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Annual mammography at age 45-49 years and biennial mammography at age 50-69 years: comparing performance measures in an organised screening setting

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Abstract:	Objective To compare the results of five years of annual mammography screening at age 45-49 with the results five years of biennial screening at age 50-54 and 55-69. Methods In an Italian screening programme, data from 1,465,335 mammograms were analysed. Recall rates, invasive assessment rates, surgical biopsy rates, and cancer detection rates were calculated for the first screen (first) and, cumulatively, for the second and subsequent screens (second+). Results The rate ratios between younger women and the two groups of older ones were: recall rate: first 1.11 and 1.11, second+ 2.10 and 2.77; invasive assessment rate: first 0.94 and 0.94, second+ 1.63 and 1.56; surgical biopsy rate: first 0.68 and 0.45, second+ 1.35 and 0.88; total detection rate: first 0.63 and 0.37, second+ 1.30 and 0.74. For the total positive predictive value of surgical biopsy, the ratios were: first 0.93 and 0.82, second+ 0.96 and 0.83. Both at the first and second+ screens, stage distribution of screen-detected cancers did not vary by age group. Conclusion Five years of annual screening at age 45-49 were associated with 2-3-fold higher cumulative recall rates at second+ screens and with more limited differences in the frequency and positive predictive value of surgical biopsy.
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Author Comments:	21 June 2018 Editorial Office European Radiology Dear Sirs, Enclosed please find a manuscript entitled "Annual mammography at age 45-49 years and biennial mammography at age 50-69 years: comparing performance measures in an organised screening setting" that is submitted for publication as an Original Article. The 2006 European guidelines for quality assurance in breast cancer screening did not recommend mammography screening of women younger than 50 years. Women aged 40-49 years (or 45-49 years) are invited to screening only in some small European countries and some regional areas, with a two-year screening interval. Recently, however, the situation has changed. For asymptomatic women aged 45 to 49 years at average risk of breast cancer, the European Commission Initiative on Breast Cancer (ECIBC) Guideline Development Group has suggested mammography screening in the context of organised programmes. In this perspective, the main problem concerns the choice of the screening interval. The recommendation from the ECIBC Guideline Development Group is more vague than for women aged 50-69 years and is not based on sound evidence, with models producing inconsistent results. In fact, virtually no published studies exist on the performance measures of an annual screening protocol for European women aged 45-49 years in a public health screening setting. The article I submit, which has a high degree of novelty, is a contribution to bridge this knowledge gap. In 2009, in a biennial screening programme covering a large administrative region of northern Italy, the target age range of 50-69 years was extended to 45-74 years. Women aged 45-49 years are invited annually. The article reports a study of the main performance measures of annual screening at this age. Thank you for your attention. I look forward to hearing from you. Best regards. Lauro Bucchi, MD* *Corresponding author at: Romagna Cancer Registry, Romagna Cancer Institute (Istituto Scientifico Romagnolo per lo Studio e la Cura dei Tumori, IRST, IRCCS), Meldola, Forlì, Italy. Tel.: +39-0543-739-455, Fax: +39-0543-739-459. E-mail: lauro.bucchi@irst.emr.it
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Annual mammography at age 45-49 years and biennial mammography at age 50-69 years: comparing performance measures in an organised screening setting

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Annual mammography at age 45-49 years and biennial mammography at age 50-69 years: comparing performance measures in an organised screening setting

Abstract

Objective To compare the results of five years of annual mammography screening at age 45-49 with the results five years of biennial screening at age 50-54 and 55-69.

Methods In an Italian screening programme, data from 1,465,335 mammograms were analysed. Recall rates, invasive assessment rates, surgical biopsy rates, and cancer detection rates were calculated for the first screen (first) and, cumulatively, for the second and subsequent screens (second+).

Results The rate ratios between younger women and the two groups of older ones were: recall rate: first 1.11 and 1.11, second+ 2.10 and 2.77; invasive assessment rate: first 0.94 and 0.94, second+ 1.63 and 1.56; surgical biopsy rate: first 0.68 and 0.45, second+ 1.35 and 0.88; total detection rate: first 0.63 and 0.37, second+ 1.30 and 0.74. For the total positive predictive value of surgical biopsy, the ratios were: first 0.93 and 0.82, second+ 0.96 and 0.83. Both at the first and second+ screens, stage distribution of screen-detected cancers did not vary by age group.

Conclusion Five years of annual screening at age 45-49 were associated with 2-3-fold higher cumulative recall rates at second+ screens and with more limited differences in the frequency and positive predictive value of surgical biopsy.

Key Points

At repeated screens, cumulative recall rate was 2-3-fold higher for younger women.

Differences in cumulative surgical referral and surgical biopsy rates were moderate.

Differences in positive predictive value of surgical biopsy were particularly small.

