Optimizing breast reconstructive surgery in the Netherlands using clinical audit data

Bommel, A.C.M. van

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CHAPTER 1

General introduction and outline of this thesis

GENERAL INTRODUCTION AND OUTLINE OF THIS THESIS

Systematically monitoring treatment outcomes was first described over a century ago by Ernest A. Codman. In his view, the results of every treated case ought to be registered and at all times accessible for evaluation by members of the staff, trustees, administration or other authorized investigators. In his time, evaluating and improving healthcare by reflecting on actively collected outcome data was a progressive thought.[1]

Today, many have adopted the view that evaluating care by the analysis of outcomes of treated patients is an important step in the "Plan Do Check Act (PDCA)" cycle to improve healthcare quality.[2] Clinicians, hospitals, and countries have collectively embraced clinical auditing and adhere to the concept of systematically measuring and subsequently improving quality of care. While individual professionals and institutions aim to evaluate and improve their own performances in relation to peers, society calls for transparency of the quality of care to enable patients to choose a healthcare provider based on reliable information. Other stakeholders such as healthcare insurance companies and the healthcare inspectorate also demand transparency of the quality of care given in hospitals.

In the Netherlands, nationwide clinical auditing on an institutional level was catalyzed by the increased interest of the national healthcare inspectorate (IGJ)[3] in the relationship between hospital volume and outcomes of surgical care at the beginning of the 21st century. Following the nationwide query of the institutional volume of esophageal surgery in 2006 and the publication of institutional rates of tumor positive margins in patients undergoing breast conserving surgery in 2008,[3,4] nationwide clinical auditing was swiftly implemented for several surgical oncological disorders.

The Initiation of a National Breast Cancer Audit in the Netherlands

The National Breast Cancer Organization Netherlands (NABON) was established in 1999 to improve multidisciplinary care for breast cancer patients, an initiative started by clinicians.[5] Initially, NABON pursued publishing national treatment guidelines

as well as guidelines to optimize institutional infrastructures. In 2011, NABON, the Dutch Institute for Clinical Auditing (DICA)[6] and the Comprehensive Cancer Organization the Netherlands (IKNL)[7] joined forces and initiated the NABON Breast Cancer Audit (NBCA).[8] Representatives of all medical specialties involved in breast cancer care defined a number of multidisciplinary quality indicators to measure different aspects of breast cancer care. These indicators reflected adherence to existing diagnostic work-up and treatment guidelines. Full participation of all Dutch hospitals in the Netherlands was realized within a few years.

The primary goal of the NBCA is to monitor the quality of provided breast cancer care in hospitals in the Netherlands by offering participating individual hospitals feedback on their results in relation to "real-time" national benchmark information with case-mix adjustment if needed. The second objective, comparison of hospital performances using quality indicators, is a more complex endeavor weighing multiple factors, and interpreting the results should be done with caution. First, defining unambiguous quality indicators reflecting the quality of breast cancer treatment is not as easy as it seems and is still an ongoing process. Second, case-mix adjustment can only compensate for variation in outcomes as long as the involved confounding factors are identified. Moreover, even following case-mix adjustment, interpreting the remaining hospital variation has to be done with certain caution. Exploring observed variation on a national level serves as the "Check" step, and may result in the adjustment of guidelines as an "Act" to close the PDCA cycle.

In the present form of the NBCA, (reconstructive) surgical items are well covered. Breast conserving surgery has been performed in the majority of patients diagnosed with breast cancer during the last 40 years and consequently has been the cornerstone of surgical breast cancer care. Combining mastectomy with an immediate breast reconstruction was introduced more recently and its increasing use on a national level demonstrates the increased awareness of the importance of esthetic outcomes after breast cancer surgery. Zooming in on an institutional level, variation in collaboration between surgical oncologists and plastic surgeons as well as in hospital organizational factors may result in substantial variation in the

use of immediate breast reconstruction across the Netherlands. In addition, the increasing use of systemic therapy in the neo-adjuvant setting and more extensive radiotherapy following breast conserving surgery as well as after mastectomy are to be addressed in a national audit to understand variation in treatment patterns over time or between hospitals.

The ultimate treatment goals in breast cancer care are to improve survival and the quality of life of patients. The risk of life-threatening short-term treatment-related complications is very low and long-term prognosis is very good in patients diagnosed with primary breast cancer. Therefore, there is an increasing interest in patient-reported outcome measures (PROMs) as a means to better understand the effects of the disease and its treatment on the quality of life as perceived by patients. For example, esthetic outcomes after breast cancer surgery and breast reconstruction are undoubtedly important from a patient perspective and should therefore also be considered by clinicians together with patients in the decision-making process.

The aims of this thesis were to describe the nationwide implementation of clinical auditing of breast cancer treatment in the Netherlands, to investigate the hospital variation of (reconstructive) surgical breast cancer care, and to identify factors which may reduce the variation found and may optimize the use of breast reconstructive surgery. This is outlined in the following chapters:

- The institution of the NBCA, the initially used quality indicators and the results of the first four years of nationwide clinical auditing are reported in **Chapter 2**.
- The evolution of meaningful quality indicators is an ongoing process. The NBCA traditionally used the quality indicator "proportion of patients undergoing breast conserving surgery" as cosmetic outcome of breast cancer surgery, however, other treatment modalities may contribute to a favorable cosmetic outcome as well. **Chapter 3** describes the development of a quality indicator that comprises all efforts to preserve or restore the breast contour: Breast-contour-preserving procedure (BCPP).

- Practice patterns and hospital variation with respect to the treated population of patients who underwent immediate breast reconstruction following mastectomy for restoration of their breast mound is analyzed in **Chapter 4**. To adjust for institutional differences, this chapter analyzes which patient and tumor case-mix factors contribute to the observed hospital variation and to what extent variation remains after adjustment for these factors.
- Aside from patient case-mix factors, hospital and hospital organizational factors affecting the use of immediate breast reconstruction after mastectomy for ductal carcinoma in situ (DCIS) and invasive breast cancer are investigated in **Chapter 5**.
- Trying to identify all possible factors affecting the use of immediate breast reconstruction led to the analyses in **Chapter 6**, evaluating differences in the attitudes of surgeons and plastic surgeons towards immediate breast reconstruction following mastectomy.
- The effect of being informed about immediate breast reconstruction on the likelihood of receiving an immediate breast reconstruction accentuates the importance of pre-operative information provision, which is described in **Chapter 7**.
- In **Chapter 8** a breast surgery specific PROM is used to compare quality of life of patients after mastectomy with immediate breast reconstruction and following mastectomy only, because patient-reported outcomes are important to improve counseling and shared decision-making of all patients treated for breast cancer.

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CHAPTER 2

Clinical auditing as an instrument for quality improvement in breast cancer care in the Netherlands

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On behalf of the NABON Breast Cancer Audit

J Surg Oncol. 2017 Mar;115(3):243-249.

ABSTRACT

Background: In 2011, the NABON Breast Cancer Audit (NBCA) was instituted as a nation-wide audit to address quality of breast cancer care and guideline adherence in the Netherlands. The development of the NBCA and the results of 4 years of auditing are described.

Methods: Clinical and pathological characteristics of patients diagnosed with invasive breast cancer or in situ carcinoma (DCIS) and information regarding diagnosis and treatment are collected in all hospitals (n=92) in the Netherlands. Thirty-two quality indicators measuring care structure, processes and outcomes were evaluated over time and compared between hospitals.

Results: The NBCA contains data of 56,927 patients (7,649 DCIS and 49,073 invasive cancers). Patients being discussed in pre- and post-operative multidisciplinary team meetings improved (2011: 83% and 91%; 2014: 98% and 99%, respectively) over the years. Tumor margin positivity rates after breast conserving surgery for invasive cancer requiring re-operation were consistently low (~5%). Other indicators, for example, the use of an MRI-scan prior to surgery or immediate breast reconstruction following mastectomy showed considerable hospital variation.

Conclusions: Results show an overall high quality of breast cancer care in all hospitals in the Netherlands. For most quality indicators improvement was seen over time, while some indicators showed yet unexplained variation.

INTRODUCTION

Quality of health care has become subject of public debate. Until recently, quality of breast cancer care was merely enhanced by national organizations such as the National Breast Cancer Organization Netherlands (NABON) that defined and distributed guidelines that contained multidisciplinary criteria for providing good quality breast cancer care as well as actual treatment guidelines.[1] Today's society demands transparency, resulting in a call for the evaluation of quality of care as provided by the individual institutions.

In the Netherlands, the Dutch Health Care Inspectorate started querying surgical departments a decade ago for a number of quality aspects and national media began to report on the observed variation of hospital-specific indicator results. In 2008, the Dutch Health Care Inspectorate observed a high rate of tumor-positive margins after breast conserving surgery in a number of hospitals in the Netherlands[2], urging the need for a national audit for the monitoring of the quality of breast cancer care in individual hospitals. Concurrently, clinicians of various disciplines were seeking benchmarked performance information to monitor the quality of their delivered breast cancer care which could catalyze quality improvements in the care delivered to their patients.[3]

The aims of the present study were to describe the development of the NABON Breast Cancer Audit (NBCA) and report on the results of the first 4 years of nationwide clinical auditing of multidisciplinary breast cancer care in the Netherlands.

METHODS

The creation of the NABON Breast Cancer Audit (NBCA)

Close cooperation of the NABON, the Comprehensive Cancer Organization the Netherlands (IKNL) and the Dutch Institute for Clinical Auditing (DICA) led to the institution of the NBCA in 2011.[4] NABON is a Dutch breast cancer working group that aims to improve breast cancer care in the Netherlands by developing

national guidelines, defining quality indicators and standards of care, and by organizing post-graduate symposia. IKNL is a quality institution for oncological and oncological palliative care, which hosts the Netherlands Cancer Registry (NCR), in which data of all newly diagnosed malignancies in the Netherlands are registered since 1989. Information regarding treatment and outcomes of breast cancer is extracted from the medical records by specially trained data-managers in each hospital in the Netherlands. Moreover, IKNL is the NABON and NBCA secretary. DICA was founded in 2011 with the objective to facilitate the start-up of new nation-wide clinical audits, following the successful initiation of the Dutch Surgical Colorectal Audit (DSCA) in 2009.[5]

In 2009, the NABON established a scientific committee to initiate the NBCA. The scientific committee consisted of mandated members of all medical associations involved in breast cancer care in order to constitute a national clinical audit: the Dutch Radiological Society (NVvR), the Dutch Society for Pathology (NVvP), the Association of Surgeons of the Netherlands (NVvH), the Netherlands Society for Plastic Surgery (NVPC), the Dutch Society of Radiotherapy and Oncology (NVRO) and the Dutch Society of Medical Oncology (NVMO). The Breast Cancer Patients Association (BVN) participated to represent the patients' voice. Later, a representative of the Dutch health care insurance companies (ZN) joined the scientific committee and in 2015 a mandated member of the Dutch Society for Clinical Genetics (VKGN) joined the working group.

