PERSONALISATION OF FOLLOW-UP CARE IN WOMEN TREATED FOR BREAST CANCER: A RETROSPECTIVE COHORT STUDY

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Health Technology & Services Research 23-8-2016

UNIVERSITY OF TWENTE.



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ABSTRACT

Purpose Breast cancer follow-up is intended to be more personalized in the Netherlands with respect to detection of loco regional recurrences according to the new guideline. In contrast, the previous guideline recommended the same follow-up for all patients despite the variance in risk of recurrences for individuals. To give insight in the personalisation of follow-up care, we studied whether follow-up practice differs between patients diagnosed before and after implementation of a new, more personalized intended guideline for arrangement of follow-up, whether the follow-up practices differs from the old and current guidelines and whether individual follow-up care plans are compiled.

Methods A retrospective cohort study was performed reviewing 250 patient charts of curatively treated patients for primary invasive breast cancer diagnosed in 2010, 2012 or 2013 in five hospitals in the Netherlands. Patients were selected from the Netherlands cancer registry. Data about follow-up visits with the purpose of detecting of loco-regional recurrences was extracted from patient charts. The number of follow-up visits were tested for differences and Poisson regression was used to determine whether the amount of visits depended on known risk factors for recurrence.

Results Patients of both cohorts received more follow-up visits than recommended by the different guidelines. The total number of follow-up visits increased when a radiotherapist was involved, the patient was younger and had a lower tumour stage. An underuse of mammography was found. The follow-up plans that were found showed no evidence of personalisation based on risk of recurrence.

Conclusions Despite providing different recommendations, follow-up of patients diagnosed with breast cancer before and after publication of the 2012 guideline was almost similar concerning the visits with the purpose of detection of LRRs, during the first three years of follow-up. Influence of age, tumour stage and receiving radiotherapy on the number of follow-up visits suggests some personalisation of follow-up.

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Keywords follow-up care, breast cancer, recurrence, guideline, mammography

1 INTRODUCTION

Every year more than 14,000 women are diagnosed with invasive mamma carcinoma and receive treatment aimed at curation of their disease [1]. Following curative treatment for breast cancer, patients receive follow-up care. This follow-up care has three aims: providing psychosocial support, monitoring of treatment side-effects and early detection of both loco-regional recurrences (LRR) and second primary breast cancer (SPBC). In particular, LRR is searched for, because of the high risk for distant metastasis. Early detection of LRR improves survival compared to late symptomatic detection [2]. In general, follow up is not aimed at detection of metastasis, because early detection of metastasis does not improve survival [3, 4].

LRRs are defined as ipsilateral events in the breast (local) and/or in axillary, infraclavicular, supraclavicular, internal mammary/parasternal or intramammary lymph nodes (regional) [5]. Known risk factors for LRR are tumour size, age, tumour grade, vascular invasion, multifocality, hormone receptor status an treatment of primary tumours [6]. The majority of LRRs occur in the first five years after curative treatment [7]. The incidence of LRR within five years following primary treatment is 2,6% after lumpectomy and 3,5% after mastectomy [8].

The arrangement of follow-up care is described in the guidelines (Figure 1) [9, 10]. In 2012, a new guideline was published in which a more personalized follow-up schedule was advised, in line with trends in cancer care. Until 2012, the guideline developed in 2002 was valid. According to 2002 guideline all woman received similar follow-up care regardless of the individual differences in risk of recurrences [9]. The 2002 guideline prescribed that women should visit the hospital every three months during the first year of follow-up, every six months during the second year and once a year in the remaining three years. The consultations can be performed by one or more specialists. Additionally, women should be physically examined during every visit and they should receive a mammogram once a year. The start of the follow-up is defined as the date of the end of treatment (date of surgery or end date of adjuvant radiotherapy and/or chemotherapy).



FIGURE 1 ARRANGEMENT OF VISITS AND MAMMOGRAPHY IN 2012 AND 2002 GUIDELINES

According the 2012 guideline, the care provider has to develop a personalized follow-up plan in consultation with the patient [10]. This plan contains arrangements concerning specialists involved in the follow-up, the frequency of follow-up visits and diagnostic tests (physical examination, mammogram and MRI). According to the guideline women are physically examined and receive a mammogram once a year, both during a five year follow-up and more if indicated. To improve continuity of follow-up care the visits must be performed by the same specialist. In this guideline, the start of the follow-up is defined as the date of last surgery.

From several studies into the adherence to the 2002 guideline, overuse as well as underuse of strategies for detection of LRR were reported [11-13]. In the first year of follow-up, an underuse of follow-up visits with physical examination was seen. From the third year till the fifth year an overuse of these visits was seen. An underuse of mammograms was noticed for all follow-up years. According to these studies, the yield of physical examinations and mammography in detecting LRR's is limited, which indicates overtreatment.

During follow-up visits, 34% of recurrences are found asymptomatically, showing the benefit of follow-up visits [11]. Remarkably, almost half of the recurrences are found in between routine follow-up visits due to manifestation of symptoms in response to the patient's self-examination [12]. Following from these results and the low LRR incidence rates, the frequency and length of follow-up are debatable. In fact the differences in risk of recurrences between individuals call for a more personalized follow-up. For this reason the 2012 guideline recommends that clinicians draw up an individual follow-up plan in consultation with the patient taking the risk of recurrence into account. The extent to which follow-up is really personalized in practice is still unclear. This leads to the overall research question:

"Do breast cancer patients who are curatively treated with surgery, adjuvant radiotherapy and/or adjuvant systemic therapy receive personalized follow-up after implementation of the 2012 guideline?"

Therefore we explore: (1) whether follow-up care of patients treated according the 2012 guideline differs from follow-up practice of patients treated according to the 2002 guideline with respect to detection of LRR, (2) whether the 2002 guideline and 2012 guideline are followed in practice with respect to detection of LRR and (3) the availability of follow-up plans and their content.

2 METHODS

Design

To address above mentioned research question a retrospective cohort study was conducted.

Patients

Patients with primary invasive breast cancer were identified from the Netherlands Cancer Registry (NCR). This registry includes all newly diagnosed malignancies in the Netherlands based on notification by the national pathology archive (PALGA) [14] and is hosted by Comprehensive Cancer Centre the Netherlands (IKNL) [15]. Inclusion criteria were women with primary invasive breast cancer who underwent breast surgery and received follow-up care in the participating hospitals. Exclusion criteria were women with positive BRCA 1/2 gen, earlier or synchronous tumours, neo-adjuvant systemic therapy, no surgery or surgery abroad, TNM staging pT=4 or pT=0, macroscopic residue and microscopic residue without adjuvant treatment.

The study population comprises a cohort treated according to the 2002 guideline and a cohort treated according to the 2012 guideline. The cohort treated according to 2002 guideline consisted of patients diagnosed between the first of January 2010 and the first of January 2011 (n=9675), the cohort treated according to the 2012 guideline consisted of patients diagnosed between the first of March 2012 guideline consisted of patients diagnosed between the first of March 2013 (n=9735) (Figure 1).

To answer the research question a sample was taken of eligible patients of five teaching and nonteaching hospitals in eastern Netherlands. Twenty-five patients per hospital from the 2012 cohort were selected at random (Figure 1), resulting in a cohort sample of 125 patients. Following the frequency matching method [16], every selected patient from the 2012 cohort sample was matched with a patient from the 2010 cohort based on combination of the following characteristics: age, hospital of surgery, tumour size, degree of differentiation and received treatments. When more than one patient from the 2010 cohort had the same combination of characteristics, a matching patient was selected from these at random. This led to the inclusion of 250 patients in total.