Younger women benefited the most from the high specificity of diagnostic work-up.

Keywords

Mass Screening; Mammography; Breast Neoplasms; Premenopause; Biopsy

Abbreviations

DCIS Ductal carcinoma in situ

ECIBC European Commission Initiative on Breast Cancer

FNA Fine-needle aspiration

GISMa Italian Group for Mammography Screening

NCB Needle core biopsy

ONS (Italian) National Centre for Screening Monitoring

PPV Positive predictive value

VAB Vacuum-assisted biopsy

Introduction

The benefit of mammography screening for women younger than 50 years is considered less, and less certain, than for older ones. Since 2006, the European guidelines for quality assurance in breast cancer screening have recommended that organised mammography screening programmes be targeted at women aged 50-69 years [1]. Screening recommendations from leading international agencies have substantially supported this age restriction [2, 3]. This explains why, in Europe, biennial screening programmes for women aged 40-49, or 45-49, years have so far been introduced only in Iceland, Czech Republic, Hungary, and some regional areas [4]. In the United Kingdom, the target age range is currently being extended but with the age threshold set at 47 years. [5].

In 2017, the situation has changed. For women aged 45-49 years at average risk of breast cancer, the European Commission Initiative on Breast Cancer (ECIBC) Guideline Development Group has issued a conditional recommendation for mammography screening in the context of organised programmes [6]. The extent to which this will influence public health screening policies in Europe remains to be seen. There is some possibility, however, that the new guidelines will interact synergistically with the American Cancer Society guidelines of 2015, which state that average-risk women should begin having annual mammograms at age 45 years, and can change to having mammograms every other year beginning at age 55 years [7].

It must be noted, conversely, that a conditional recommendation is challenging for organised screening programmes. When a recommendation is conditional, the majority of women may need more discussion with healthcare professionals. This implies that participation could not be the best choice for all of them. Invitation strategies must account for this uncertainty, and high participation may not be a desired outcome in all situations.

Another challenging issue for organised screening programmes will be the choice of the screening interval for women aged 45-49 years. The recommendation from the ECIBC Guideline

Development Group is more vague than for women aged 50-69 years and is not based on sound evidence, with models producing inconsistent results [6]. This uncertainty is coupled with doubts on the costs and, in part, on the balance between desirable and undesirable effects.

In this scenario, it would be useful to have robust estimates of detection, recall, and surgical referral and biopsy rates of annual screening of European women aged 45-49 years in an organised screening setting. The few available data concern the effectiveness of the procedure [8]. For this reasons, the new European guidelines state that future evaluations of screening services for this population should consider their results in the context of evolving diagnosis and treatment protocols and in relation to the screening interval [6].

This article is an initial contribution to bridge this knowledge gap. In a large administrative region of Italy, women aged 45-49 years have been invited to participate annually in an organised mammography screening programme since 2010. We report here a study of the performance measures of annual screening in this age group.

Materials and methods

Background: Italian screening guidelines for younger women

In Italy, mammography screening of women aged 40-49 years was approved, with conditions, more than 10 years ago. According to the 2006 guidelines from the Italian Group for Mammography Screening (GISMa), the extension of organised programmes to the age range 40-49 years – albeit not recommended – can be taken into consideration provided that: coverage of women aged 50-69 years has been completed; budget is sufficient; priority is given to the age group 45-49 years; information on pros and cons of screening at this age is given; mammography is offered annually; mammograms are taken in two views and double-read; and the process is monitored [9].

Setting

Since 1995-1997, depending on the health care district, the Emilia-Romagna Region (northern Italy) has been targeted by a free-of-charge, two-yearly, two-view, double-read mammography screening programme for women aged 50-69 years. The programme is run on a local-level basis under the responsibility of 11 health care district screening units. Details are reported elsewhere [10, 11]. The results of all Italian regional screening programmes are annually surveyed by the GISMa and published by the National Centre for Screening Monitoring (ONS) [12].

In 2009, for the first time in Italy, the regional Administration extended the target age range of the programme to women aged 45-49 years (and 70-74 years) [13]. The above GISMa guidelines were adhered to, except for the provision of information on the uncertainties surrounding screening of younger women.

Time period

Women aged 45-49 years began to be invited in 2010. Their enrolment increased progressively and was completed in 2014 [13]. We evaluated the performance of screening among women invited in the 5-year period between 2011 and 2015. The year 2010 was excluded from the study due to the low invitation rate and a possible selection bias.

Data sources

The data for the study were taken from the annual national surveys conducted by the GISMa and the ONS. These surveys collect data in aggregate form from local screening units. Each year, the data are checked for internal consistency between different aggregates. In many publications, their quality for statistical purposes has been shown to be acceptable [12, 14].