The primary goal of the NBCA is the nation-wide monitoring of quality of care and the provision of feedback to the participating individual hospitals on their outcomes in relation to "real-time" national benchmark information as a first step to improve the quality of breast cancer care in the Netherlands by enabling institutions to evaluate their data and start improvement projects. The aforementioned scientific committee is responsible for the draft and development of a multidisciplinary set of indicators used to express and monitor the various qualitative aspects of care. Other tasks include in-depth outcomes research and preparation of annual reports for public use to improve transparency.

Quality indicators: monitoring of the structure, process and outcome of breast cancer care

Quality indicators are as much evidence-based as possible. These quality indicators are used to evaluate guideline adherence and outcomes of breast cancer care and they cover different aspects of the multidisciplinary care path for breast cancer patients, from diagnostic work-up to the different treatment options. For 2015, 32 quality indicators measuring structure, processes and outcomes of breast cancer care are available for benchmarked feedback and public transparency. Each indicator consists of a nominator and a denominator, the latter describing the selection of patients under consideration (**Supplementary Appendix 1**). For 10 indicators, a professional standardized norm is available, that is, a generally accepted cut-off value, implying that a hospital should perform above (e.g., in case of pre-operative multi-disciplinary team [MDT] meeting) or below (e.g., in case of tumor-positive margins) a predefined standard. These norms are based on consensus of the multidisciplinary scientific committee. For some indicators, such as tumor-positive margins, norms are based on national guidelines/international literature. For other indicators, where total adherence was expected and desirable, thresholds were set at 90%. Other indicators were merely defined to explore institutional variation in treatment patterns. Standardized cut-off values denominating a level of quality are not (yet) available for these indicators. The NBCA quality indicators are evaluated annually by the scientific committee on their validity and existing indicators may be adapted or removed when considered redundant whereas new indicators are developed based on new insights. Currently, some indicators are merged (pre- and post-operative MDT meeting with a more strict norm), others are deleted (estrogen and progesterone receptor positivity), while others are adjusted (such as the frequency of tumor-positive margins which will be presented in relation to the proportion of patients who subsequently undergo re-excisions).

Dataset and registration of NBCA data

All surgically treated patients diagnosed with primary invasive breast cancer or ductal carcinoma in situ (DCIS) in the Netherlands are included in the NBCA. Patients diagnosed with lobular carcinoma in situ, phyllodes tumors, sarcomas and lymphomas are not included. Patients are included based on the date of the

histological confirmed diagnosis. Information regarding diagnostic procedures, surgery, reconstructive surgery, radiotherapy, neo-adjuvant and adjuvant systemic treatment is collected. For case-mix adjustment, baseline characteristics of the patient (e.g., age, previous breast surgery) and tumor characteristics (e.g., histology, tumor stage, receptor status) are collected. Depending on the treatments given, a maximum of 75 items is registered per patient.

Participating hospitals can either register the data themselves (facilitated by the web-based data-collection system of DICA) or have the data registered by IKNL-data-managers. A manual is available to secure uniform data acquisition. When data are registered by IKNL, hospitals can check the indicators and data on patient level for possible inconsistencies before the data are transferred to the DICA-system, in which data of all participating hospitals are gathered. Patient information is anonymized before transfer of the data to the national database. Hospitals registering the data themselves (through data-managers or specialized nurses) enter the data directly into the secured web-based system of DICA.[5] A third trusted party de-identifies data directly after data entry.[6] Data are continuously collected. Entry and accuracy of data remain the responsibility of the participating hospitals.

Benchmarking and transparency of quality indicator results

Throughout the year, individual hospitals have continuous insight into their own performance on the quality indicators, along with other baseline information such as patient, tumor and treatment characteristics that are updated weekly on their secured MyNBCA website. The quality indicators are nationally benchmarked against the other (anonymously presented) hospitals. Funnel plots are used to present indicator results in conjunction with the benchmark results. Annually, comprehensive reports with performance on all quality indicators of all institutions are disclosed to other parties, such as the national health care inspectorate and health care providers. In addition, an annual report with in depth research is available online for the public.

Analyses

Information of all patients who were operated for invasive breast cancer or DCIS between 1 January 2011 and 30 September 2014 was available for analysis. Results

of the 32 quality indicators were calculated for all 92 institutions and changes over the 4-year-period were evaluated using a χ^2 trend test. Since information regarding adjuvant treatments requires a longer period (~9 months) to be completed, information of the quality indicators involving adjuvant treatments was not available for 2014. A P-value <0.05 is considered statistically significant. Comparisons of indicator results between the individual hospitals are visualized by funnel plots and presented in relation to the mean or norm (if applicable) using funnels to represent 95% confidence intervals. Boxplots with median hospital performance and interquartile ranges were used to analyze changes over the years. All analyses were performed using SPSS 20 (IBM-SPSS, Inc., Chicago, IL).

RESULTS

Hospitals

In the Netherlands, breast cancer care is provided in 92 hospitals. Full participation of all hospitals was realized in 2012, the second year of registration. One hospital stopped treating breast cancer patients in 2012, and one new hospital was founded in 2013. About one third of the hospitals registered the data themselves and a high rate of case ascertainment was found after comparing data with those registered by the NCR for these hospitals (data not shown).

Patient and tumor characteristics

After 4 years of auditing the NBCA database contained data of 56,927 patients: 7,649 patients with DCIS, 49,073 with invasive cancer (**Table 1**). In 205 patients (0.4% of all patients), DCIS or invasive cancer was not specified. Most patients were aged between 50 and 65 years (57% for DCIS and 43% for invasive breast cancer, respectively) at the time of diagnosis. Patients diagnosed with invasive breast cancer most frequently had relatively small tumors (pT1, 63%) and the majority had no axillary lymph node metastases (pN0, 64%).

Quality indicators

An overview of the overall results for all NBCA-indicators per year is displayed in **Table 2**.

Table 1. Patient, tumor and treatment characteristics of patients included in the NABON Breast Cancer Audit (NBCA) stratified by invasive breast cancer and ductal carcinoma in situ (DCIS) (2011–2014).

			DCIS		Invasive breast cancer	
			(n=7,649)	%[a]	(n=49,073)	%[a]
Patient	Age	Below 50	990	13%	9,587	20%
		50 - 65	4,323	57%	21,100	43%
		65 or above	2,334	31%	18,368	37%
	Gender	Female	7,621	100%	48,774	99%
		Male	28	0%	299	1%
Tumor	BI-RADS classification	BI-RADS 0	19	0%	95	0%
		BI-RADS 1 - 2	230	3%	392	1%
		BI-RADS 3 - 5	7,127	93%	47,739	97%
		Unknown	273	4%	847	2%
	Palpable	No	6,176	81%	17,057	35%
		Yes	1,308	17%	31,340	64%
		Unknown	165	2%	676	1%
	Multifocal	No	7,044	92%	41,443	85%
		Yes	605	8%	7,630	16%
	Histology	Ductal	7,164	94%	39,822	81%
		Lobular	0	0%	5,465	11%
		Combination	141	2%	1,264	3%
		Unknown	344	5%	2,522	5%
	Grade	1	1,188	16%	11,127	23%
		2	2,691	35%	20,783	42%
		3	3,323	43%	12,726	26%
		Unknown	447	6%	4,437	9%
	TNM-pT	pTo / cTx / Unknown	n.a.	n.a.	2,359	5%
		pT1	n.a.	n.a.	30,996	63%
		pT2	n.a.	n.a.	13,644	28%
		pT3	n.a.	n.a.	1,636	3%
		pT4	n.a.	n.a.	438	1%
	TNM-pN	pNx / Unknown	n.a.	n.a.	1,981	4%
		pN0	n.a.	n.a.	31,193	64%
		pN1	n.a.	n.a.	11,996	24%
		pN2	n.a.	n.a.	2,463	5%
		pN3	n.a.	n.a.	1,440	3%

Table 1. Patient, tumor and treatment characteristics of patients included in the NABON Breast Cancer Audit (NBCA) stratified by invasive breast cancer and ductal carcinoma in situ (DCIS) (2011–2014). (continued)

			DCIS		Invasive breast cancer	
			(n=7,649)	%[a]	(n=49,073)	%[a]
Treatment	Neo-adjuvant therapy	Yes	n.a.	n.a.	6,262	13%
	Type of first surgery	Breast conserving surgery	5,210	68%	29,070	59%
		Ablative surgery	2,381	31%	19,506	40%
	Immediate reconstruction[b]	Yes	1,012	43%	3,364	17%
	Sentinel node procedure	Yes	4,844	64%	39,839	82%
	Axillary lymph node dissection	Yes	86	1%	12,388	25%
	Postoperative chemotherapy[c]	Yes	n.a.	n.a.	12,423	40%
	Postoperative radiotherapy[c]	Yes	3,169	52%	24,454	63%

BI-RADS, Breast Imaging-Reporting and Data System; n.a., not applicable.
[a] Percentages are rounded off, which in some cases leads to a total of above 100;
[b] in case of ablative surgery;
[c] calculated for 2011, 2012 and 2013 only.

Table 2. Quality indicators for breast cancer health care in the NABON Breast Cancer Audit (NBCA) and mean percentages per year from 2011 to 2014.