Data collection

Patient, tumour and treatment characteristics were obtained from the NCR. Comorbidities were registered following the Charlson comorbidity index [17]. Additional data about follow-up visits during which physical examination, here after referred to as 'visits', was performed were collected retrospectively from medical charts. The following items of every visit with the purpose of detection LRR (performing physical examination and/or mammogram) were recorded: consultations at the surgical, medical oncologist or radiotherapy department, medical oncologist, radiotherapist and breast care nurse, reason of visit (regular follow-up visit or initiated by the patient), performer of consultation, patient complaints, physical examination, diagnostic tests and outcome of consultation. When only a diagnostic test, e.g. mammogram, was performed during a visit, the test and date of the test were registered with the visit in which the result of the test was discussed. Additionally, presence of follow-up plans including content were registered. Date of last surgery was defined as the start of follow-up and follow-up ended after five years, following the 2012 guideline. The cut-off point of one follow-up year was 365 days. Disease relapse, lost-to-follow-up and decease of the patient were also considered as end of follow-up. Data was collected over a follow-up period of five years for the 2010 cohort sample. For the 2012 cohort sample the followup was completed to the third year. Data collection took place from April 2016 until June 2016.



FIGURE 2 FLOW CHART OF PATIENT INCLUSION

Ethical considerations

This study is not subject to the Dutch Medical Research Involving Human Subjects Act (Wet medisch-wetenschappelijk onderzoek met mensen), because the patients were not subjected to procedures or are required to follow rules of behaviour. As a consequence no ethical permission was required. To confirm this statement, the research proposal was submitted to the Research Ethics Committee region Arnhem-Nijmegen. For access to the medical records, surgeons with specialisation in oncology, medical oncologists and/or radiotherapists of the participating hospitals were asked for permission. Anonymity of the patients and hospitals was guaranteed. Furthermore, the data collectors have signed a confidentiality agreement. The Committee of Privacy and supervisory board of the Comprehensive Cancer Organisation the Netherlands (IKNL) consented with this study.

Statistical analysis

Descriptive data are presented in percentages and means. Guideline adherence of follow-up visits and mammograms was assessed by using a two independent sample t-test to compare the mean number of visits and mammograms.

To determine differences between the number of follow-up visits (dependent variable) among subgroups of patient's age (≤ 60 , 61-75, >75), tumour stage (1, 2 and 3), tumour grade (I, II or III) and whether or not patients received chemo-, radio- or hormone therapy (independent variables) a one-way analysis of variance (ANOVA) was performed. A Poisson regression analysis was performed to determine if the known risk factors for recurrence age, tumour grade, tumour size and treatments (independent variables) influence the number of follow-up visits (dependent variable). For all analyses the significance level was set at 5% (p=0.05) and all analysis were performed using STATA (version 14.1).

3 RESULTS

Patient characteristics

In table 1 the characteristics of the two patient cohort samples and cohorts are presented. During the follow-up period 18 (7%) patients died, 7 (3%) patients had a recurrence and 8 (3%) patients were lost to follow-up. The mean ages of the 2010 and 2012/2013 cohort samples were 60.3 and 60.1 years respectively. In both cohort samples, comorbidity was present in 52 of 125 patients (42%). No significant differences were found in percentages and means between both cohort samples. The characteristics of both cohort samples are comparable to the characteristics of both cohorts, no significant differences were found (Table 1).

	2012/2013 cohort	2010 cohort	2012/2013 cohort	2010 cohort
	sample	sample		
	N=125	N=125	N=9735	N=9675
	(N (%))	(N (%))	(N (%))	(N (%))
Age at diagnosis (in yea	rs)			
mean	60.1	60.3	60.2	59.2
≤60	63 (50)	57 (46)	4872 (50)	5196 (54
61-75	52 (42)	57 (46)	3921 (40)	3513 (36)
>75	10 (8)	11 (8)	942 (9)	966 (10)
Tumour stage				
1	82 (66)	87 (70)	6630 (68)	6273 (65)
2	40 (32)	38 (30)	2803 (29)	3079 (31)
3	3 (2)	0 (0)	247 (2)	268 (3)
Unknown	-	-	44 (1)	55 (1)
Tumour grade				
1	35 (28)	37 (30)	2487 (26)	2284 (24)
II	50 (40)	57 (46)	4172 (43)	4213 (43)
III	39 (31)	29 (23)	2669 (27)	2708 (28)
IV	-	-	2 (0)	2 (0)
Unknown	1 (1)	2 (1)	425 (4)	468 (5)
Treatment				
Surgery				
Mastectomy	50 (40)	51 (41)	3190 (33)	3568 (37)
Breast conserving	75 (60)	74 (59)	6541 (67)	6098 (63)
Coincidence finding	-	-	4 (0)	10 (0)
mamma reduction				
Adjuvant				
Chemotherapy	47 (38)	45 (36)	3876 (40)	4166 (43)
Radiotherapy	81 (65)	82 (66)	7022 (72)	6510 (67)
Hormone therapy	55 (44)	62 (50)	5291 (54)	5357 (55)

LRR detection: visits and mammograms

Concerning the differences between guideline and practice, it was seen that for all follow-up years of the 2012/2013 cohort sample significant more visits were performed than recommended by the 2012 guideline (p<0.01) (Table 2). In the first year the overuse was the highest; patients received 2.02 visits were one was recommended. For the 2010 cohort sample significant differences in the number of visits were found for all follow-up years, except for the second year. In the first year of follow-up less visits were observed (2.35) than recommended by the guidelines (4). Meanwhile

N=250	N=250 2012/2013 cohort sample (N=125)			2010 coho	2010 cohort sample (N=125)							
	NABON ¹	Ν	Mean (95% confidence interval)	Less than recommended	As recommended	More than recommended	NABON ¹	Ν	Mean (95% confidence interval)	Less than recommended	As recommended	More than recommended
Consultations												
Year 1	1	125	2.02* ² (1.77-2.26)	12 (10%)	40 (32%)	73 (58%)	4	125	2.35 ^{* 2} (2.13-2.57)	104 (83%)	14 (11%)	7 (5%)
Year 2	1	113	1.84* (1.65-2.03)	7 (6%)	38 (34%)	68 (60%)	2	120	1.93 (1.77-2.10)	36 (30%)	59 (49%)	25 (21%)
Year 3	1	107	1.69* (1.51-1.88)	7 (6%)	43 (40%)	57 (53%)	1	119	1.63* (1.48-1.80)	7 (6%)	50 (42%)	62 (52%)
Year 4	1	-	-	-	-	-	1	109	1.50* (1.35-1.64)	6 (5%)	53 (49%)	50 (46%)
Year 5	1	-	-	-	-	-	1	107	1.36* (1.22-1.51)	7 (6%)	64 (60%)	36 (34%)
Mammograms												
Year 1	1	125	0.53* (0.43-0.62)	62 (50%)	60 (48%)	3 (2%)	1	125	0.52* (0.42-0.62)	64 (51%)	57 (46%)	4 (3%)
Year 2	1	113	0.81* (0.71-0.92)	29 (26%)	76 (67%)	8 (7%)	1	120	0.83* (0.73-0.94)	29 (24%)	84 (70%)	7 (6%)
Year 3	1	107	0.84* (0.75-0.93)	22 (20%)	80 (75%)	5 (5%)	1	119	0.82* (0.73-0.92)	29 (24%)	82 (69%)	8 (7%)
Year 4	1	-	-	-	-	-	1	109	0.90** (0.81-0.99)	19 (18%)	82 (75%)	8 (7%)
Year 5	1	-	-	-	-	-	1	107	0.79* (0.71-0.88)	23 (21%)	83 (78%)	1 (1%)