The median interscreening interval in days was assessed using the database of screening mammography records at the Department of Health of the regional Administration.

Objectives, rationale, and endpoints

The primary study question was: what is the incidence of recall, diagnostic assessment, and surgical biopsy among women undergoing five years of annual screening between age 45 and 49 as compared with women undergoing five years of biennial screening in the age range 50-54 and 55-69? Our objectives were, first, to report descriptively the standard performance measures of screening in the three age groups and, second, to calculate their ratio comparing younger women versus both groups of older ones. Our rationale was that this approach would allow for a more direct understanding of the results of annual screening between 45 and 49 years of age.

The study endpoints were as follows: recall rate; non-invasive and invasive assessment rates; surgical referral and surgical biopsy rates; detection rates of benign breast lesion and of breast cancer by pT and pN status; ductal carcinoma in situ (DCIS):invasive cancer ratio; pT and pN distribution of invasive cancers; positive predictive value (PPV) mammography, surgical referral, and surgical biopsy for invasive cancer and for DCIS and invasive cancer; and proportion of cancers treated conservatively.

Design

We considered that, numbering from 1 to 5 the years during which women aged 45-49 years receive an annual mammogram, older women are screened in years 1, 3 and 5. This suggested that younger and older women can be compared for the results of the first screen and, then, for the cumulative results of their subsequent screens over an equal 4-year time period. In this way, we made allowance for the fact that women aged 45-49 years are exposed to the procedure twice as often as older ones [15]. The 5-year cumulative rates were also calculated as summary measures.

In all age groups, the recall rate, the non-invasive and invasive assessment rates, the surgical referral and surgical biopsy rates, and the detection rates per 1000 first-screen mammograms and, separately, per 1000 mammograms at second and subsequent screens were calculated as average

values of the study period. These values were used to calculate the cumulative rates according to standard methods [16].

Like the above rates, the DCIS:invasive cancer ratio, the pT and pN percent distribution, the percent PPV of mammography, surgical referral, and surgical biopsy; and the percent proportion of cancers conservatively treated were separately calculated for women at their first and subsequent screens as average values of the study period. These measures, describing the clinical characteristics of screen-detected abnormalities, did not undergo any further treatment.

Data analysis

Attending women of all ages who reported a recent (<12 months) spontaneous mammography were not screened nor included in the number of women invited. Women who were unreachable (letter returned to sender) were considered non-attenders. The participation rate was defined as the proportion of invited women undergoing screening mammography.

Women aged 45-49 years were compared with older ones by calculating the ratios of performance measures and the 95% confidence intervals around them.

Results

Number of invitations and mammograms

On 1 January 2011, the target population included 176,440 women aged 45-49 years, 156,026 women aged 50-54 years, and 407,155 women aged 50-69 years.

During the study period, 243,066 invitations to the first screen were sent to women aged 45-49 years, 51,857 to those aged 50-54 years, and 28,448 to those aged 55-69 years, for a total of 323,371. The number of invitations to the second and subsequent screens was 537,623 among

women aged 45-49 years, 364,614 among those aged 50-54 years, and 940,272 among those aged 55-69 years, for a total of 1,842,509. Overall, 2,165,880 invitations were sent.

The upper row of Table 1 shows the total number of screening mammograms performed. The participation rate by age group was 71.9%, 86.4%, and 94.1%, respectively, at the first screen and 64.2%, 62.6%, and 68.7%, respectively, at the second and subsequent screens.

The frequency of testing by age group was very near to the nominal one, with a median interscreening interval of 391 days, 746 days, and 744 days, respectively.

Recall rate, assessment rate, surgical referral rate, surgical biopsy rate, and detection rate

The second and subsequent rows of Table 1 show the number of recalls for assessment, the number of assessments performed by type, the number of surgical referrals and biopsies, and the number of benign and malignant screen-detected lesions in the three age groups. For all age groups, the response rate to recall was >94% at the first screen and >98% at the second and subsequent screens.

Table 2 shows the recall rate, the assessment rates, the surgical referral rate, the surgical biopsy rate, and the detection rates per 1,000 screened women at the first screen and at the second and subsequent screens.

For all of these rates, Table 3 shows the ratio between younger women and women aged 50-54 years and 55-69 years. At the first screen, the recall rate was 11% higher for younger women compared with both groups of older ones. The non-invasive assessment rate was moderately higher but no excess invasive assessment rate was observed. All surgical referral and surgical biopsy rates were less by approximately 30% to 55%. The detected prevalence of DCIS was approximately one-third lower compared with both groups of older women. The yield of invasive cancer too was less, with a ratio of 0.31 versus women aged 55-69 years.