Discipline	Indicator	Pre-defined norm	2011 (n=12,562)	2012 (n=15,929)	2013 (n=16,451)	2014[a] (n=11,985)	P-value[b]
Radiology	BI-RADS classification used in radiology report	>90%	97%	98%	98%	99%	<0.001
	Breast MRI in patients treated with neo-adjuvant chemotherapy		n.a.[f]	83%	87%	89%	<0.001
	Breast MRI in patients treated with primary surgery		n.a.[f]	28%	30%	31%	<0.001
Pathology	Pathology report as defined[c]	>90%	83%	93%	97%	97%	<0.001
	HER-2 positive measurement		12%	15%	13%	13%	<0.001
	Estrogen positive measurement		83%	83%	85%	84%	<0.001
	Progesterone positive measurement		65%	67%	69%	69%	<0.001
Surgery	Tumor positive margins after first breast conserving surgery for invasive breast cancer after neo-adjuvant therapy[c]		5,0%	8,3%	6,5%	6,8%	0.193
	Tumor positive margins after first primary breast conserving surgery for invasive breast cancer[d]	<15%	5,9%	5,4%	4,8%	4,6%	0.007
	Tumor positive margins after first primary breast conserving surgery for DCIS[e]	<30%	25%	20%	22%	18%	0.002
	Sentinel node procedure for pNo(i-) tumors, with more than 5 nodes excised	<5%	2,3%	1,9%	1,9%	1,7%	0.274
	Sentinel node procedure for pNo(i+) tumors, with more than 5 nodes excised	<5%	4,6%	2,6%	1,9%	3,7%	0.123
	Breast conserving surgery for invasive breast cancer without a re-intervention		94%	92%	93%	93%	0.004
	Breast conserving surgery for DCIS without a re-intervention		85%	83%	82%	86%	0.054

Table 2. Quality indicators for breast cancer health care in the NABON Breast Cancer Audit (NBCA) and mean percentages per year from 2011 to 2014. (continued)

Discipline	Indicator	Pre-defined norm	2011 (n=12,562)	2012 (n=15,929)	2013 (n=16,451)	2014[a] (n=11,985)	P-value[b]
Plastic surgery	Immediate reconstructions with first ablative surgery for invasive breast cancer (total)		14%	16%	19%	21%	<0.001
	Immediate reconstructions with first ablative surgery for DCIS (total)		41%	38%	45%	46%	0.013
Radiotherapy	Prior to neo-adjuvant chemotherapy seen by radiation oncologist		36%	42%	46%	n.a.[g]	<0.001
	Radiotherapy for locally advanced breast cancer (excluding T_3N_0) treated with mastectomy		75%	80%	81%	n.a.[g]	<0.001
	Radiotherapy for DCIS treated with breast conserving surgery		75%	81%	84%	n.a.[g]	<0.001
Systemic therapy	Neo-adjuvant chemotherapy for invasive Mo breast cancer		8%	9%	12%	14%	<0.001
	Post-operative chemotherapy for invasive Mo breast cancer		34%	32%	31%	n.a.[g]	<0.001
	Neo-adjuvant or post-operative chemotherapy for invasive Mo breast cancer		42%	40%	42%	n.a.[g]	<0.001
Multi-disciplinary	Number of records completed in NBCA	>90%	97%	98%	99%	99%	<0.001
	Pre-operative multi-disciplinary team meeting including digital report	>90%	83%	94%	97%	98%	<0.001
	Post-operative multi-disciplinary team meeting including digital report	>90%	91%	97%	99%	99%	<0.001

Table 2. Quality indicators for breast cancer health care in the NABON Breast Cancer Audit (NBCA) and mean percentages per year from 2011 to 2014. (continued)

Discipline	Indicator	Pre-defined norm	2011 (n=12,562)	2012 (n=15,929)	2013 (n=16,451)	2014[a] (n=11,985)	P-value[b]
Transit times	Transit time ≤ 5 weeks between diagnosis and start neo-adjuvant chemotherapy		66%	74%	79%	81%	<0.001
	Transit time ≤ 5 weeks between diagnosis and primary surgery (without immediate reconstruction)	>90%	81%	85%	85%	88%	<0.001
	Transit time ≤ 5 weeks between diagnosis and primary surgery (with immediate reconstruction)		43%	47%	50%	56%	<0.001
	Transit time ≤ 5 weeks between final operation and start radiotherapy		38%	43%	51%	n.a.[g]	<0.001
	Transit time ≤ 5 weeks between end chemotherapy and start radiotherapy		77%	77%	82%	n.a.[g]	<0.001
	Transit time ≤ 5 weeks between final operation and start chemotherapy		65%	66%	64%	n.a.[g]	<0.001
	Transit time ≤ 5 weeks between end radiotherapy and start chemotherapy		93%	93%	94%	n.a.[g]	<0.001

NABON, National Breast Cancer Consultation Netherlands; BI-RADS, Breast Imaging-Reporting and Data System; MRI, magnetic resonance imaging; DCIS, ductal carcinoma in situ.

See **Supplementary Appendix 1** for definitions of quality indicators.

[a] 2014 consists of 9 months: January–October.

[b] Using x2 tests.

[c] Pathology report addresses estrogen receptor-, progesterone receptor-, and HER2-status, malignancy grade, tumor size, margin involvement and number of positive lymph nodes (when sentinel node procedure or axillary node dissection was performed).

[d] Tumor positive for invasive breast cancer is defined as tumor cells (>4 mm) in the surgical resection.

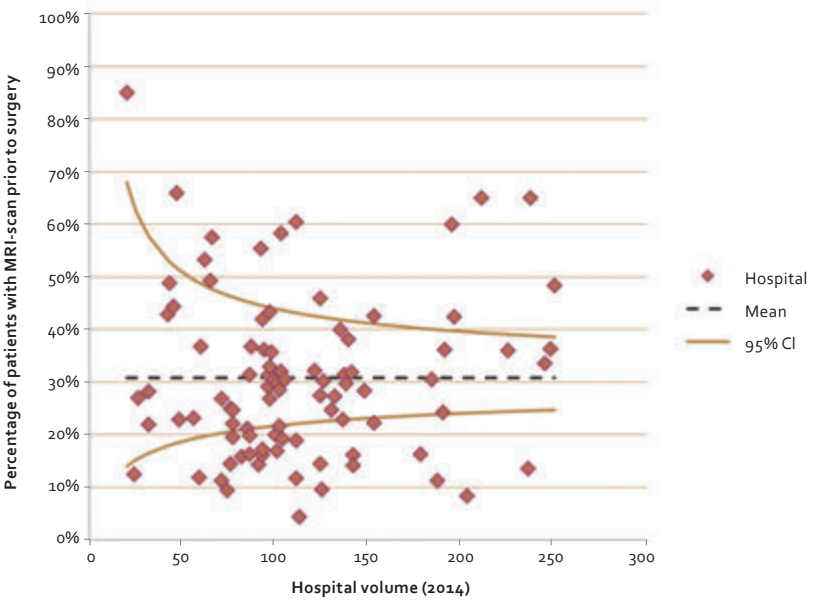
[e] Tumor positive for DCIS is defined as any tumor present in a surgical resection margin.

[f] n.a.: not applicable, registration of use of MRI-scan started in 2012.

[g] n.a.: not applicable, for adjuvant indicators there are no results yet available for 2014.

Radiology. A final Breast Imaging-Reporting and Data System (BI-RADS) classification was used in breast imaging reports in 98% of the patients (97% in 2011 and 99% in 2014; see **Table 2**). Over the years 2011–2014, the percentage of patients who underwent breast MRI increased (from 83% to 89% before neo-adjuvant treatment and from 28% to 31% before upfront surgery). The use of breast MRI varied largely between hospitals both for patients undergoing primary surgery (2014: range 4–84%; **Figure 1**) as well as for patients treated with neo-adjuvant systemic treatment (2014: range 0–100%).

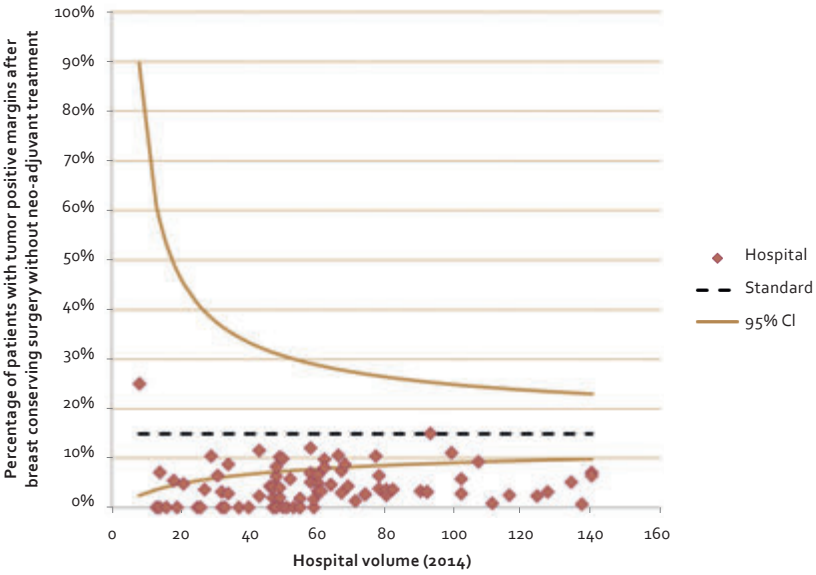
Figure 1. Funnel plot of variation between hospitals in the percentage of patients with invasive Mo breast cancer or ductal carcinoma in situ (DCIS) having a Magnetic Resonance Imaging (MRI)-scan prior to surgery in 2014. The 95% confidence intervals are displayed around the mean (31%).



Pathology. The proportion of patients with complete pathology reports increased significantly over the years. In 2014, 97% of the pathology reports contained all required pathology items (**Table 2**), and nearly every hospital (90 out of 92) reached the norm of 90% for this indicator compared to 66% of the hospitals reaching this norm in 2011.

Surgery and reconstructive surgery. Fifty-nine percent and 68% of the patients underwent breast conserving therapy for invasive breast cancer and DCIS, respectively (**Table 1**). The percentage of patients with tumor involved resection margins requiring re-operation after initial breast conserving surgery for invasive breast cancer was stable over the years: ~5% (**Figure 2**). After neo-adjuvant chemotherapy, this percentage was higher (7%) and highest for patients undergoing breast conserving surgery for DCIS (20%). All hospitals had results significantly below the predefined norm of 15% for invasive breast cancer and 30% for DCIS.

Figure 2. Funnel plot of variation between hospitals in the percentage of patients with invasive breast cancer and more than focal tumor-positive margins after breast conserving surgery without neo-adjuvant treatment (2014). The 95% confidence intervals are displayed around the standard (15%).



An immediate breast reconstruction was performed in 17% (range 0–66%) of patients with invasive cancer and in 43% (range 0–84%) of patients diagnosed with DCIS who underwent a mastectomy. The percentage of patients receiving an immediate breast reconstruction increased over the years with a 50% relative

increase over the 4 years for invasive breast cancer (14–21%), and 12% relative increase for DCIS (41–46%).

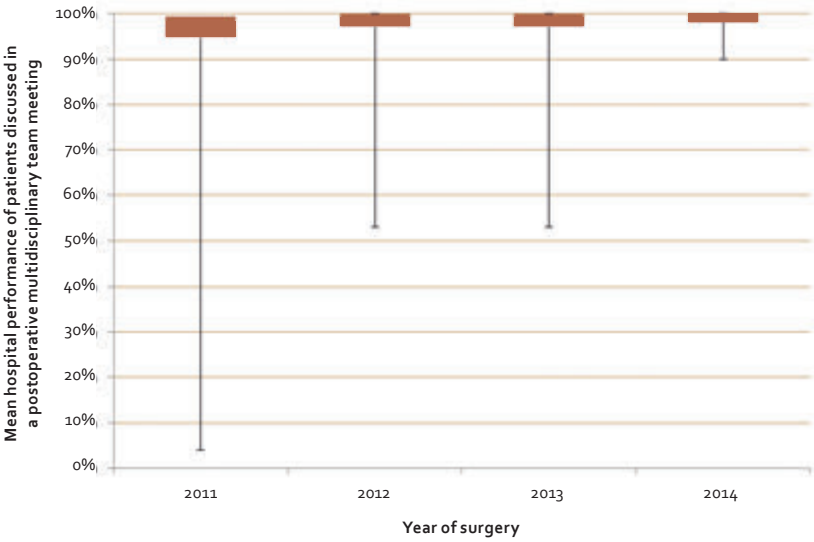
Radiotherapy. Eighty-one percent of the patients diagnosed with locally advanced breast cancer who underwent a mastectomy received additional radiotherapy in 2013. Of the patients undergoing breast conserving surgery for DCIS, 84% received radiotherapy.