TABLE 2 GUIDELINE ADHERENCE OF CONSULTATIONS AND MAMMOGRAMS FOR 2012/2013 AND 2010 COHORT SAMPLES

¹ The number of visits according to the National Breast Cancer Network Netherlands (NABON) guideline

² Significant difference between 2010 and 2012/2013 cohort sample in mean number of consultations by means of two independent t-test (only comparison of first three years was possible)

* p<0.01, ** p<0.05

significant more visits were observed during the third until the fifth year. In the second year the mean number of visits was according to the 2002 guideline.

In addition the average number of mammograms was significant less than the recommendations for both cohort samples during all follow-up years (Table 2). In particular during the first year of follow-up; the 2012/2013 cohort sample (50%) and the 2010 cohort sample (51%) received less than one mammogram.

When comparing the mean number of visits for both cohort samples using a two independent ttest a significant difference was only found in the first year; the 2012/2013 cohort sample received 2.02 visits and the 2010 cohort sample 2.35 visits (Table 2). No significant differences were found comparing mean number of mammograms between the two cohort samples.

As an overuse was found in number of consultations, a one-way ANOVA was performed in order to identify subgroups which show differences in the average total number of consultations during three years follow-up for both cohort samples and during five year for the 2010 cohort sample (Table 3).

Comparing three years of follow-up of both cohort samples, no significant differences were found in the means of total number of consultations for different subgroups based on tumour grade, receiving hormone therapy and receiving chemotherapy (p<0.05). For the subgroups based on receiving radiotherapy a significant (p<0.05) increase in number of follow-up visits was found for patients who did receive radiotherapy (6.8 visits) compared to patients who did not receive radiotherapy (4.4 visits) in 2012/2013 cohort sample. For the 2010 cohort sample with three year follow-up, no significant difference was found.

The differences in total of visits for different tumour stages were significant for the 2012/2013 cohort sample, lower tumour stages received more visits. Additional analysis showed that patients with low tumour stages often received adjuvant radiotherapy; in both cohort samples about 76% (n=82 for 2012/2013 cohort sample and n=87 for 2010 cohort sample) of tumour stage 1 patients received adjuvant radiotherapy and about 48% of patients with tumour stage 2 (n=40 for 2012/2013 cohort sample and n=38 for 2010 cohort sample).

No significant differences between tumour stage subgroups were found for the 2010 cohort sample with three year follow-up. Subcategories in age significantly increased the total number of visits for younger patients in the 2012/2013 cohort sample. No significant difference was found in mean number of visits for different ages for the 2010 cohort sample with three year follow-up.

Because we also retrieved data about the five year follow-up of the 2010 cohort sample, also a one-way ANOVA was performed on this data in order to identify subgroups which show differences in the average total number of visits (Table 3). A significant increase of the number of visits was found for patients who received radiotherapy (8.65) compared to patients who did not receive radiotherapy (7.47). No significant differences were found in subgroups based on age, tumour stage, tumour grade, receiving chemotherapy and receiving hormone therapy in the 2010 cohort sample when analysing five year follow-up.

	2012/2013 cohort sample		ort sample	2010 cohort sample			2010 cohort sample		
	Three year follow-up		w-up	Five year follow-up			Five year follow-up		
	N	Mean number of visits	p-value ¹	Ν	Mean number of visits	p-value ¹	Ν	Mean number of visits	p-value ¹
Age at diagnosis (in years)			0.006**			0.249			0.053***
≤60	63	6.41		57	6.04		57	8.68	
61-75	52	5.75		57	5.65		57	8.16	
>75	10	3.40		11	5.00		11	6.36	
Tumour stage			<0.001*			0.986			0.464
1	82	6.62		87	5.77		87	8.37	
2	40	4.53		36	5.76		38	7.95	
3	3	4.33		-	-		-	-	
Tumour grade			0.822			0.333			0.197
I	35	5.66		37	6.22		37	9.05	
II	50	6.18		57	5.72		57	8.05	
III	39	5.77		29	5.34		29	7.55	
Unknown	1	5.00		2	5.00		2	8.5	
Radiotherapy			<0.001*			0.093***			0.032**
Yes	81	6.81		82	5.99		82	8.65	
No	44	4.40		43	5.35		43	7.47	
Chemotherapy			0.484			0.320			0.543
Yes	45	6.13		47	6.00		47	8.45	
No	80	5.76		78	5.63		78	8.12	
Hormone therapy			0.808			0.818			0.335
Yes	66	5.95		62	5.73		62	7.98	
No	59	5.83		63	5.81		63	8.49	

TABLE 3 MEAN NUMBER OF VISITS IN TOTAL FOR DIFFERENT SUBGROUPS

¹ From one-way ANOVA

* p<0.01), ** p<0.05, ***p<0.1

To identify whether the effect of age, tumour stage tumour differentiation, radiotherapy, hormone therapy and chemotherapy on the total number of visits during three years of follow-up differs between both cohorts a Poisson regression was performed (Table 4). The effects of age, hormone therapy and chemotherapy on the number of visits did not significantly differ between both cohorts. The interaction between year of diagnosis and tumour stage was significant; 25% less visits for patients from 2012/2013 cohort sample with tumour stage 2 and compared to the reference group (p=0.040). The effect of tumour differentiation and number of visits was also significant; 43% more visits for patients of 2012/2013 cohort sample with tumour stage II (p=0.042). Patients of 2012/2013 cohort sample who received radiotherapy received 31% more visits (p=0.040) compared to the reference group.

Follow-up plans

According to the 2012 guideline, specialists are recommended to write a personalized follow-up plan in consultation with the patient. In total nine follow-up plans (7.2% of the 2012/2013 cohort sample) were registered in patient charts, all in one hospital. In all plans the potential physical and