At second and subsequent screens, younger women experienced a 2- to 3-fold higher recall rate. This led to a larger increase in non-invasive assessment rate, with the invasive assessment rate being only approximately 60% higher than among both groups of older women. The excess of

surgical referral rates was even less pronounced and was found only comparing younger women with women aged 50-54 years. Taking women aged 55 years and older as a reference, younger women had 10% lower surgical rates. In terms of yield of disease, the situation was similar. The total detection rate of cancer among women aged 45-49 years was 30% higher than among women aged 50-54 years and approximately 25% lower than among older women. Compared with these, however, younger ones retained a moderate excess prevalence of DCIS.

The 5-year cumulative rates are shown in the Electronic Supplementary Material Table S1. Their ratios are shown in the Electronic Supplementary Material Table S2.

DCIS:invasive cancer ratio, tumour stage, PPV, and patterns of treatment

These indicators are shown in Table 4 and are compared in Table 5. Whether at the first screen or subsequent screens, the DCIS:invasive cancer ratio did not differ significantly between women aged 45-49 years and the intermediate age group. A significant excess of intraepithelial diseases was observed if comparing younger women with women aged 55 years or older.

Both the pT and pN distribution of invasive cancers showed only modest and nonsignificant differences between age groups, except for a 27% excess prevalence of pN-positive cancers among younger women compared with those aged 55-69 years.

The PPVs showed the same pattern at all screens. For younger women, the PPVs of mammography for DCIS and invasive cancer were approximately 40% and 70% lower than in the other two age groups, whereas the differences in the PPV of surgical biopsy were between 7% and 18%. The proportion of invasive cancers undergoing conservative surgery was similar across the age groups both at the first screen and at the subsequent ones.

Discussion

Comments to the results

It is commonly supposed that higher recall and surgical referral and biopsy rates are unavoidable consequences of screening women aged 40-49 years [9, 17, 18]. If this was the case, this would have a negative impact on the feasibility and affordability of the procedure. As the prevalence of cancer decreases with decreasing age, a rise in recall and surgical referral and biopsy rates would cause the PPV of mammography and surgical indication to be much poorer among younger women.

Our results confirmed only in part these assumptions. We actually found a 2- to 3-fold higher cumulative recall rate at second and subsequent screens over a 4-year time period, which included four screens for women aged 45-49 years and two for older ones. At the first screen, the recall rate was only about 11% greater. With respect to surgical referrals and surgical biopsies, younger women had a 30% to 55% lower rates at the first screen. At the second and subsequent screens, they had 30-35% higher rates if compared with women aged 50-54 years, and approximately 10% lower rates compared with those aged 55 years or older.

These findings are explained by the fact that, over recent years, the increasing use of percutaneous sampling techniques has greatly improved the specificity of the diagnostic work-up of screen-detected abnormalities. When the PPV of surgical referral and surgical biopsy approaches 100%, a poorer prevalence of disease (which is the case for women aged 45-49 years compared with the third age group) automatically translates into a lower rate of unnecessary referrals and biopsies [19].

Two more points regarding the diagnostic assessment of screen-detected abnormalities should be made. At the first screen, the invasive assessment rate was the same for younger women as for the older ones. At subsequent screens, they experienced a much larger increase in non-invasive than invasive assessment rate. With a 2- to 3-fold higher recall rate, the cumulative invasive

assessment rate among women aged 45-49 years was only 60% higher than in both groups of older women. It appears that mammographic abnormalities detected in younger women generated a lower level of clinical suspicion at assessment, which confirms that there is room for improvement of the basic screening process.

The second issue of the diagnostic assessment to be mentioned is that younger women benefited from a larger increase in the PPV of surgical biopsy versus that of mammography. For them, the PPV of mammography for DCIS and invasive cancer was 40% to 70% less than for older women whereas the PPV of surgical biopsy was only 7% to 18% less. This indicates that percutaneous sampling techniques have a particularly favourable impact on younger women.

The rationale of short-interval rescreen is to balance the poorer sensitivity of mammography that is due to the greater breast density and the more rapid tumor growth [20]. There is evidence that an increased breast density explains most of the excess odds of women aged 40-49 years having an interval cancer in the first interval year, and that a rapid tumour growth contributes mostly to the excess odds of interval cancer during the second year [21]. A 12-month screening interval is expected to reduce the adverse impact of fast-growing tumours. Our results are compatible with this rationale, since the percentage of large-sized tumours was very similar to that found in both groups of older women undergoing biennial screening.

Conversely, and by implication, our data provide only limited support to the recommendation for annual screening of women aged 50-54 years [7]. In comparative terms, their tumour stage distribution was not adversely affected by the 24-month screening interval. Previous studies have already suggested that women between 45 and 54 years of age are not a mammographically homogeneous population. While women under 50 years undergoing biennial screening are more likely to have late-stage disease at diagnosis than those screened annually, there is apparently no such increase for women aged ≥50 years with a 2-year versus a 1-year screening interval [22-25].