(Neo-)adjuvant systemic therapy. Neo-adjuvant chemotherapy was increasingly administered over the study period (from 8% in 2011 to 14% in 2014, **Table 2**), and there was a significant variation between hospitals (0–48% in 2014). In 2014, 9% of the patients diagnosed with a cT2 tumor received neo-adjuvant chemotherapy (range 0–57%). The proportion of patients who received either adjuvant or neo-adjuvant chemotherapy decreased slightly over the years (**Table 2**).

Multidisciplinary care process. Ten quality indicators provide insight in the multidisciplinary care process logistics, and four of them have a standardized cut-off value (**Table 2**). Compared to 2011, more patients were discussed in pre- and post-operative MDT meetings: pre-operative this percentage rose from 83% to 98%, postoperative from 91% to 99%. In addition, variation between the hospitals decreased; in 2014, none of the hospitals discussed significantly less patients than the 90% norm in a post-operative MDT meeting (**Figure 3**). A similar trend was observed for the pre-operative MDT meeting.

Transit times. Time between diagnosis and primary treatment improved, more patients were treated within the predefined time frame of 5 weeks. An immediate breast reconstruction negatively affected the proportion of patients being operated within 5 weeks since diagnosis: from 56% to 88% when immediate breast reconstruction was not performed. The proportion of patients operated timely was lower in hospitals with larger patient volumes. However, an improvement over the years was observed for all time intervals.

Figure 3. Boxplot of variation between hospitals in the percentage of patients with either invasive breast cancer or ductal carcinoma in situ (DCIS) discussed in a post-operative multidisciplinary team meeting, and digital report available (2011–2014) with median hospital performance and interquartile ranges. 2014 contains 9 months; from January 2014 to October 2014.



DISCUSSION

This paper describes the implementation of a system monitoring the quality of breast cancer care in the Netherlands via a nationwide multidisciplinary audit. All 92 hospitals currently delivering breast cancer care in the Netherlands participate in the NBCA and the results of the first 4 years of auditing show an overall high quality of care, areas where clear improvement has been achieved as well as unexplained variation.

The collection of data in all hospitals in the Netherlands resulted in 56,927 patients for whom detailed information regarding their work-up and treatment was available for analysis. Several initiatives have shown that improvement of quality of care can be established by measuring quality indicators over time[7–12]; however, to the best of our knowledge we are the first to report on a nationwide breast cancer audit with full participation of all hospitals. The use of quality indicators embedded in a

national audit providing benchmark information to participating hospitals catalyzes quality improvement and insurance on various levels in the healthcare system.[13] An example of improvement on hospital level is a hospital that recognized itself as an outlier on the indicator "frequency of HER2-positive tumors". Having observed a significant higher frequency they evaluated their pathology processes and found out that their laboratory used a different method of tracking HER2 positivity. This was subsequently adjusted. Another hospital observed low rates of patients discussed in a pre-operative MDT meeting, identifying that this was associated with a lack of meetings during holiday periods and they changed their clinic days to make sure every patient is discussed in an MDT meeting. On another level, regional cancer centers have organized network meetings reflecting on observed differences between the institutions within the network.

Apart from the actions of the individual hospitals that were triggered by benchmarking their results, the comprehensive audit outcomes have led on a national level to in depth research into hospital variation in breast MRI use and immediate breast reconstruction facilitated by research grants of the Dutch Cancer Society. As such, the NBCA serves as a monitor to identify variation as well as a database that identifies factors explaining variation and eventually ought to catalyze guideline adjustments.

The absence of consistency between indicator sets used by different other audits internationally is a limitation of individual audits as only uniform definitions of quality indicators can enable international benchmarking.[7–9,14,15] Nevertheless, guidelines may well differ between countries and therefore differences in quality parameters will remain, as the main goal of an audit is the quality assurance in a particular area.

Process indicators

A number of trends were observed since the introduction of the audit in 2011. For most quality indicators with a predefined quality norm, the mean value of all hospitals improved and the variation between the hospitals decreased, as was observed at an earlier moment in the Netherlands.[16] Significant changes were

seen for the indicators reflecting the process of provided care. Over time, all hospitals reached the norm of 90% of patients being discussed in MDT meetings. This demonstrates that a multidisciplinary approach is widely adopted in the Netherlands as is advised by national guidelines. A similar study reported a variety of patients being discussed in an MDT meeting in Belgium, with improvement from 61.4% in 2003 to 80% in 2006.[7] Although a slight improvement was seen in the time to operation, in 2014 still a number of hospitals were not able to reach the 90% norm of patients undergoing surgical treatment within 5 weeks after diagnosis. It was also shown that a number of factors, such as combining surgical resection with reconstructive surgery, affect this process indicator.

Outcome indicators

The consistent low rate of tumor-positive margins in patients who underwent breast conserving surgery for invasive breast cancer is remarkable as well as reassuring, since concerns about the rate of incomplete resections were one of the drivers to initiate this clinical audit. Compared to earlier studies in the Netherlands, improvement was observed, although various definitions of margin involvement have been applied over the years, making direct comparison difficult.[17] The NBCA adheres to the current guideline, defining a positive margin for invasive breast cancer as a margin that is more than focally (>4 mm) involved, because this is the cut off where re-excision or continuation of treatment with radiotherapy is advised. Altogether, a positive margin rate for invasive breast cancer of 5% in the 4 years' study period, with no hospital performing significantly worse than the 15% norm was seen. Room for further improvement seems limited. The same applies to the positive margin rate following breast conserving surgery for DCIS.

Apart from the quality indicators with a standardized norm, other indicators were designed to explore current patterns of care. Some of these indicators showed large variation between hospitals and its causes and clinical relevance need to be explained. The preoperative use of breast MRI varied from 4% to 85% between hospitals. Routine use of breast MRI in the preoperative setting is discouraged by national guidelines, while MRI is considered to be indicated in patients who receive chemotherapy in a neo-adjuvant context (for patients treated with neo-

adjuvant chemotherapy it is recommended to perform breast MRI prior to the start of therapy as the optimal means to monitor response to treatment).[18] Apparently, interpretation of this definition varies between hospitals as demonstrated by the observed variation. Another example is the proportion of patients undergoing an immediate reconstruction following a mastectomy for invasive breast cancer or DCIS and variation in neo-adjuvant chemotherapy. The NBCA may serve as a database to identify factors explaining the observed hospital variation. Identifying areas of variation provides insight, opens discussions among clinicians and enables further research to understand the variation, allowing future guideline recommendations and improving quality of care for all breast cancer patients.

Limitations

Participation of all hospitals in the audit enables valid comparisons. However, completeness of the data by all participating hospitals is required in order to understand observed differences. Especially in the first year of registration, not all data were complete or correctly coded in the system. For example, it was difficult to retrieve from hospital records by IKNL-trained registrars whether a patient was discussed in an MDT meeting in the first year of registration. We chose not to make missing data an advantage; in case that a hospital had not reported if patients were discussed in an MDT meeting, it was assumed that these patients were not discussed in such a meeting. The results should be interpreted within this context and can only lead to an underestimation of actual performances. Furthermore, the present results also underline that the NBCA remains "work-in-progress" as reproducible quality indicators were not available for all involved disciplines, this is expected to change within the next few years. Lastly, it is of note that the observed trends cannot be attributed fully to the audit, as these improvements may well be the result of other changes in breast cancer practice such as new operation techniques to reduce tumor-positive margins or awareness for immediate breast reconstructions. Moreover, indicators for patients without surgery should be defined and these patients should be included in future.

Future directions of the audit

A future challenge is the development of more robust and reproducible quality indicators for all disciplines involved in the treatment of patients with breast cancer. At the moment, the NBCA has a data verification process to achieve reliable hospital comparisons. In the near future, more extensive data verification will be done in order to secure the quality of the data. For indicators without norms, reasons for the observed variation should be addressed by evaluating the audit data and further in-depth research. The availability of these data enables us not only to investigate and understand the variation found, but also to inspect hospitals on their performances and learn from best practices to further improve quality of breast cancer care for each hospital, throughout the country.

Furthermore, a balance is required between capturing all valuable information on the one hand and spending an acceptable amount of time needed for data entry on the other hand. At the moment, the 32 current quality indicators are calculated based on 75 registered items. Developing new quality indicators of interest should be accompanied by deleting indicators that have become redundant. A modest and acceptable investment of time (and finances) is one of the major challenges for the NBCA. Various ways to reduce the registration burden are explored.

Lastly, since patient-centered care is becoming more and more focused on the perceived quality of care, the NBCA will start measuring patient-reported outcome measures (PROMs) in order to evaluate the patient's outcomes with the care delivered, also on a longer term. PROMs will be implemented in 2016 and the dataset will be aligned with other initiatives focusing on patient-centered care such as the International Consortium for Health Outcomes Measurement (ICHOM).[19] This leads to an increased number of outcome indicators along with the process indicators and opportunities for international comparisons. The outcome indicators for recurrent disease will become available after 5 years.

CONCLUSION

The goals of the NBCA to establish a nation-wide multidisciplinary evaluation of quality parameters in breast cancer care, to evaluate guideline adherence and to facilitate benchmarking have been achieved within 4 years' time with full participation of all hospitals. Present results show an overall high quality of breast cancer care in the Netherlands and provide insight in fields and items for improvement. Future challenges include the development of robust quality indicators and understanding the variation of several indicators, accurate data verification and reducing the time necessary for data collection. With these efforts, we will be able to monitor and improve breast cancer care in the Netherlands.

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SUPPLEMENTARY APPENDIX 1

Overview of 32 quality indicators and their definitions used in the NABON Breast Cancer Audit

Radiology

BI-RADS classification described in radiology report (Standard >90%)

- Numerator: Number of patients with BI-RADS category reported in diagnostic phase on mammography, ultrasound or breast MRI.
- Denominator: Number of patients surgically treated for invasive breast cancer or DCIS.

Breast MRI prior to neo-adjuvant chemotherapy

- Numerator: Number of patients with breast MRI exam prior to neo-adjuvant chemotherapy.
- Denominator: Number of patients with invasive breast cancer treated with neo-adjuvant chemotherapy.

Preoperative breast MRI

- Numerator: Number of patients with preoperative breast MRI exam.
- Denominator: Number of patients with invasive breast cancer or DCIS treated with primary surgery.