Year of diagnosis * Age $-2010 \text{ cohort sample} - Age: \leq 60 0.8895 0.356 2012 >75 0.7180 0.237 Year of diagnosis * Tumour stage -2010 \text{ cohort sample} - Tumour stage: 1 0.7180 0.237 2010 3 -2010 \text{ cohort sample} - Tumour stage: 1 1 \text{ (empty)} 0.744 0.040^* 2012 2 0.744 0.040^* 1 \text{ (omitted)} 0.281 Year of diagnosis * Tumour differentiation 2010 \text{ cohort sample} - Tumour differentiation: 1 1 \text{ (empty)} 0.281 2012 11 1 \text{ (omitted)} 1 \text{ (omitted)} 0.42^* Year of diagnosis * Radiotherapy 2010 \text{ cohort sample} - Radiotherapy: no 0.042^* Year of diagnosis * Radiotherapy -2010 \text{ cohort sample} - Radiotherapy: no 0.042^* Year of diagnosis * Hormone therapy -2010 \text{ cohort sample} - Radiotherapy: no 0.042^* Year of diagnosis * Hormone therapy -2010 \text{ cohort sample} - Hormone therapy: no 0.245 Year of diagnosis * Chemotherapy -2010 \text{ cohort sample} - Chemotherapy: no 0.8410 0.281 $	Interaction term	Reference group	Incidence rate ratio	p-value ¹
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2012 III1.42700.042*Year of diagnosis * Radiotherapy 2012 yes- 2010 cohort sample - Radiotherapy: no- 1.30680.042*Year of diagnosis * Hormone therapy 2012 yes- 2010 cohort sample 	2012 II		1.1631	0.281
Year of diagnosis * Radiotherapy- 2010 cohort sample - Radiotherapy: no2012 yes1.30680.042*Year of diagnosis * Hormone therapy 2012 yes- 2010 cohort sample - Hormone therapy: no1.15790.245Year of diagnosis * Chemotherapy 2012 yes- 2010 cohort sample - Chemotherapy: no0.84100.281	2012 III		1.4270	0.042*
2012 yes1.30680.042*Year of diagnosis * Hormone therapy 2012 yes- 2010 cohort sample - Hormone therapy: no1.15790.245Year of diagnosis * Chemotherapy 2012 yes- 2010 cohort sample - Chemotherapy: no0.84100.281	Year of diagnosis * Radiotherapy	- 2010 cohort sample - Radiotherapy: no		
Year of diagnosis * Hormone therapy 2012 yes- 2010 cohort sample - Hormone therapy: no2012 yes1.15790.245Year of diagnosis * Chemotherapy - Chemotherapy: no- 2010 cohort sample 	2012 yes		1.3068	0.042*
2012 yes 1.1579 0.245 Year of diagnosis * Chemotherapy - 2010 cohort sample - Chemotherapy: no - 2012 yes 0.8410 0.281	Year of diagnosis * Hormone therapy	- 2010 cohort sample - Hormone therapy: no		
Year of diagnosis * Chemotherapy- 2010 cohort sample - Chemotherapy: no2012 yes0.84100.281	2012 yes		1.1579	0.245
2012 yes 0.8410 0.281	Year of diagnosis * Chemotherapy	- 2010 cohort sample - Chemotherapy: no		
	2012 yes		0.8410	0.281

From Poisson regression

* p<0.05

psychologic consequences of breast cancer (treatment) and signals to consult specialists were described. In most of the plans the specialists involved in follow-up, frequency of physical examinations and mammograms were mentioned. The frequency of visits including physical examinations and mammogram was according to the minimum recommended by the guideline in all cases, no differentiation was encountered in all cases. In all plans visits with a variation of specialists were found including surgeon, medical oncologist, radiotherapist and breast care nurse.

Disciplines

According to the 2012 guidelines patients should receive follow-up care by one specialist. No significant differences (p<0.05) were found in the percentages of patients who received a certain treatment (surgery, radiotherapy or hormone and/or chemotherapy) between the cohort samples (Table 5). In addition, no significant differences (p<0.05) were found between both cohort samples in percentages of patients who visited a certain specialist. No changes were detected between both cohort samples. Patients still visit more specialists, when more specialists are involved due to adjuvant therapy.

TABLE 5 PATIENTS WHO RECEIVED TREATMENT AND VISITED THE SP	TABLE 5 PATIENTS WHO RECEIVED TREATMENT AND VISITED THE SPECIALIST				
	2012/2013	2010 cohort			
	cohort sample	sample			
	(N (%))	(N (%))			
Underwent surgery	125 (100)	125 (100)			
Visited surgeon	122 (98)	125 (100)			
Visited breast care nurse	92 (74)	103 (82)			
Received radiotherapy	81 (65)	82 (66)			
Visited radiotherapist	65 (52)	63 (56)			
Received hormone and/or chemotherapy	80 (64)	76 (61)			
Visited medical oncologist	19 (15)	15 (12)			

MRI scan of mamma

Women with dense breasts often got MRI scans instead of mammograms, because the mammograms are hard to assess. In both the 2012/2013 and 2010 cohort sample, ten patients with dense breasts received one or more MRI scans of the mamma instead of mammography. In the 2012/2013 cohort sample, seven women were 50 or younger and three were aged between 50 and 65. In the 2010 cohort sample five women were younger than 50 and five women were aged between 50 and 65. Of the 2012/2013 cohort sample seven patients received one MRI scan in three years of follow-up and three patients received two MRI scans. Five patients of the 2010 cohort sample received one MRI during five year follow-up, four patients received three MRI scans and one patient got four MRI-scans. Despite the low number of patients an underuse of MRI scans is indicated.

4 DISCUSSION AND CONCLUSION

Despite providing different recommendations, follow-up of patients diagnosed with breast cancer before and after publication of the 2012 guideline was almost similar concerning the visits with the purpose of detection of LRRs, during the first three years of follow-up. In fact, before 2012 specialists already act in accordance with the 2012 guideline, suggesting that the new guideline might have been a formalisation the current practice at that time. For patients diagnosed in 2012/2013 the number of visits was increased when a radiotherapist was involved, the patient was younger and had a lower tumour stage. An underuse was found for mammograms. Also an underuse of MRI scans was indicated for patients with dense breasts. The follow-up plans that were found showed no evidence of personalisation based on risk of recurrence. Involvement of different specialists during follow-up did not change.

In comparison with other studies on adherence of the 2002 guideline, differences are seen in the number of patient charts and patient groups. This study compared two patient groups and compared both groups, in total 250 patients, with associated guideline, were other studies compare one cohort with the 2002 guideline in 196 and 144 patients respectively [11, 12].

Other studies in adherence of the 2002 guideline found an overuse of 4 and 31% for visits in the first follow-up year, we found 5% overuse [11, 12]. The same studies found an overuse ranging from 51-86% for the second to the fifth year of follow-up [11, 12]. We found less overuse, but the overuse pattern was similar. Of both cohorts about 50% of the patients received a mammogram in the first year. This is a large decrease in the use compared to 76% reported by other studies during the 2002 guideline [11, 12]. From year two to five, the percentages of patients who got one or more mammograms per year varied between 74% and 83%. Other studies reported a slightly higher use of mammography (81%-87%) [11, 12]. In comparison with other studies on adherence of the 2002 guideline, differences are seen in the number of patient charts and patient groups. This study compared two patient groups and compared both groups, in total 250 patients, with associated guideline, were other studies compare one cohort with the 2002 guideline in 196 and 144 patients respectively [11, 12]. Differences in results may be caused by the inclusion of different incidence years: this study included patients diagnosed in 2010, while the other studies included patients diagnosed in 2003 and 2004. Over the years, hospitals may have changed internal protocols.

Having received radiotherapy was found as a factor influencing the number of visits for patients diagnosed in 2012/2013, this outcome is in accordance with the literature [12]. Not only subgroups based on receiving radiotherapy showed other results, but also subgroups based on age and tumour stage resulted in significant differences in mean number of visits. Young patients and patients with a high tumour stage have an increased risk of recurrences [18]. Specialists have the ability to plan more follow-up visits when patients have a high risk of recurrences. This study shows that younger patients received more follow-up visits, which might indicate somewhat personalisation of the follow-up visits. Paradoxically, patients with a high tumour stage did receive less visits than patients with a low tumour stage. Additional analyses showed that patients with a low tumour stage received radiotherapy more often, which may have resulted in more follow-up visits.