Policy implications

Screening services are currently sized so as to guarantee regular biennial mammography and subsequent investigations to women aged 50-69 years. In the decision to invite women aged 45-49 years to annual screening and, if the decision is taken, in the planning of the service, the very high cumulative burden of recalls for assessment should be given primary consideration. The adverse effects of the low age of women on the frequency and PPV of surgical referral and biopsy have a relatively lesser magnitude. Screening younger women requires a relatively higher level of investment in outpatient diagnostic work-up services than in inpatient surgical services.

Strengths and weaknesses

The are many strengths in this study. First, its large multicentre basis and its uncommon statistical power, resulting in a high precision of estimates, allow for the results to be safely generalised to other settings.

Second, all breast imaging procedures were administered by the same personnel in the same facilities during the same screening and assessment sessions, which ensures the comparability of results between the three woman's age groups.

Third, the timeliness of the study should be noted. It was undertaken a few months after the publication of the ECIBC recommendations for women aged 45-49 years. The results may offer some useful clarifications about the uncertainties surrounding the new guidelines [6].

Fourth and last, the study has a remarkable degree of novelty. We are not aware of comparable literature data. The few previous studies of mammography screening comparing women 40-49 years of age with older ones have dealt with biennial screening in the opportunistic setting. Some authors, but not all [26, 27], have reported results consistent with ours, i.e., a higher recall rate at second and subsequent screens, a lower PPV of mammography, and a lower surgical biopsy rate [24, 28].

A weakness of this study is that the data were collected in an aggregate form, causing two considerable drawbacks. The first is that we were unable to identify the women undergoing multiple recalls, assessments, and surgical biopsies. We can exclude, however, that there were women with multiple breast cancer diagnoses, since Italian women with a previous diagnosis of the disease are generally excluded from invitation to screening.

The second problem with the data is that their consistency could not be assessed in a direct manner. However, as they were taken from annual national surveys conducted for 15 years by two important specialised bodies, we assume that their quality was acceptable [12, 14].

Other limitations of the study lie in its design. Data for the first screen at age 55 years and above were necessarily based on the relatively small population of women who had never been screened previously. Previous spontaneous mammograms, too, might alter the results of the first screen, especially for younger women.

Finally, it must be acknowledged that the study would be incomplete without including an assessment of the incidence of interval breast cancer and, consequently, of the cumulative incidence of breast cancer using a cohort design. The complex methodological issues involved in these approaches, however, warrant a separate analysis. In addition, at the time we are writing this article, a substantial part of negative mammography results issued in 2011-2015 cannot yet be followed-up due to the latency time of the regional breast cancer registry.

Conclusions

In summary, this study yielded multifaceted results. Compared with five years of biennial screening in the age range 50-54 and 55-69, five years of annual screening between age 45 and 49 were associated with a two- to three-fold higher cumulative recall rates at second and subsequent screens, and with much more limited differences in the frequency and PPV of surgical referral and biopsy. The high specificity of current assessment techniques for screen-detected abnormalities had a

greater impact on younger women. Screening women aged 45-49 years requires a relatively higher level of investment in outpatient diagnostic work-up services than in inpatient surgical services.

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Titles of Tables

Table 1 Number of screening mammograms, recalls, assessments by type, surgical referrals and surgical biopsies, and detected benign and malignant breast lesions at the first screen and at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

Table 2 Recall rate, assessment rate by type, surgical referral and surgical biopsy rates, and breast cancer detection rates at the first screen and homologous cumulative rates at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

Table 3 Recall rate, assessment rate by type, surgical referral and surgical biopsy rates, and breast cancer detection rates at the first screen and homologous cumulative rates at the second and subsequent screens: ratio between women aged 45-49 years and women aged 50-54 years and 55-69 years. Emilia-Romagna Region mammography screening programme (2011-2015)

Table 4 DCIS:invasive cancer ratio, pT and pN distribution, positive predictive value of mammography, surgical referral and surgical biopsy, and proportion of conservative treatments for breast cancer at the first screen and at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

Table 5 DCIS:invasive cancer ratio, pT and pN distribution, positive predictive value of mammography, surgical referral and surgical biopsy, and proportion of conservative treatments for breast cancer at the first screen and at the second and subsequent screens: ratio between women

aged 45-49 years and women aged 50-54 years and 55-69 years. Emilia-Romagna Region mammography screening programme (2011-2015)

Table

Table 1 Number of screening mammograms, recalls, assessments by type, surgical referrals and surgical biopsies, and detected benign and malignant breast lesions at the first screen and at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