Pathology

Pathology report as defined (Standard >90%)

- Numerator: Number of patients with standard pathology report including information about estrogen receptor percentage, progesterone receptor percentage, HER2, grade, tumor size, resection margin and number of positive lymph nodes.
- Denominator: Number of patients with a pathology report of invasive breast cancer of at least 1cm without neo-adjuvant therapy.

HER-2 positive measurement

- Numerator: Number of patients with HER2 positive tumor.
- Denominator: Number of patients with primary invasive breast cancer and availability of HER2 status.

Estrogen positive measurement

- Numerator: Number of patients with estrogen receptor positive tumor (≥ 10% of the tumor cells is positive).
- Denominator: Number of patients with primary invasive breast cancer and availability of estrogen receptor status.

Progesterone positive measurement

- Numerator: Number of patients with progesterone receptor positive tumor (≥ 10% of the tumor cells is positive).
- Denominator: Number of patients with primary invasive breast cancer and availability of progesterone receptor status.

Surgery

Tumor positive margins after first breast conserving surgery for invasive breast cancer after neo-adjuvant therapy

- Numerator: Number of patients with more than focal (>4 mm) tumor in resection margin after first breast conserving surgery.
- Denominator: Number of patients treated with neo-adjuvant therapy and breast conserving surgery for invasive breast cancer.

Tumor positive margins after first primary breast conserving surgery for invasive breast cancer (Standard <15%)

- Numerator: Number of patients with more than focal (>4 mm) tumor in resection margin after first breast conserving surgery.
- Denominator: Number of patients treated with breast conserving surgery for invasive breast cancer.

Tumor positive margins after first primary breast conserving surgery for DCIS (Standard <30%)

- Numerator: Number of patients with focal or more than focal (>4 mm) tumor in resection margin after first breast conserving surgery.
- Denominator: Number of patients treated breast conserving surgery for DCIS.

Sentinel node procedure for pN0(i-) tumors, with more than 5 nodes excised (Standard <5%)
- Numerator: Number of patients with removal of more than 5 lymph nodes.
- Denominator: Number of patients with pN0(i-) after primary surgical treatment with sentinel node biopsy without axillary lymph node dissection of a primary pT1-2N0M0 breast cancer.

Sentinel node procedure for pN0(i+) tumors, with more than 5 nodes excised (Standard <5%)
- Numerator: Number of patients with removal of more than 5 lymph nodes.
- Denominator: Number of patients with pN0(i+) after primary surgical treatment with sentinel node biopsy without axillary lymph node dissection of a primary pT1-2N0M0 breast cancer.

Breast conserving surgery for invasive breast cancer without a re-intervention
- Numerator: Number of patients with one breast conserving surgery as final surgical treatment.
- Denominator: Number of patients with invasive breast cancer treated surgically (either one or multiple times) of whom the first operation was breast conserving without prior neo-adjuvant systemic treatment.

Breast conserving surgery for DCIS without a re-intervention
- Numerator: Number of patients with one breast conserving surgery as final surgical treatment.
- Denominator: Number of patients with DCIS treated surgically (either one or multiple times) of whom the first operation was breast conserving.

Plastic surgery

Immediate reconstructions with first ablative surgery for invasive breast cancer (total)
- Numerator: Number of patients with immediate breast reconstruction.
- Denominator: Number of patients with a primary mastectomy for invasive breast cancer.

Immediate reconstructions with first ablative surgery for DCIS (total)
- Numerator: Number of patients with immediate breast reconstruction.
- Denominator: Number of patients with a primary mastectomy for DCIS.

Radiotherapy

Prior to neo-adjuvant chemotherapy seen by radiation oncologist
- Numerator: Number of patients seen by radiotherapist prior to neo-adjuvant systemic treatment.
- Denominator: Number of patients with invasive breast cancer treated with neo-adjuvant systemic therapy, surgery and postoperative radiation therapy.

Radiotherapy for locally advanced breast cancer (excluding T_3N_0) treated with mastectomy
- Numerator: Number of patients receiving radiotherapy.
- Denominator: Number of patients with primary invasive locally advanced breast cancer (clinical T_3, T_4, any N, M0 and T, N_{2-3}, M0) treated with mastectomy.

Radiotherapy for DCIS treated with breast conserving surgery
- Numerator: Number of patients receiving radiotherapy.
- Denominator: Number of patients with DCIS treated with breast conserving surgery.

Systemic therapy

Neo-adjuvant chemotherapy for invasive M0 breast cancer
- Numerator: Number of patients receiving neo-adjuvant chemotherapy.
- Denominator: Number of patients with invasive breast cancer treated surgically.

Post-operative chemotherapy for invasive M0 breast cancer
- Numerator: Number of patients receiving post-operative chemotherapy.
- Denominator: Number of patients with invasive breast cancer treated surgically.

Neo-adjuvant or post-operative chemotherapy for invasive M0 breast cancer
- Numerator: Number of patients receiving neo-adjuvant or post-operative chemotherapy.
- Denominator: Number of patients with invasive breast cancer treated surgically.

Multi-disciplinary

Number of records completed in NBCA (Standard >90%)

- Numerator: Number of patients of whom the information in the registry is complete and approved by the breast cancer care team.
- Denominator: Number of surgically treated patients with primary invasive breast cancer or DCIS.

Pre-operative multi-disciplinary tumor board meeting including digital report (Standard >90%)

- Numerator: Number of patients discussed in a pre-operative MDT and the report is electronically available.
- Denominator: Number of patients surgically treated for primary invasive breast cancer or DCIS.

Post-operative multi-disciplinary tumor board meeting including digital report (Standard >90%)

- Numerator: Number of patients discussed in a post-operative MDT and the report is electronically available.
- Denominator: Number of patients surgically treated for primary invasive breast cancer or DCIS.

Transit times

Transit time ≤ 5 weeks between diagnosis and start neo-adjuvant chemotherapy

- Numerator: Number of patients receiving neo-adjuvant chemotherapy within ≤5 weeks after diagnosis (date of biopsy).
- Denominator: Number of patients with neo-adjuvant chemotherapy for invasive breast cancer.

Transit time ≤ 5 weeks between diagnosis and primary surgery (without immediate reconstruction) (Standard >90%)

- Numerator: Number of patients receiving surgery within ≤5 weeks after diagnosis (date of biopsy).
- Denominator: Number of patients with primary surgery without immediate breast reconstruction for invasive breast cancer or DCIS.

Transit time ≤ 5 weeks between diagnosis and primary surgery (with immediate reconstruction)

- Numerator: Number of patients receiving surgery within ≤5 weeks after diagnosis (date of biopsy).
- Denominator: Number of patients with primary surgery with immediate breast reconstruction for invasive breast cancer or DCIS.

Transit time ≤ 5 weeks between final operation and start radiotherapy

- Numerator: Number of patients receiving radiotherapy within ≤5 weeks after surgery.
- Denominator: Number of patients with invasive breast cancer or DCIS treated with surgery and radiotherapy (without chemotherapy between the two treatments).

Transit time ≤ 5 weeks between end chemotherapy and start radiotherapy

- Numerator: Number of patients receiving radiotherapy within ≤5 weeks after chemotherapy.
- Denominator: Number of patients with invasive breast cancer with chemotherapy and radiotherapy.

Transit time ≤ 5 weeks between final operation and start chemotherapy

- Numerator: Number of patients receiving chemotherapy within ≤5 weeks after surgery.
- Denominator: Number of patients with invasive breast cancer with surgery and chemotherapy (without radiotherapy between the two treatments).

Transit time ≤ 5 weeks between end radiotherapy and start chemotherapy

- Numerator: Number of patients receiving chemotherapy within ≤5 weeks after radiotherapy.
- Denominator: Number of patients with invasive breast cancer with radiotherapy and chemotherapy.

Abbreviations

NABON: National Breast Cancer Consultation Netherlands;
BI-RADS: Breast Imaging-Reporting and Data System;
MRI: Magnetic Resonance Imaging;
DCIS: Ductal Carcinoma in Situ.

CHAPTER 3

Breast-contour-preserving procedure as a multidisciplinary parameter of esthetic outcome in breast cancer treatment in the Netherlands

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ABSTRACT

Background: The rate of breast conserving surgery (BCS) is used as an esthetic outcome parameter, while other treatments contribute also, such as neo-adjuvant chemotherapy (NAC) enabling BCS or immediate breast reconstruction (IBR). This study explores these efforts to preserve the patient's breast contour.

Patients and Methods: All patients who underwent surgery for invasive breast cancer in the Netherlands between January 2011 and December 2015 were selected from the Dutch national breast cancer audit (n=61,309). The breast-contour-preserving procedure (BCPP) rate was defined as the rate of primary BCS, BCS after NAC, or mastectomy with IBR. BCPP rates were calculated and compared by year of diagnosis, age categories, and individual hospitals.

Results: The rate of primary BCS remained stable (53%) while the BCPP rate increased from 63% in 2011 to 71% in 2015 due to an increase in patients receiving BCS after NAC and mastectomy with IBR. Primary BCS rates increased with age (from 17% in patients aged <30 years to 63% in patients aged 60–69 years), while the proportion of patients undergoing mastectomy with IBR decreased from 44% in patients <30 years to 1% in patients ≥70 years. The BCPP rate was similar for all age groups except for patients >70 years. BCPP rates varied between the different hospitals in the Netherlands, ranging from 47 to 88%.

Conclusions: The chance of preserving the breast contour for patients with breast cancer has increased substantially over recent years. BCPP provides a comprehensive parameter of esthetic outcome of breast cancer surgery.

INTRODUCTION

The quality of breast cancer treatment has received considerable attention in recent years. Identification of parameters that represent quality of breast cancer care is challenging. As survival rates for patients with primary breast cancer have improved considerably over the recent decades[1] and local recurrence rates have decreased significantly,[2] more effort is being directed to improve esthetic outcomes, reflecting an important aspect of quality of life. Previously, the proportion of patients undergoing breast conserving surgery (BCS) has been used as a parameter reflecting esthetic outcome in breast cancer treatment. Recent population-based studies report stable BCS rates over the past years of approximately 60%,[3,4] suggesting that esthetic outcomes of local treatment may not have improved over recent years.

Nonsurgical treatment modalities contribute to local esthetic outcome as well. The use of neo-adjuvant systemic therapy influences the ability to perform BCS.[5,6] Moreover, immediate breast reconstruction following mastectomy (IBR) or delayed breast reconstruction may also lead to desirable esthetic outcomes. Both neo-adjuvant chemotherapy (NAC) and IBR are increasingly being used,[4] and institutional preferences regarding the use of the former and surgical expertise with the latter have an impact on the surgical choice for BCS or mastectomy.