This study has several important strengths. For this study, patients were selected from the NCR in which all cancer patients in the Netherlands are registered, which means no selection bias was encountered. Also, both cohort samples have similar characteristics which indicates proper matching of patients. Furthermore, both cohort samples have the same characteristics as the patient cohorts, which might indicate high generalisability. Data extraction took place directly from patient charts, instead of automatic extraction of data. For this reason only the visits related to follow-up and detection of LRRs were registered instead of all visits.

Despite these strengths the results concerning guideline adherence should be interpreted with caution. This study included patients diagnosed after two weeks after publication of the guidelines; 25 (20%) patients were diagnosed within three months after the publication. As it is not known to what degree and at what time the new guidelines were implemented in the different hospitals directly after being issued, it is unknown what the effects are on the results. As a consequence of including patients diagnosed after implementation of new guideline in February 2010, only a follow-up of three years could be registered. In a couple of years the guideline adherence and degree of personalisation can be researched for five years of follow-up.

The start of follow-up is defined as the day of last surgery for both patient groups, which is not in line with 2002 guideline. This was done to be able to compare both groups. However, this can lead to an overestimation of follow-up visits of patients diagnosed before 2012. A cut-off point of 365 days for every follow-up year may have led to more visits in one year and less in another when patients had delayed or advanced visits. The number of mammograms may be underestimated due to the fact that women with dense breast receive a routine MRI examination instead of a mammogram. About 8% of the women in this study had dense breast in accordance with the literature [19]. Although breast cancer care is delivered based on nationwide guidelines, this study was conducted in five hospitals in the east of the Netherlands, which might limit the generalizability to some extent.

Due to increased survival rates and incidence in breast cancer the demand for follow-up care increases [20]. In this study only the visits with the purpose of detecting LRRs are included. In addition, the patients also visit breast care nurses for psycho-social care. When receiving hormone therapy patients also visit the medical oncologist regularly, but the oncologists rarely do physical examinations. For this reason the results of this study are an underestimation of the total care utilisation. This study shows the current demand for health care. The demand could become less, because breast care patients visit the hospital more than necessary in the context of detection of LRR following the 2012 guideline. The new guideline provides space for less frequent visits. Maybe the guidelines still needs some implementation time and the burden of care utilisation decreases as a consequence of less visits. However, the need for psycho-social care is left out of consideration in this study.

Personalized care is of increasing importance in health care to prevent under- and overuse of health care and to manage the growing demand for care. The 2012 guidelines provides opportunities for personalized follow-up care in breast cancer patients after treatment. This study shows that there might be some personalization in follow-up care practice in the first three years after publication of the 2012 guideline, seeing the influence of age and tumour stage on number of follow-up visits. Meanwhile the risk of recurrence is not noticed in patient charts, thus seems not to be involved in the decision making. The question arises why specialists provide more visits than recommended and why they seem not to provide personalized follow-up. It could be that professionals are in need of more guidance on arrangement of personalized follow-up schedules. Future research is needed on what specialists need to be able to provide personalized follow-up.

Besides advising a personalized follow-up, the 2012 guideline also recommends shared decisionmaking about the follow-up plan including the arrangement of the follow-up in line with recommendations of the Institute of Medicine [21]. Compiling a follow-up plan prevents losing breast cancer patients after treatment [22]. All plans found were part of another study. Future research that looks into processes of shared decision-making in compiling follow-up plans is needed to improve the degree of personalization in follow-up of breast cancer patients.

As patients already underwent less clinical visits aimed at early recurrence detection than prescribed, the issuing of the new, less intensive follow-up guideline in 2012 did not result in much change. The number of follow-up visits were significantly influenced by age, tumour stage and involvement of radiotherapists, suggesting perhaps some individualization in follow-up of breast cancer patients.

REFERENCES

- 1. IKNL. Incidence and mortality breast cancer. 2016 23-3-2016].
- 2. Lu, W.L., et al., Impact on survival of early detection of isolated breast recurrences after the primary treatment for breast cancer: a meta-analysis. Breast Cancer Res Treat, 2009. **114**(3): p. 403-12.
- 3. Ghezzi, P.P., et al., Impact of follow-up testing on survival and health-related quality of life in breast cancer patients: A multicenter randomized controlled trial. JAMA, 1994. **271**(20): p. 1587-1592.
- Rosselli Del Turco, M., et al., Intensive diagnostic follow-up after treatment of primary breast cancer. A randomized trial. National Research Council Project on Breast Cancer follow-up. JAMA, 1994.
 271(20): p. 1593-7.
- 5. Moossdorff, M., et al., *Maastricht Delphi consensus on event definitions for classification of recurrence in breast cancer research.* J Natl Cancer Inst, 2014. **106**(12).
- 6. Witteveen, A., et al., *Personalisation of breast cancer follow-up: a time-dependent prognostic nomogram for the estimation of annual risk of locoregional recurrence in early breast cancer patients.* Breast Cancer Res Treat, 2015. **152**(3): p. 627-36.
- 7. Demicheli, R., et al., *Recurrence dynamics does not depend on the recurrence site.* Breast Cancer Research, 2008. **10**(5): p. 1-8.
- van der Heiden-van der Loo, M., Ho, V.K.Y, Damhuis, R.A.M., Siesling, S., Menke, M.B.E., Peeters, P.H.M. & Rutgers, E.J.T., *Weinig lokaal recidieven na mammachirurgie: goede kwaliteit van de Nederlandse borstkankerzorg.* Nederlands Tijdschrift voor Geneeskunde, 2010. 154:A1984.
- 9. NABON, *Richtlijn: behandeling van het mammacarcinoom.* Vereniging van Integrale Kankercentra, 2005.
- 10. NABON, *Richtlijn: mammacarcinoom*. Intergaal Kankercentrum Nederland, 2012.
- 11. Geurts, S.M., et al., *Pattern of follow-up care and early relapse detection in breast cancer patients.* Breast Cancer Res Treat, 2012. **136**(3): p. 859-68.
- 12. Grandjean, I., et al., *Evaluation of the adherence to follow-up care guidelines for women with breast cancer.* Eur J Oncol Nurs, 2012. **16**(3): p. 281-5.
- 13. Lu, W., et al., Underuse of long-term routine hospital follow-up care in patients with a history of breast cancer? BMC Cancer, 2011. **11**: p. 279.
- 14. PALGA. <u>http://www.palga.nl/</u>. 2016.
- 15. IKNL. <u>https://www.iknl.nl/home</u>. 2016; Available from: <u>https://www.iknl.nl/home</u>.
- 16. Rothman, K.J., Greenland, S., Lash, T.L., *Modern epidemiology*. 3rd ed. 2008, Philadelphia: Lippincott Williams & Wilkins.
- 17. Janssen-Heijnen, M.L., et al., *Prognostic impact of increasing age and co-morbidity in cancer patients: a population-based approach.* Crit Rev Oncol Hematol, 2005. **55**(3): p. 231-40.
- 18. Kraeima, J., et al., *Individual risk profiling for breast cancer recurrence: towards tailored follow-up schemes.* Br J Cancer, 2013. **109**(4): p. 866-71.
- Emaus, M.J., et al., MR Imaging as an Additional Screening Modality for the Detection of Breast Cancer in Women Aged 50-75 Years with Extremely Dense Breasts: The DENSE Trial Study Design. Radiology, 2015. 277(2): p. 527-37.
- Molino, A., What is the best follow-up methodology in early breast cancer? Breast, 2008. 17(1): p. 1-2.
- 21. Hewitt, M., Greenfield, S., Stovall, E., *From Cancer Patient to Cancer Survivor: Lost in Transition*. 2006, Institute of Medicine: Washington, D.C.
- 22. Earle, C.C., Failing to plan is planning to fail: improving the quality of care with survivorship care plans. J Clin Oncol, 2006. **24**(32): p. 5112-6.