	First screen				Second and subsequent screens				Total
	45-49	50-54	55-69	Total	45-49	50-54	55-69	Total	
Screening mammograms	174,657	44,801	26,761	246,219	345,235	228,106	645,775	1,219,116	1,465,335
Recalls	18,102	4187	2494	24,783	18,032	11,370	24,393	53,795	78,578
Assessments									
Non-invasive	13,732	2959	1695	18,386	14,755	8731	16,622	40,108	58,494
Invasive									
FNA	2184	654	317	3155	1544	1180	3637	6361	9516
NCB, VAB	1838	442	342	2622	1549	1330	3778	6657	9279
Total invasive	4022	1096	659	5777	3093	2510	7415	13,018	18,795
Total assessments	17,754	4055	2354	24,163	17,848	11,241	24,037	53,126	77,289
Surgical referrals	1091	410	377	1878	1056	1057	4423	6536	8414
Surgical biopsies	1026	387	352	1765	991	968	4192	6151	7916
Detected benign breast lesions	243	69	38	350	191	162	264	617	967
Detected breast cancers									
DCIS	225	88	55	368	187	191	653	1031	1399
Invasive cancer									
pT1mic-a-b	175	79	90	344	197	206	1310	1713	2057
pT1c	222	83	96	401	244	259	1303	1806	2207
pT2-4	97	41	59	197	97	99	460	656	853
pTX, missing pT information	25	11	10	46	37	21	146	204	250
pN-negative	346	148	165	659	399	414	2455	3268	3927
pN-positive	153	52	79	284	137	156	603	896	1180
pNX, missing pN information	13	7	7	27	39	15	160	214	241
Total invasive cancers*	522	214	258	994	578	588	3234	4400	5394
Total breast cancers*	747	302	313	1362	765	779	3887	5431	6793

FNA fine-needle aspiration; *NCB* needle core biopsy; *VAB* vacuum-assisted biopsy; *DCIS* ductal carcinoma in situ

Recall indicates recall for further assessment. Non-invasive assessment indicates one or more among ultrasound, diagnostic mammography, breast physical examination, and other tests without pathologic evaluation. Surgical referral indicates referral for open biopsy. Surgical biopsy indicates open biopsy. Second and subsequent screens indicate the second, third, fourth and fifth annual screen for women aged 45-49 years, and the second and third biennial screen for women aged 50-54 years and 55-69 years

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

Table

Table 2 Recall rate, assessment rate by type, surgical referral and surgical biopsy rates, and breast cancer detection rates at the first screen and homologous cumulative rates at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

	Rate at the first screen			Cumulative rate at the second and subsequent screens		
	45-49	50-54	55-69	45-49	50-54	55-69
Recall rate	103.6	93.5	93.2	208.9	99.7	75.5
Assessment rates						
Non-invasive assessment	78.6	66.0	63.3	171.0	76.6	51.5
Invasive assessment						
FNA	12.5	14.6	11.8	17.9	10.3	11.3
NCB, VAB	10.5	9.9	12.8	17.9	11.7	11.7
Total invasive assessment	23.0	24.5	24.6	35.8	22.0	23.0
Surgical referral rate	6.2	9.2	14.1	12.2	9.3	13.7
Surgical biopsy rate	5.9	8.6	13.2	11.5	8.5	13.0
Detection rate of benign breast lesion	1.4	1.5	1.4	2.2	1.4	0.8
Detection rates of breast cancer						
DCIS	1.3	2.0	2.1	2.2	1.7	2.0
Invasive cancer						
pT1mic-a-b	1.0	1.8	3.4	2.3	1.8	4.1
pT1c	1.3	1.9	3.6	2.8	2.3	4.0
pT2-4	0.6	0.9	2.2	1.1	0.9	1.4
pN-negative	2.0	3.3	6.2	4.6	3.6	7.6
pN-positive	0.9	1.2	3.0	1.6	1.4	1.9
Total invasive cancer*	3.0	4.8	9.6	6.7	5.2	10.0
Total breast cancer*	4.3	6.7	11.7	8.9	6.8	12.0

FNA fine-needle aspiration; *NCB* needle core biopsy; *VAB* vacuum-assisted biopsy; *DCIS* ductal carcinoma in situ

Recall indicates recall for further assessment. Non-invasive assessment indicates one or more among ultrasound, diagnostic mammography, breast physical examination, and other tests without pathologic evaluation. Surgical referral indicates referral for open biopsy. Surgical biopsy indicates open biopsy. Second and subsequent screens indicate the second, third, fourth and fifth annual screen for women aged 45-49 years, and the second and third biennial screen for women aged 50-54 years and 55-69 years

All rates are per 1,000 screening mammograms

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

Table

Table 3 Recall rate, assessment rate by type, surgical referral and surgical biopsy rates, and breast cancer detection rates at the first screen and homologous cumulative rates at the second and subsequent screens: ratio between women aged 45-49 years and women aged 50-54 years and 55-69 years. Emilia-Romagna Region mammography screening programme (2011-2015)