A parameter that comprises the combined efforts to preserve the breast contour may therefore be more appropriate to evaluate local esthetic outcome in breast cancer treatment. For this purpose, we defined ''breast-contour-preserving procedure (BCPP)'' as a parameter that encompasses all strategies to preserve the contour of the breast (primary BCS, BCS after NAC, and mastectomy with IBR). Within the NABON Breast Cancer Audit (NBCA),[3] we explored BCPP as a local outcome parameter by evaluating trends over time in relation to age, and compared the frequencies of BCPP with primary BCS rates.

PATIENTS AND METHODS

Data source

Demographic and clinicopathological patient characteristics (age, histological subtype, grade, tumor–node– metastasis (TNM) classification) together with comprehensive multidisciplinary treatment information (surgical and medical adjuvant and neo-adjuvant therapy) were collected prospectively for all newly diagnosed Dutch patients with breast cancer in the NABON Breast Cancer Audit (NBCA) since 2011.[4] Registration was done by registrars of the Netherlands Cancer Registry and personnel of the individual hospitals. Patients receiving primary systemic treatment without subsequent surgical treatment were not registered in the NBCA. All female patients with primary invasive breast cancer without distant metastases diagnosed between January 1, 2011 and December 31, 2015 were extracted from the NBCA.

Categories/Definitions

The surgical procedure was categorized as BCS or mastectomy as determined by the final operative procedure for the primary tumor. Patients who underwent BCS with subsequent mastectomy as a second or third operative procedure were categorized as having had a mastectomy. Patients who had undergone a mastectomy were subdivided by receipt of IBR. Of patients who had undergone BCS, those who had received NAC were identified and categorized as such. The endpoint of interest was BCPP, which was the final outcome of local treatment obtained by one of the following treatment strategies: (1) primary BCS, (2) BCS after NAC, and (3) mastectomy followed by IBR. The remaining patients underwent a mastectomy either primary or following NAC.

Analysis

Descriptive statistics were used to describe the baseline characteristics of the study population. The proportions of patients who had undergone primary BCS were addressed for the study period of 5 years, and the effect of age on the rate of primary BCS was evaluated, as well as the variation in these proportions between individual hospitals. Similarly, the proportions within the categories that

constituted the group of patients who had undergone BCPP were assessed and evaluated over time and in relation to age. Time trends of the rate of patients who had received primary BCS were compared with BCPP. All analyses were performed using SPSS 20 (IBM-SPSS Inc., Chicago).

RESULTS

During the study period, 61,309 patients were diagnosed and surgically treated for primary invasive breast cancer in 89 Dutch hospitals. Patient and tumor characteristics are summarized in **Table 1**. The median age of the patients was 61 years, and 74% of the patients were younger than 70 years old. The majority of patients were diagnosed with invasive ductal carcinoma (81%), and most tumors were staged as T1–2 (88%) and N0 (82%).

The frequencies of the treatment strategies leading to preservation of the breast contour are listed in **Table 2**. In 67% of all patients, the breast contour was preserved (BCPP): 53% of all patients (n=32,520) underwent BCS as the primary and definitive surgical treatment, 5% had BCS following NAC (n=3328), and 8% (n=5023) of all patients underwent mastectomy combined with IBR. Patients who had received NAC accounted for one-tenth of all patients who had undergone BCS, while one-fifth of patients undergoing a mastectomy received IBR. Chemotherapy was administered to 41% of all patients: 5% of patients received NAC and subsequently underwent BCS, 7% of the patients received NAC and subsequently had a mastectomy, while 29% of patients received adjuvant chemotherapy.

Table 1. Patient and tumor characteristics of 61,309 patients with invasive breast cancer in 2011–2015.

		n (61309)	%
Age (years)	Below 30	305	1%
	30 - 39	2291	4%
	40 - 49	9139	15%
	50 - 59	16058	26%
	60 - 69	17788	29%
	70 or above	15708	26%
Histological subtype	Ductal	49677	81%
	Lobular	6936	11%
	Combination of ductal and lobular	1601	3%
	Other or unknown	3095	5%
Grade	Grade I	1[42]33	23%
	Grade II	26340	43%
	Grade III	15431	25%
	Unknown	5305	9%
Clinical tumor stage	cTx	1946	3%
	cT0	72	0%
	cTis	1488	2%
	cT1	35495	58%
	cT2	18304	30%
	cT3	2943	5%
	cT4	1061	2%
Clinical nodal stage	cNx	1582	3%
	cN0	50142	82%
	cN1	8697	14%
	cN2	323	1%
	cN3	565	1%
Receptor type	HR positive, HER2 negative	43280	71%
	HR positive, HER2 positive	5006	8%
	HR negative, HER2 positive	2400	4%
	Triple negative	6498	11%
	Unknown	4125	7%

HR, hormone receptor; HER2, human epidermal growth factor receptor 2.

Table 2. Surgical treatment strategies for patients diagnosed with invasive breast cancer, separated by year of diagnosis, age group and hospital differences.

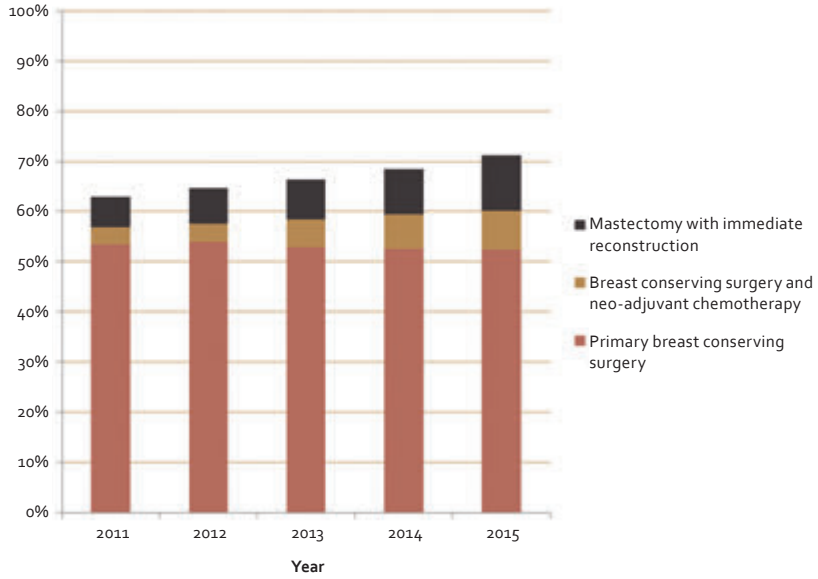
		BCS		BCS		Mastectomy		**BCPP**	Mastectomy	
		NAC -		NAC +		IBR +			IBR -	
	TOTAL	32520	53%	3328	5%	5023	8%	**67%**	20438	33%
Year of diagnosis	2011	5699	54%	367	3%	682	6%	**63%**	3905	37%
	2012	7283	54%	501	4%	920	7%	**64%**	4801	36%
	2013	7152	53%	748	6%	1102	8%	**67%**	4525	34%
	2014	7308	53%	957	7%	1286	9%	**69%**	4377	31%
	2015	5078	52%	755	8%	1033	11%	**71%**	2830	29%
Age group	Below 30	52	17%	39	13%	133	44%	**73%**	81	27%
	30 - 39	619	27%	311	14%	593	26%	**67%**	768	34%
	40 - 49	3522	39%	1084	12%	1566	17%	**68%**	2967	33%
	50 - 59	9107	57%	1147	7%	1715	11%	**75%**	4089	26%
	60 - 69	11281	63%	662	4%	839	5%	**72%**	5006	28%
	70 or above	7931	51%	83	1%	175	1%	**52%**	7519	48%
Hospitals	Mean	n.a.	53%	n.a.	5%	n.a.	8%	**67%**	n.a.	33%
	Min	n.a.	34%	n.a.	0%	n.a.	0%	**47%**	n.a.	12%
	Max	n.a.	67%	n.a.	21%	n.a.	28%	**88%**	n.a.	53%

NAC, Neo-adjuvant chemotherapy; IBR, immediate breast reconstruction; BCS, breast conserving surgery; BCPP, breast-contour-preserving procedure; n.a., not applicable.

Trends over time

During 2011–2015, use of BCS following NAC and mastectomy with IBR both increased, from 3 to 8% and 6 to 11% of all patients, respectively. As a result, the overall frequency of BCPP increased significantly, from 63% in 2011 to 71% in 2015 (P<0.001; **Figure 1**; **Table 2**), and the proportion of patients who underwent a mastectomy without reconstruction decreased from 37 to 29%, i.e., a relative reduction of 22%. The proportion of patients undergoing mere BCS for invasive cancer in the Netherlands remained stable during the study period. A gradual increase was observed in the overall use of NAC, from 8% in 2011 to 16% in 2015.

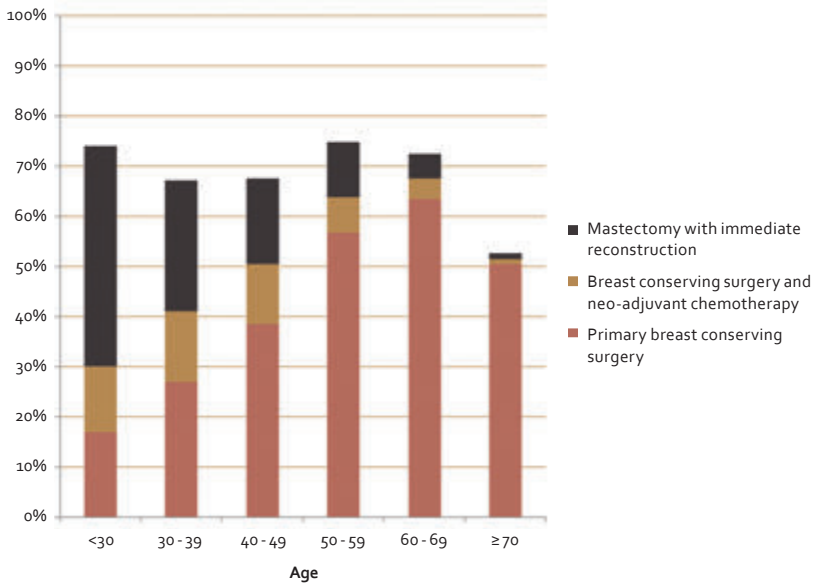
Figure 1. The annual proportion of patients who undergo a breast-contour-preserving procedure (BCPP) separated by the multiple treatment modalities (2011-2015).



Age-specific frequency of BCS and BCPP

Table 2 presents the frequencies of the treatment strategies per age group. The overall frequency of BCPP was similar (approximately 70%) for all age categories, except for patients ≥70 years old (52%). The means used to preserve the breast contour varied per age group. The proportion of patients who underwent primary BCS was lowest under 30 years (17%) and highest (63%) in patients aged 60–69 years. With increasing age, both BCS after NAC and mastectomy with IBR rates decreased. Above the age of 70 years, a substantially lower percentage of primary BCS was observed (51%), and only a very low percentage of BCS after NAC (1%) and IBR (1%). Almost half of the oldest patients underwent a primary mastectomy. **Figure 2** shows the cumulative age-specific proportions of the three treatment strategies to preserve the breast contour.

