.32 (0-1)	0.16 (0-1)	n/a	0.19 (0-1)
	FP mammogram	<0.01 (0-0)	< 5	n/a	n/a	n/a	n/a	N < 20
Lumpectomy / resection	Breast cancer	1.08 (0-2)	1.78 (1-4)	0.99 (0-2)	1.03 (0-2)	1.08 (0-2)	n/a	1.08 (0-2)
	FP mammogram	0.14 (0-1)	0.01 (0-0)	0.07 (0-1)	0.44 (0-1)	0.10 (0-1)	< 5	0.04 (0-0)
Reconstructive surgery	Breast cancer	0.20 (0-1)	0.78 (0-3)	0.19 (0-1)	0.26 (0-1)	0.28 (0-1)	n/a	0.20 (0-1)
	FP mammogram	0.01 (0-0)	<0.01 (0-0)	n/a	n/a	< 5	n/a	<0.01 (0-0)

Abbreviations. FP=false-positive. MRI=magnetic resonance imaging.

[a] Coil placement, galactography, breast cystography, needle marking