	Rate ratio (95% CI) at the first screen		Cumulative rate ratio (95% CI) at the second and subsequent screens	
	45-49 vs. 50-54	45-49 vs. 55-69	45-49 vs. 50-54	45-49 vs. 55-69
Recall rate	1.11 (1.07-1.15)	1.11 (1.07-1.16)	2.10 (2.06-2.13)	2.77 (2.73-2.80)
Assessment rates				
Non-invasive assessment	1.19 (1.14-1.24)	1.24 (1.18-1.31)	2.23 (2.20-2.27)	3.32 (3.28-3.37)
Invasive assessment				
FNA	0.86 (0.78-0.93)	1.06 (0.94-1.19)	1.73 (1.65-1.81)	1.59 (1.54-1.64)
NCB, VAB	1.07 (0.96-1.18)	0.82 (0.73-0.92)	1.54 (1.47-1.61)	1.53 (1.48-1.59)
Total invasive assessment	0.94 (0.88-1.01)	0.94 (0.86-1.01)	1.63 (1.58-1.68)	1.56 (1.52-1.60)
Surgical referral rate	0.68 (0.61-0.76)	0.44 (0.39-0.50)	1.32 (1.25-1.39)	0.89 (0.86-0.93)
Surgical biopsy rate	0.68 (0.60-0.76)	0.45 (0.40-0.50)	1.35 (1.28-1.43)	0.88 (0.85-0.92)
Detection rate of benign breast lesion	0.90 (0.69-1.18)	0.98 (0.70-1.38)	1.56 (1.37-1.77)	2.71 (2.42-3.02)
Detection rates of breast cancer				
DCIS	0.66 (0.51-0.84)	0.63 (0.47-0.84)	1.29 (1.14-1.46)	1.07 (0.98-1.17)
Invasive cancer				
pT1mic-a-b	0.57 (0.44-0.74)	0.30 (0.23-0.38)	1.26 (1.12-1.42)	0.56 (0.52-0.61)
pT1c	0.69 (0.53-0.88)	0.35 (0.28-0.45)	1.24 (1.12-1.38)	0.70 (0.65-0.75)
pT2-4	0.61 (0.42-0.87)	0.25 (0.18-0.35)	1.29 (1.09-1.54)	0.79 (0.70-0.89)
pN-negative	0.60 (0.49-0.73)	0.32 (0.27-0.39)	1.27 (1.17-1.39)	0.61 (0.57-0.64)
pN-positive	0.75 (0.55-1.03)	0.30 (0.23-0.39)	1.16 (1.01-1.33)	0.85 (0.77-0.94)
Total invasive cancers*	0.63 (0.53-0.73)	0.31 (0.27-0.36)	1.30 (1.21-1.39)	0.67 (0.64-0.70)
Total breast cancers*	0.63 (0.55-0.72)	0.37 (0.32-0.42)	1.30 (1.22-1.38)	0.74 (0.71-0.77)

FNA fine-needle aspiration; *NCB* needle core biopsy; *VAB* vacuum-assisted biopsy; *DCIS* ductal carcinoma in situ; *CI* confidence interval

Recall indicates recall for further assessment. Non-invasive assessment indicates one or more among ultrasound, diagnostic mammography, breast physical examination, and other tests without pathologic evaluation. Surgical referral indicates referral for open biopsy. Surgical biopsy indicates open biopsy. Second and subsequent screens indicate the second, third, fourth and fifth annual screen for women aged 45-49 years, and the second and third biennial screen for women aged 50-54 years and 55-69 years

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

Table

Table 4 DCIS:invasive cancer ratio, pT and pN distribution, positive predictive value of mammography, surgical referral and surgical biopsy, and proportion of conservative treatments for breast cancer at the first screen and at the second and subsequent screens, by woman's age group. Emilia-Romagna Region mammography screening programme (2011-2015)

	Value at the first screen			Value at the second and subsequent screens		
	45-49	50-54	55-69	45-49	50-54	55-69
DCIS:invasive cancer ratio	0.43	0.41	0.21	0.32	0.32	0.20
pT1mic-a-b/total invasive cancer	33.5	36.9	34.9	34.1	35.0	40.5
pT1c/total invasive cancer	42.5	38.8	37.2	42.2	44.0	40.3
pT2-4/total invasive cancer	18.6	19.2	22.9	16.8	16.8	14.2
pN-negative/total invasive cancer	66.3	69.2	64.0	69.0	70.4	75.9
pN-positive/total invasive cancer	29.3	24.3	30.6	23.7	26.5	18.6
Positive predictive value						
of mammography, for invasive cancer*	2.9	5.3	11.0	3.2	5.2	13.5
of mammography, for DCIS and invasive cancer*	4.2	7.4	13.3	4.3	6.9	16.2
of surgical referral, for invasive cancer*	47.8	52.2	68.4	54.7	55.6	73.1
of surgical referral, for DCIS and invasive cancer*	68.5	73.7	83.0	72.4	73.7	87.9
of surgical biopsy, for invasive cancer*	50.9	55.3	73.3	58.3	60.7	77.1
of surgical biopsy, for DCIS and invasive cancer*	72.8	78.0	88.9	77.2	80.5	92.7
Conservatively treated/pT1	79.4	84.0	90.9	85.7	85.8	91.7
Conservatively treated/total treated†	72.7	78.8	80.1	78.8	81.1	85.7