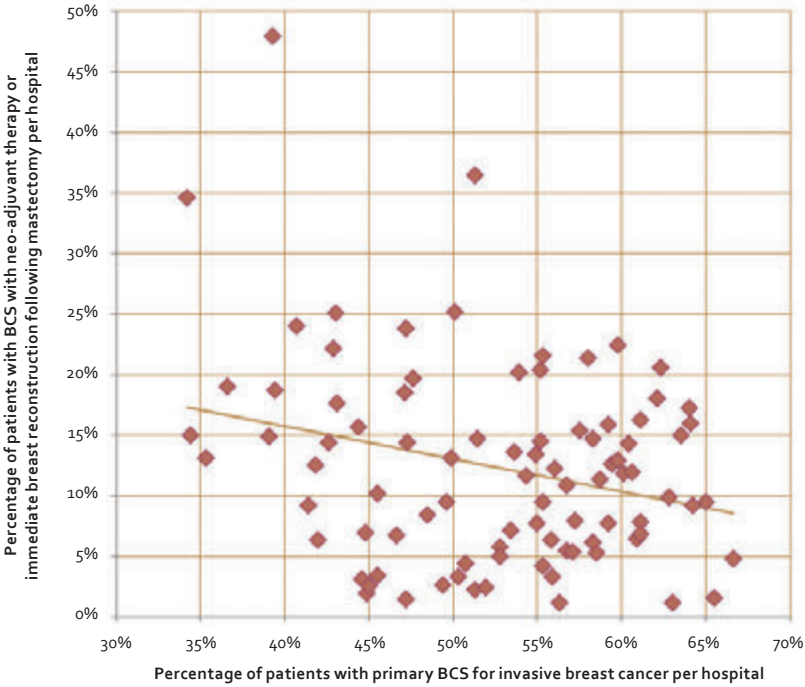
Figure 2. Multiple treatment modalities of the parameter breast-contour-preserving procedure (BCPP) for patients diagnosed with breast cancer separated by age.



Variation between hospitals

The proportion of patients undergoing BCPP varied extensively between individual hospitals, and this range of BCPP (47–88%) was wider than the observed variation of BCS (37–67%). All three treatment strategies constituting BCPP showed a wide variation between hospitals (**Table 2**). There was an inverse relationship between the proportion of primary BCS and the other two strategies to preserve the breast contour per hospital (**Figure 3**). The rates of BCS after NAC and mastectomy combined with IBR varied largely between hospitals: some hospitals never used BCS after NAC nor mastectomy with IBR, while other institutions performed BCS after NAC in up to 21% and IBR in up to 28% of patients. Hospital volume did not influence the institutional BCPP rate (data not shown).

Figure 3. Correlation per hospital between the proportion of patients who undergo primary Breast Conserving Surgery (BCS) and the cumulative proportion of patients who have BCS following neo-adjuvant chemotherapy and patients who undergo immediate breast reconstruction following mastectomy.



DISCUSSION

We present BCPP as an esthetic local outcome measure in breast cancer patients. BCPP provides a comprehensive parameter encompassing various treatment strategies to maintain the breast contour in patients treated for breast cancer. While in the Netherlands the rate of BCS remained stable during the study period, the rate of BCPP increased, from 63% in 2011 to 71% in 2015. This increase is the result of increased use of BCS after NAC and mastectomy with IBR. To the best of the authors' knowledge, no other studies have described BCPP as a composite measure to evaluate local esthetic outcome. Many studies have reported trends of the separate surgical, reconstructive, and medical modalities in patients treated

for primary breast cancer.[4,7–11] Population-based BCS rates have remained stable in recent years in Brazil[7] and the Netherlands,[4] while an increase was observed in some other European countries.[11] Over a similar time period, a decrease in the proportion of patients undergoing BCS was seen in the USA (from 66.6% in 1998 to 61.9% in 2011).[8,12–15] Other studies have reported significant institutional and regional differences in BCS rates, ranging from 20 to 84%.[11,16–20] Increased use of mastectomy combined with IBR over time, differences in IBR rates between countries,[4,7,8,21–24] as well as more frequent application of NAC have also been reported.[4,5,25–28] The observed rise in the rate of BCPP in relation to the observed stable primary BCS rate demonstrates that the composite endpoint has additional value as a local esthetic outcome parameter. This is illustrated in the present study, since a stable rate of primary BCS masks a 22% proportional decrease of patients who underwent a plain mastectomy. The BCPP rate was similar for most age groups, but the strategies used to maintain the breast contour varied largely between the different age groups. Primary BCS was increasingly used when patients were older, and a concomitant decrease was observed for the proportions of patients who underwent BCS after NAC and those who underwent mastectomy with IBR. In the very young age group, IBR accounted for half of the patients in whom the breast contour was preserved. The difference in the proportion of patients who had primary BCS in relation to the overall proportion undergoing BCPP (17% and 73%, respectively) was most profound in these very young patients (<30 years old). This is in part explained by previous guidelines advising against BCS in the young because of the higher risk of local recurrence and diagnosed genetic mutations.[29]

In patients aged >70 years, the low rate of BCPP merely reflected the rate of BCS, since BCS after NAC and mastectomy with IBR were infrequently used (1% and 1%, respectively). The absence of evidence in support of adjuvant chemotherapy in patients older than 70 years explains why NAC was hardly ever administered. The low rate of mastectomy with IBR seems conceivable too, although the extent to which patient preferences explain the observed higher mastectomy rate remains unanswered. BCPP as such was of little additional value in these elderly patients.

The rate of BCS has been promulgated as a quality indicator.[30] When performing primary BCS, a delicate balance exists between the esthetic and oncological aims of the surgery: a wider excision may lead to a worse esthetic result, while a too narrow excision may leave residual tumor tissue. Striving for a high BCS rate may unintentionally lead to the perverse incentive of aiming for the lowest possible positive margin rates by resecting larger amounts of breast tissue. BCPP serves the aim of measuring esthetic outcome more appropriately, as it appreciates at least the combined efforts and different treatment strategies to maintain the shape of the breast, which is in itself a desirable esthetic outcome.

While BCPP more or less annihilated conventional age-specific BCS rates, no such effect was observed for institutional differences. Despite an apparent interplay between the various strategies used to preserve the breast contour (illustrated by the observed inverse association between the rate of BCS and the proportion of patients who underwent BCPP), the net effect of the hospital variation in BCS after NAC and mastectomy with IBR resulted in an observed wider range of the proportion of BCPP than the hospital variation in BCS rates. Previous studies using data from the NBCA studied the variation of NAC rates[25] and the proportion of patients undergoing mastectomy combined with IBR.[21,31] Patient and tumor characteristics and hospital factors did account for institutional variation, but the number of treated patients per hospital was not a factor associated with higher rates of NAC or IBR. In another study, we also observed that surgeons' and plastic surgeons' preferences had an impact on the institutional IBR rate.[32] Much of the observed institutional variation remains unexplained. Several hospitals in the present study never applied NAC or provided IBR, which might explain the wider range of BCPP rates. As these hospitals had no means other than primary BCS to enhance their BCPP rate, these institutions fell behind as others were improving their BCPP rate. Obviously, this hypothesis urges the need for additional in-depth analysis of the observed institutional variation.

Having a national multidisciplinary audit for breast cancer care enabled us to analyze questions with large numbers of patients. This is a strength of the present study, and the population-based data are also suitable to study time trends. The absence of information regarding important patient characteristics such as smoking status and

body mass index is a limitation of the NBCA. These factors may well affect the eligibility of patients to undergo immediate breast reconstruction. Moreover, the lack of data about delayed reconstruction may limit the interpretation of results since to some extent. In addition, institutional availability and use of oncoplastic surgical techniques as well as radiotherapy indications have an impact on the desirability to perform BCS or prosthesis use, respectively. However, data regarding the use of oncoplastic techniques lacked sufficient detail to take into consideration. Referral patterns between hospitals, e.g., patients who underwent surgery at an institution another than the hospital where NAC was administered, could not be addressed. Finally, information regarding the achieved and perceived success of BCS as well as of IBR was not available, but would importantly enhance the value of BCPP as an outcome parameter.

BCPP provides insight into the various ways in which breast cancer patients can retain their breast contour, and the result reflects combined multidisciplinary efforts. Although it still lacks information about the perceived esthetic outcome, BCPP is an important step in providing more information than the rate of BCS alone. Achievement of a 100% preservation score is not considered to be an ultimate goal. We acknowledge that multiple factors influence the treatment options that can and will be offered to patients, and the patient's decision. Notwithstanding these limitations, this study supports the use of the BCPP rate as a local outcome parameter, and an institutional BCPP rate of 75% in patients younger than 70 years may well be defined as an appropriate norm value for good esthetic outcome of local treatment.

CONCLUSIONS

BCPP as a composite parameter provides insight into and understanding of the preservation of the breast contour in primary breast cancer patients, appreciating the various ways to maintain the contour of the breast. This study demonstrates that, while the BCS rate remained stable over recent years, the proportion of patients in whom the breast contour was preserved increased while the proportion who underwent a plain mastectomy decreased by one-fifth. At the same time, unexplained institutional differences in the BCS rate persist when applying the rate of BCPP as a quality indicator, and this should motivate future research.

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CHAPTER 4

Large hospital variation in immediate breast reconstruction rates after mastectomy for breast cancer in the Netherlands

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ABSTRACT

Background: The present study aimed to describe the use of immediate breast reconstruction (IBR) after mastectomy for invasive breast cancer and ductal carcinoma in situ (DCIS) in hospitals in the Netherlands and determine whether patient and tumor factors account for the variation.

Methods: Patients undergoing mastectomy for primary invasive breast cancer or DCIS diagnosed between January 1, 2011 and December 31, 2013 were selected from the NABON Breast Cancer Audit. All the 92 hospitals in the Netherlands were included. The use of IBR in all hospitals was compared using unadjusted and adjusted analyses. Patient and tumor factors were evaluated by univariate and multivariate analyses.

Results: In total, 16,953 patients underwent mastectomy: 15,072 for invasive breast cancer and 1,881 for DCIS. Unadjusted analyses revealed considerable variation between hospitals in postmastectomy IBR rates for invasive breast cancer (mean 17%; range 0–64%) and DCIS (mean 42%; range 0–83%). For DCIS, younger age and multifocal disease were factors that significantly increased IBR rates. For patients diagnosed with invasive breast cancer, IBR was more often used in younger patients, multifocal tumors, smaller tumors, tumors with a lower grade, absence of lymph node involvement, ductal carcinomas, or hormone-receptor positive/HER2-positive tumors. After case-mix adjustments for these factors, the variation in the use of IBR between hospitals remained large (0–43% for invasive breast cancer and 0–74% for DCIS).