APPENDICES

1 CODEBOOK PATIENT

VARNO	VARNAME	Codering	Omschrijving/label	Toelichting
	IKC		IKC nummer	Vul op ieder formulier het 9-cijferig GRA-nummer in
	regdat	DD/MM/JJJJ	Datum registratie	Datum waarop de patiënt geregistreerd is
	internist	0= nee 1= ja 8= ja, maar ander ziekenhuis 9= onbekend	Nacontrole door internist	Indien de patiënt systemisch behandeld is zou de internist nacontrolevisites kunnen uitvoeren. 8= als de patiënt elders gecontroleerd wordt waardoor je geen informatie hebt over deze nacontroles.
	radiotherapeut	0= nee 1= ja 8= ja, maar ander ziekenhuis 9= onbekend	Nacontrole door radiotherapeut	Indien de patiënt radiotherapeutisch behandeld is zou de radiotherapeut nacontrolevisites kunnen uitvoeren. 8= als de patiënt elders gecontroleerd wordt waardoor je geen informatie hebt over deze nacontroles.
	chirurg	0= nee 1= ja 8= ja, maar ander ziekenhuis 9= onbekend	Nacontrole door chirurg	Indien de patiënt chirurgisch behandeld is zou de chirurg nacontrolevisites kunnen uitvoeren. 8= als de patiënt elders gecontroleerd wordt waardoor je geen informatie hebt over deze nacontroles.

PRIMAIRE BEHANDELING

datfirstPTT	DD/MM/JJJJ	Datum eerste	primaire	tumor	Eerste therapiedatum, dus niet diagnose datum
		behandeling			
datlastPTT	DD/MM/JJJJ	Datum laatste behandeling	primaire	tumor	Zonder hormonale/endocriene en doelgerichte (= targeted) therapie, omdat dit samenloopt met de nacontrole

PATIENTGEGEVENS COMORBIDITEITEN

CmCOPD	0= nee 1= ja	Comorbiditeit COPD	COPD
CmCAR	0= nee 1= ja	Comorbiditeit cardiovasculaire ziekten	Cardiovasculair ziekten: myocard infarct, hartinsufficiëntie, angina pectoris, coronaire bypassoperatie
CmPAD	0= nee 1= ja	Comorbiditeit perifere arteriele ziekten	Perifere arteriele ziekten: claudicatio intermittens, abdominaal aneurysma, chirurgische ingreep
CmCER	0= nee 1= ja	Comorbiditeit cerebrovasculaire ziekten	Cerebrovasculaire ziekten: cerebrovasculair accident, hemiplegi
CmMAL	0= nee 1= ja	Comorbiditeit overige maligniteiten	Overige maligniteiten (behalve basaalcelcarcinoom)
CmHT	0= nee 1= ja	Comorbiditeit hoge bloeddruk	Hoge bloeddruk
CmDM	0= nee 1= ja	Comorbiditeit diabetes mellitus	Diabetes mellitus
CmOT	0= nee 1= ja	Comorbiditeit overige	Auto-immuunziekte (sarcoïdose, ziekte van Wegener, SLE), reumatoïde artritis (alleen ernstige), nierziekte (glomerulonefritis, pyelonefritis), gastro- intestinale (maagzweer en resectie, colitis), leverziekte (cirrose, hepatitis), dementie, chronische infecties

NAZORGPLAN

Nazorgplan	0= nee 1= ja	Nazorgplan beschreven in status	Is er een (individueel) nazorgplan beschreven in de status/patiëntendossier?
NazorgGevolgLich	0 = nee 1= ja	Lichamelijke gevolgen	Lichamelijke gevolgen van ziekte en behandeling beschreven in het nazorgplan
NazorgGevolgPsych	0 = nee 1= ja	Psychosociale gevolgen	Psychosociale gevolgen van ziekte en behandeling beschreven in het nazorgplan

NazorgInricht	0 = nee 1= ia	Wenselijkheid en inrichting	Wenselijkheid en inrichting van de nazorg beschreven in het nazorgplan
NazorgHeroverweg	0 = nee 1= ja	Moment van heroverweging	Moment van heroverweging beschreven in het nazorgplan
NazorgPunten	0 = nee 1= ja	Aandachtspunten	Aandachtspunten beschreven in het nazorgplan
NazorgLategevolg	0 = nee 1= ja	Late gevolgen behandeling	Late gevolgen behandeling beschreven in het nazorgplan
NazorgRaadpleeg	0 = nee 1= ja	Signalen raadplegen arts	Signalen die aanleiding moeten zijn om een arts te raadplegen beschreven in het nazorgplan
NazorgTaakverd	0 = nee 1= ja	Afspraken taakverdeling	Afspraken over coördinatie en taakverdeling tussen hulpverleners beschreven in het nazorgplan
NazorgInternist	0 = nee 1= ja	Nazorg door internist	In het nazorgplan staat beschreven dat de internist de nazorg zal uitvoeren
NazorgRadio	0 = nee 1= ja	Nazorg door radiotherapeut	In het nazorgplan staat beschreven dat de radiotherapeut de nazorg zal uitvoeren
NazorgChirurg	0 = nee 1= ja	Nazorg door chirurg	In het nazorgplan staat beschreven dat de chirurg de nazorg zal uitvoeren
NazorgPE	0 = nee 1= ja	Lichamelijk onderzoek tijdens nazorg	Lichamelijk onderzoek is onderdeel van de nazorg volgens het nazorgplan
NazorgPErichtlijn	0 = nee 1= ja	Frequentie PE volgens richtlijn	Frequentie van lichamelijk onderzoek zoals beschreven in het nazorgplan komt overeen met de richtlijn (jaarlijks, gedurende 5 jaar)
NazorgPEduur	jaar 9= niet gedefineerd 999= levenslang	Duur van lichamelijk onderzoek	De duur dat lichamelijk onderzoek gedaan zal worden tijdens de nazorg zoals beschreven in het nazorgplan Alleen invullen indien afwijkend van richtlijn/standaard
NazorgPEfreq	openveld	Frequentie van lichamelijk onderzoek	Alleen invullen indien afwijkend van richtlijn/standaard
NazorgMG	0 = nee 1= ja	Mammogram tijdens nazorg	Mammogram is onderdeel van de nazorg volgens het nazorgplan
NazorgMGrichtlijn	0 = nee 1= ja	Frequentie MR volgens richtlijn	Frequentie van mammogram zoals beschreven in het nazorgplan komt overeen met de richtlijn (jaarlijks, gedurende 5 jaar)