DCIS ductal carcinoma in situ

Surgical referral indicates referral for open biopsy. Surgical biopsy indicates open biopsy. Second and subsequent screens indicate the second, third, fourth and fifth annual screen for women aged 45-49 years, and the second and third biennial screen for women aged 50-54 years and 55-69 years

Except for the DCIS:invasive cancer ratio, all values are percentages

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

†Pooling DCIS cases and invasive cancers

Table

Table 5 DCIS:invasive cancer ratio, pT and pN distribution, positive predictive value of mammography, surgical referral and surgical biopsy, and proportion of conservative treatments for breast cancer at the first screen and at the second and subsequent screens: ratio between women aged 45-49 years and women aged 50-54 years and 55-69 years. Emilia-Romagna Region mammography screening programme (2011-2015)

	Ratio (95% CI) at the first screen		Ratio (95% CI) at the second and subsequent screens	
	45-49 vs. 50-54	45-49 vs. 55-69	45-49 vs. 50-54	45-49 vs. 55-69
DCIS:invasive cancer ratio	1.05 (0.77-1.42)	2.02 (1.44-2.87)	1.00 (0.78-1.26)	1.60 (1.32-1.94)
pT1mic-a-b/total invasive cancer	0.91 (0.73-1.12)	0.96 (0.78-1.18)	0.97 (0.83-1.14)	0.84 (0.75-0.95)
pT1c/total invasive cancer	1.10 (0.90-1.33)	1.14 (0.95-1.38)	0.96 (0.84-1.09)	1.05 (0.94-1.16)
pT2-4/total invasive cancer	0.97 (0.70-1.35)	0.81 (0.61-1.08)	1.00 (0.77-1.29)	1.18 (0.97-1.44)
pN-negative/total invasive cancer	0.96 (0.86-1.07)	1.04 (0.93-1.16)	0.98 (0.91-1.06)	0.91 (0.86-0.96)
pN-positive/total invasive cancer	1.21 (0.92-1.58)	0.96 (0.76-1.20)	0.89 (0.73-1.09)	1.27 (1.08-1.50)
Positive predictive value				
of mammography, for invasive cancer*	0.56 (0.48-0.65)	0.27 (0.23-0.31)	0.62 (0.55-0.69)	0.24 (0.22-0.26)
of mammography, for DCIS and invasive cancer*	0.56 (0.50-0.64)	0.32 (0.28-0.36)	0.62 (0.56-0.68)	0.27 (0.25-0.29)
of surgical referral, for invasive cancer*	0.92 (0.82-1.02)	0.70 (0.64-0.77)	0.98 (0.91-1.06)	0.75 (0.71-0.79)
of surgical referral, for DCIS and invasive cancer*	0.93 (0.87-1.00)	0.82 (0.78-0.88)	0.98 (0.93-1.03)	0.82 (0.79-0.86)
of surgical biopsy, for invasive cancer*	0.92 (0.83-1.02)	0.69 (0.64-0.76)	0.96 (0.89-1.03)	0.76 (0.71-0.80)
of surgical biopsy, for DCIS and invasive cancer*	0.93 (0.87-0.99)	0.82 (0.78-0.86)	0.96 (0.92-1.00)	0.83 (0.80-0.86)
Conservatively treated/pT1	0.95 (0.87-1.03)	0.87 (0.80-0.95)	1.00 (0.95-1.05)	0.93 (0.89-0.98)
Conservatively treated/total treated†	0.92 (0.85-1.01)	0.91 (0.82-1.01)	0.97 (0.92-1.03)	0.92 (0.87-0.97)

DCIS ductal carcinoma in situ; *CI* confidence interval

Surgical referral indicates referral for open biopsy. Surgical biopsy indicates open biopsy. Second and subsequent screens indicate the second, third, fourth and fifth annual screen for women aged 45-49 years, and the second and third biennial screen for women aged 50-54 years and 55-69 years

*Including pTX and pNX invasive cancers and invasive cancers with missing pT and pN information

†Pooling DCIS cases and invasive cancers

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