			Alleen invullen indien afwijkend van richtlijn/standaard
NazorgMGduur	jaar 9= niet gedefineerd 999= levenslang	Duur van mammogram	De duur dat mammogram gedaan zal worden tijdens de nazorg zoals beschreven in het nazorgplan Alleen invullen indien afwijkend van richtlijn/standaard
NazorgMGfreq	openveld	Frequentie van mammogram	Alleen invullen indien afwijkend van richtlijn/standaard
Nazorgothertest	0 = nee 1= ja	Overige test benoemd in het nazorgplan	Overige test is onderdeel van de nazorg volgens het nazorgplan
Nazorgotherinfo	Open veld	Overige informatie nazorgplan	Ruimte om overige informatie uit het nazorgplan te beschrijven

LAATSTE CONTACTDATUM

datlastFU	DD/MM/JJJJ	Laatste contact datum	De laatste datum waarop de patiënt gezien is.
lastFUcond	1= tijdens primaire behandeling 2= in follow-up, geen therapie 3= in follow-up, hormonale of doelgerichte therapie 4= recidief, metastase, tweede primaire mammacarcinoom, curatieve behandeling 5= recidief, metastase, tweede primaire mammacarcinoom, palliatieve behandeling 6= lost to follow-up 8= ontslagen uit de nacontrole, no evidence of disease 9= overleden 99= onbekend	Toestand bij laatste contact datum	In welk stadium van de ziekte bevind zich de patiënt op bij de laatste contactdatum?
EndNacontrole	0= nee 1= ja	Einde nazorg	Ontslagen uit de nazorg
EndNacontroledat	DD/MM/JJJJ	Datum einde nazorg	Datum waarop de patiënt ontslagen is uit de nazorg

VerwGP	0= nee	Terugverwijzing huisarts	Na het ontslag uit de nazorg is de patiënt
	1= ja		(terug)verwezen naar de huisarts voor controle
VerwBOB	0= nee	Terugverwijzing bevolkingsonderzoek	Na het ontslag uit de nazorg is de patiënt
	1= ja	borstkanker	(terug)verwezen naar het bevolkingsonderzoek voor
			borstkanker
opmS1		Overige opmerkingen S1	

2 CODEBOOK FOLLOW-UP VISITS

VARNO	VARNAME	Codering	Omschrijving/label	Toelichting
	IKC		IKC nummer	Vul op ieder formulier het 9-cijferig GRA-nummer in
	FUdat	DD/MM/JJJJ	Datum nacontrole	De datum waarop de patiënt voor nacontrole komt.
				Dus niet de data waarop de testen uitgevoerd zijn.
			_	
	FUreason	1= routine	Soort nacontrole	1= ingeplande visite, trial gerelateerd en
		2= interval		bevolkingsonderzoek is ook routine
		9= onbekend		2= visite tussendoor, patient geïnitieerd
	FUrecidief	0= nee	Reden van visite, controle recidief	Controle recidief is de reden van visite
		1= ja		
		9= onbekend		
	FUhormoon	0= nee	Reden van visite, hormoon therapie	Hormoon therapie is de reden van visite
		1= ja		
		9= onbekend		
	FUtherapie	0= nee	Reden van visite, late therapie effecten	Late therapie effecten zijn de reden van visite; Late
		1= ja		therapie effecten zijn alle effecten die niet direct na
		9= onbekend		de behandeling optreden
	FUpsycho	0= nee	Reden van visite, psychosociale zorg	Psychosociale zorg is de reden van visite
		1= ja		
		9= onbekend		
	FUarts	1= arts	Uitvoerende zorgprofessional	Uitvoerende zorgprofessional van de nacontrole
		2= verpleegkundige		Onder verpleegkundige verstaan we mammacare
		8= anders		verpleegkundige, nurse physician etc.
	FUartsother		Andere uitvoerende zorgprofessional	Een andere zorgprofessional dan bovengenoemde
		= indien FUarts= 1 of 2		voert de nacontrole uit
	FUspec	1= medisch oncoloog	Uitvoerend specialisme	Het specialisme waartoe de uitvoerende
		2= chirurg		zorgprofessional behoort die de nacontrole uitvoert
		3= radiotherapeut		
		4= gynaecoloog		
		8= anders namelijk		
		9= onbekend		

FUspecother	= indien FUspec= 1-4 of 9	Ander specialisme	Een ander specialisme voert de nacontrole uit dan bovengenoemde specialismen
FUtype	1= poliklinisch 2= telefonisch 8= anders 9= onbekend	Type nacontrole	
FUtypeother	= indien FUtype = 1, 2 of 9	Ander type nacontrole	
FUlastmeter	0= nee 1= ja 9= onbekend	LASTmeter ingevuld	LASTmeter ingevuld tijdens controle
FUlastverw	0= nee 1= ja 9= onbekend	Doorverwezen ivm LASTmeter	Patient doorverwezen ivm LASTmeter

SYMPTOMEN

FUsymp	0= nee	Symptomen of klachten wijzend op	Klachten die wijzen op een recidief. Bijwerkingen
	1= ja	recidief aanwezig	therapie zoals opvliegers vallen hier <i>niet</i> onder.
	9= onbekend		
FUsympbone	1= botklachten	Bot klachten	
FUsympgeneral	1= algemene klachten	Algemene klachten	Voorbeelden van algemene klachten zijn: koorts,
	-	-	misselijkheid, vermoeidheid, hoofdpijn
FUsymplung	1= long	Long gerelateerde klachten	Hoest, benauwdheid, longontsteking
FUsympNS	1= neurologische klachten	Neurologische klachten	
FUsympskin	1= huidafwijkingen	Huidafwijkingen	
FUsympbreast	1= knobbel in de borst	Knobbel in de borst	
FUsympbreastother	1= klachten borst	Klachten borst	Rode borst, zwelling borst, ontsteking borst, klachten
			tepel
FUsymplymph	1= lymfeklieren	Vergrootte lymfeklieren	
FUsymparm	1= klachten arm	Klachten in de arm	
FUsympshoulder	1= klachten schouder	Klachten in de schouder	
FUsymppainchest	1= pijnklachten borst/oksel regio	Pijnklachten borst/oksel regio	Pijn in de borst/oksel regio
FUsymppainother	1= pijnklachten overige	Pijnklachten overige	Pijn overige bijv. ribben, rug
FUsympedema	1= oedeem/zwelling	Oedeem	Oedeem/zwelling
FUsympstomach	1= buikklachten	Buikklachten	Buik- en maagklachten
FUsymptypeother		Andere klachten	

FUsympunknown	1= onbekend	Type klachten onbekend	
COMORBODITEIT + LO + MAMI	MOGRAM		
FUCORMORB	0= nee 1= ja 9=onbekend/niet benoemd	Nieuwe comorbiditeit	Nieuwe comorbiditeit ontdekt gedurende de nazorg
FUPE	1= ja 2= niet benoemd	Lichamelijk onderzoek	
OutPE	0= negatief 1= positief 9= onbekend	Bevinding lichamelijk onderzoek	De uitslag van het lichamelijk onderzoek ter controle van recidieven; positief=aanwijzingen voor recidief, negatief=geen aanwijzingen voor recidief Deze variabele dient alleen ingevuld te worden bij routine afspraken en niet bij een interval afspraak
OutPEterecht	0= fout positief 1= terecht positief	Terechte bevinding lichamelijk onderzoek	Indien een positief lichamelijk onderzoek, de conclusie na vervolgonderzoek betreffende het resultaat van het lichamelijk onderzoek Deze variabele dient alleen ingevuld te worden bij routine afspraken en niet bij een interval afspraak
FUMG	1= ja 2= niet benoemd	Mammogram	
FUMGdat	DD/MM/JJJJ	Datum mammogram	Datum waarop de mammogram is uitgevoerd
OutMG	0= negatief 1= positief 9= onbekend	Bevinding Mammogram	De uitslag van het mammogram ter controle van recidieven; positief=aanwijzingen voor recidief, negatief=geen aanwijzingen voor recidief Deze variabele dient alleen ingevuld te worden bij routine afspraken en niet bij een interval afspraak
OutMGterecht	0= fout positief 1= terecht positief	Terechte bevinding Mammogram	Indien een positief mammogram, de conclusie na vervolgonderzoek betreffende het resultaat van de mammogram

Deze variabele dient alleen ingevuld te worden bij routine afspraken en niet bij een interval afspraak

BEELDVORMING + ONDERZOEK

FUMRIm	1= ja	MRI-scan mamma	
	2= niet benoemd		
FUMRImdat	DD/MM/JJJJ	Datum MRI-scan mamma	Datum waarop de MRI-scan mamma is uitgevoerd
FUbone	0= niet benoemd 1= ja	Bot-scan	Skeletscintigrafie: Indien doel is om osteoporose te monitoren, dan niet vermelden! Alleen indien controle op recidief.
FUbonedat	DD/MM/JJJJ	Datum bot-scan	Datum waarop de bot-scan is uitgevoerd
FUlvc	0= niet benoemd 1= ja	Lumbar vertebral column scan	Ruggengraat scan
FUlvcdat	DD/MM/JJJJ	Datum Lumbar vertebral column scan	Datum waarop de Ruggengraat scan is uitgevoerd
FUMRIw	0= niet benoemd 1= ja	MRI-scan wervelkolom	
FUMRIwdat	DD/MM/JJJJ	Datum MRI-scan wervelkolom	Datum waarop de MRI-scan wervelkom is uitgevoerd

FUPET	0= niet benoemd 1= ja	fdg-PET scan	
FUPETdat	DD/MM/JJJJ	Datum fdg PET-scan	Datum waarop de PET-scan wervelkom is uitgevoerd
FUCTT	0= niet benoemd 1= ja	CT-scan v/d thorax	
FUCTTdat	DD/MM/JJJJ	Datum CT-scan thorax	Datum waarop de CT-scan v/d thorax is uitgevoerd
FUCTbrain	0= niet benoemd 1= ja	CT-scan hersenen	
FUCTbraindat	DD/MM/JJJJ	Datum CT-scan hersenen	Datum waarop de CT-scan v/d hersenen is uitgevoerd
FUCTabd	0= niet benoemd 1= ja	CT-scan van pelvic area/ abdomen	
FUCTabddat	DD/MM/JJJJ	Datum CT-scan pelvic area/abdomen	Datum waarop de CT-scan pelvic area/abdomen is uitgevoerd
FUXrayT	0= niet benoemd	X-ray thorax	

	1= ja		
FUXrayTdat	DD/MM/JJJJ	Datum X-ray thorax	Datum waarop X-ray thorax is uitgevoerd
FUXrayrib	0= niet benoemd	X-ray rib (detail)	X-ray rib (detail)
	1 = ja		
FUXrayribdat	DD/MM/JJJJ	Datum X-ray rib (detail)	Datum waarop X-ray rib (detail) is uitgevoerd
FUXrayw	0= niet benoemd	X-ray wervelkolom	X-ray wervelkolom
	1 = ja		
FUXraywdat	DD/MM/JJJJ	Datum X-ray wervelkolom	Datum waarop X-ray wervelkolom is uitgevoerd
FUechoM	0= niet benoemd	Echografie mamma/axilla	
	1= ja		
FUechoMdat	DD/MM/JJJJ	Datum Echografie mamma/axilla	Datum waarop echografie mamma/axilla is uitgevoerd
FUechoA	0= niet benoemd	Echografie upper abdomen	
	1= ja		
FUechoAdat	DD/MM/JJJJ	Datum Echografie upper abdomen	Datum waarop echografie upper abdomen is
			uitgevoerd
FUechoN	0= niet benoemd	Echografie hals	Echografie hals
	1 = ja		
FUechoNdat	DD/MM/JJJJ	Datum Echografie hals	Datum waarop echografie hals is uitgevoerd
FUCBC	0= niet benoemd	Complete blood count	Bloedbeeld: rode en witte bloedcellen en
	1= ja	-	bloedplaatjes
FUCBCdat	DD/MM/JJJJ	Datum complete blood count	Datum waarop compleet bloedbeeld is uitgevoerd
FUlft	0= niet benoemd	Lever functie test	ALT en AST
	1= ja	-	
FUlftdat	DD/MM/JJJJ	Datum Lever functie tes	Datum waarop ALT en AST is uitgevoerd
FUCA15_3	0= niet benoemd	Tumormarker CA 15-3	
	<u>1= ja</u>		
FUCA15_3dat	DD/MM/JJJJ	Datum Tumormarker CA 15-3	Datum waarop Tumormarker CA 15-3 is uitgevoerd
FUCEA	0= niet benoemd	Tumorkmarker CEA	Carcinoembryonic antigen
	1 = ja		
FUCEAdat	DD/MM/JJJJ	Datum Tumormarker CEA	Datum waarop Carcinoembryonic antigen test is
	0 mint han a small		ultgevoerd Diagtage de marge (alegele lastage generation and a
FUDIOPIMAMMA		Biopt mamma/oksei	Biopi van de mamma/oksei: net verzamelen van een
		Detum bient memme/ekcel	reepje weetsel met een dikke naald
FUDIOPIMAMMAdat		Datum piopt mamma/oksel	Datum waarop blopt van de mamma/oksel is
			genomen

FUbioptother	0= niet benoemd 1= ja	Biopt overige	Biopt overige: het verzamelen van een reepje weefsel met een dikke naald
FUbioptotherdat	DD/MM/JJJJ	Datum biopt overige	Datum waarop biopt overige is genomen
FUpuncturemamma	0= niet benoemd 1= ja	Punctie borst/oksel	Punctie borst/oksel: het verzamelen van losse cellen met een dunne naald
FUpuncturemammadat	DD/MM/JJJJ	Datum punctie borst/oksel	Datum waarop punctie van borst/oksel is genomen
FUpunctureother	0= niet benoemd 1= ja	Punctie overige	Punctie overige: het verzamelen van losse cellen met een dunne naald
FUpunctureotherdat	DD/MM/JJJJ	Datum punctie overige	Datum waarop punctie overige is genomen
FUothertype	. = Nee	Type andere test	
FUothertypedat	DD/MM/JJJJ	Datum andere test	Datum waarop een andere test dan hierboven genoemd is uitgevoerd
FUrec	0= nee 1= ja 9= onbekend	Recidief ontdekt?	Is op basis van deze controle een recidief ontdekt?
FUlocal	0= nee 1= ja 9= onbekend	Recidief in ipsilaterale borst	Recidief in ipsilaterale borst
FUregional	0= nee 1= ja 9= onbekend	Recidief in ipsilaterale oksel	Recidief in ipsilaterale oksel/lymfeklieren
FUcontralateraal	0= nee 1= ja 9= onbekend	Tweede primarire	Borstkanker in de contralaterale borst of lymfeklieren
FUdistant	0= nee 1= ja 9= onbekend	Metastasen	Kanker ontdekt in andere regio dan borst
opmS2		Overige opmerkingen S2	