Conclusions: A large variation between hospitals was found in postmastectomy IBR rates in the Netherlands for both invasive breast cancer and DCIS even after adjustment for patient and tumor factors.

INTRODUCTION

Breast cancer is the most frequently diagnosed cancer in women in the Netherlands. Curative surgical treatment for breast cancer consists of breast conserving therapy or mastectomy. Mastectomy is performed in approximately 40% of patients with invasive breast cancer[1,2] and in 33% of patients with ductal carcinoma in situ (DCIS).[3]

To restore the breast contour following mastectomy, a breast reconstruction can be performed. Breast reconstruction during initial breast cancer surgery is known as immediate breast reconstruction (IBR); delayed breast reconstruction is reconstruction at a later time.[4] Reasons to offer patients IBR are of both esthetic and psychosocial nature. IBR generally leads to higher patient satisfaction, improved body image, and increased self-esteem compared to delayed reconstruction.[5] Therefore, guidelines suggest considering IBR in all patients who undergo mastectomy.[6,7] However, the percentage of patients actually undergoing IBR or delayed reconstruction after mastectomy is generally low and varies significantly from 5% to 30% in population-based studies.[8] Several factors such as patient factors, tumor-related factors, hospital factors, and demographic factors may contribute to the final decision to perform IBR.[8]

Current practice patterns of postmastectomy IBR in the Netherlands are unknown. Evaluating hospital performances using case-mix-adjusted data can identify true variation between hospitals and ultimately help to reduce undesirable variation in clinical practice and improve the quality of care for breast cancer patients. Therefore, the present study aimed to investigate the variation in the use of IBR after mastectomy for invasive breast cancer and DCIS between all hospitals in the Netherlands and identify whether the variation could be attributed to patient and tumor factors influencing the use of IBR.

MATERIALS AND METHODS

Data source

Data were derived from the NABON (National Breast Cancer Consultation Netherlands) Breast Cancer Audit (NBCA),[9] a continuous national multidisciplinary quality improvement project in which a wide range of variables concerning patient, diagnostics, and treatments are prospectively collected by the hospitals themselves or the Netherlands Cancer Registry. The NBCA contains data registered in all 92 hospitals performing breast cancer surgery in the Netherlands.[10] The information concerning individual patients and hospitals is de-identified for this study, allowing comparisons without identification.

Study population

Data from all female patients who underwent a mastectomy for either primary DCIS or nonmetastatic invasive breast cancer diagnosed between January 1, 2011 and December 31, 2013 were selected. Information available in the NBCA on patient characteristics (age) and tumor characteristics (TNM classification, histological subtype, grade, and receptor status) were extracted. Four types of IBR were defined: implant breast reconstruction (including tissue expander), autologous breast reconstruction, a combination of both, and reconstruction not otherwise specified.

Statistical analyses

Invasive breast cancer and DCIS patients were analyzed separately. Differences in the use of IBR between hospitals were compared using a funnel plot. Patient and tumor- specific factors potentially affecting the use of IBR were compared between women with and without IBR. Subsequently, to investigate which factors were related to the use of IBR, univariate regression analyses were performed. Next, factors with p-values of <0.10 were included into multivariate regression analyses using an enter model. These multivariate regression analyses were used to identify independent factors determining the use of IBR, corrected for the other factors that were included into the model.

A second analysis was performed to identify variation in the use of IBR between hospitals using the adjusted data based on observed/expected calculations (i.e., case-mix adjustment for predicting factors of IBR). All statistical analyses were performed using SPSS (SPSS for MAC Version 20.0; SPSS Inc., Chicago, IL).

RESULTS

Patient characteristics

In total, 16,953 patients underwent a mastectomy for invasive M0 breast cancer (n=15,072) or DCIS (n=1881) in one of the 92 hospitals in the Netherlands. Results are separately presented for invasive breast cancer and DCIS. Patient and tumor characteristics by reconstruction status are shown in **Table 1** for invasive breast cancer and **Table 2** for DCIS.

Table 1. Baseline characteristics of 15,072 invasive breast cancer patients treated with a mastectomy by reconstruction status between 2011 and 2013 in the Netherlands.

		Immediate reconstruction			
		No		Yes	
		n	%	n	%
Age	Below 50	2471	68%	1170	32%
	50 to 65	4222	79%	1153	22%
	65 or above	5836	97%	211	4%
Clinical tumor stadium	cTx / Unknown	752	72%	288	28%
	cT1	4596	79%	1248	21%
	cT2	5228	86%	864	14%
	cT3	1365	92%	125	8%
	cT4	595	98%	11	2%
Clinical lymph node stadium	cNx / Unknown	487	82%	108	18%
	cN0	8614	80%	2098	20%
	cN1	3141	91%	307	9%
	cN2	113	93%	9	7%
	cN3	181	93%	14	7%
Multifocal	No	9164	85%	1681	16%
	Yes	3372	80%	855	20%
Histology	Ductal	9444	82%	2025	18%
	Lobular	2027	88%	265	12%
	Combination	400	80%	103	21%
	Unknown	665	82%	143	18%
Grade	1	1944	79%	513	21%
	2	5445	84%	1065	16%
	3	3779	85%	685	15%
	Unknown	1368	83%	273	17%
Receptor groups	HR positive, Her2 negative	8140	84%	1608	17%
	HR positive, Her2 positive	1140	80%	294	21%
	HR negative, Her2 positive	682	84%	135	17%
	Triple negative	1455	83%	292	17%
	Unknown	1119	84%	207	16%

HR,Hormone Receptor.
Percentages are rounded off, which in some cases leads to a total of above 100%.

Table 2. Baseline characteristics of 1,881 patients with ductal carcinoma in situ treated with a mastectomy by reconstruction status between 2011 and 2013 in the Netherlands.

		Immediate reconstruction			
		No		Yes	
		n	%	n	%
Age	Below 50	128	33%	265	67%
	50 to 65	500	53%	452	48%
	65 or above	466	87%	69	13%
Multifocal	No	942	60%	627	40%
	Yes	153	49%	159	51%
Grade	1	93	54%	80	46%
	2	354	57%	271	43%
	3	596	60%	398	40%
	Unknown	52	58%	37	42%

Percentages are rounded off, which in some cases leads to a total of above 100%.

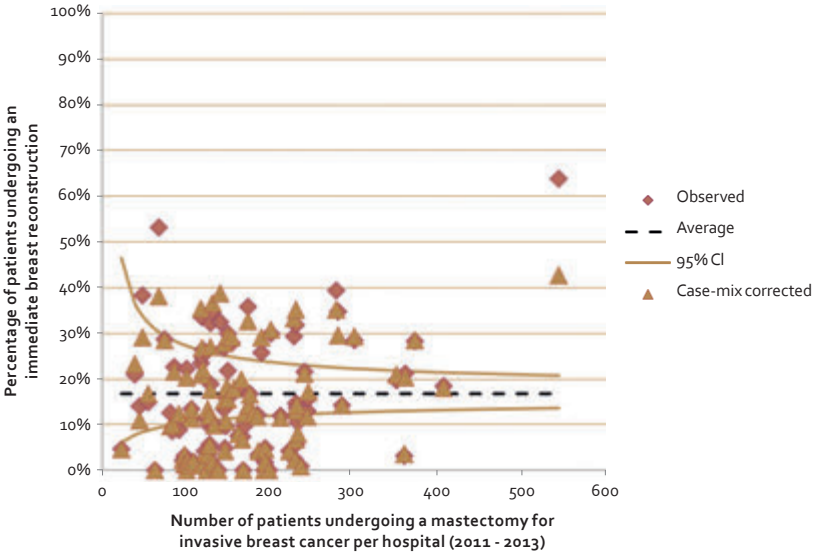
Invasive breast cancer

Variation in use of immediate breast reconstruction

On average, 16.8% (n=2536) of all patients with a mastectomy for invasive breast cancer underwent IBR. An increase in the mean use and range of IBR was seen over the years from 14.6% (range 0–54%) in 2011 to 19.3% (range 0–74%) in 2013. There was a decrease in the number of hospitals not performing IBR from 23 in 2011 to 11 in 2013. Unadjusted IBR rates for all hospitals combining 3 years together varied from 0% to 64% (**Figure 1**).

Immediate implant-based breast reconstructions were performed most frequently (89%). Immediate autologous reconstructions and a combination of autologous and implant reconstructions were both used in less than 5% of the patients who underwent IBR, and in 1.9% the reconstruction was not otherwise specified.

Figure 1. Funnel plot showing hospital differences in percentage of patient with invasive Mo breast cancer treated with mastectomy and immediate breast reconstruction, unadjusted (terra squares) and adjusted for age, clinical tumor stage, clinical nodal stage, multifocality, histology, grade and receptor status (ocher triangles) (2011 – 2013).



Predictive factors for immediate breast reconstruction

The percentage of patients receiving IBR significantly decreased with increasing age. Younger patients (<50 years) had more frequent IBR [Odds Ratio (OR) 1.73; 95% Confidence Interval (95% CI) 1.58–1.91] compared to older patients (50–65 years). IBR was less often used in patients with larger tumors and patients with involved lymph nodes. Patients who were treated for a clinical T3 tumor had a three times lower chance of receiving IBR than those treated for a clinical T1 tumor (OR 0.34; 95% CI 0.28–0.41). For lymph node-positive tumors, a similar lower chance of receiving IBR was observed; a patient with a clinical N2 tumor had a three times lower chance of receiving IBR than those with lymph node-negative tumors (95% CI 0.17–0.65).

Patients with multifocal tumors had a higher chance of receiving IBR. Being diagnosed with a ductal carcinoma increased the chance of undergoing IBR compared to lobular carcinoma diagnosis. IBR was more frequently used in lower tumor grades. Hormone Receptor positive (HR+)/ HER2-positive tumors were associated with a

higher likelihood of IBR than the reference category of HR+/HER2-negative tumors (OR 1.31; 95% CI 1.14–1.50). Compared to the reference category, patients with triple-negative tumors had a similar chance of receiving IBR. All predictive factors (age, TNM classification, multifocality, histology, tumor grade, and receptor groups) remained statistically significant in multivariate analyses (**Table 3**).

Table 3. Univariate and multivariate analyses of factors determining the use of immediate breast reconstruction after mastectomy in 15,072 invasive breast cancer patients operated between 2011 and 2013 in the Netherlands.

			Univariate Analysis		Multivariate Analyses	
		n	OR	95% CI	OR	95% CI
Age	Below 50	1170	1.73	1.58 - 1.91	2.09	1.89 - 2.32
	50 to 65	1153	ref		ref	
	65 or above	211	0.13	0.11 - 0.15	0.13	0.11 - 0.15
Clinical tumor stadium	cTx / Unknown	288	1.41	1.22 - 1.64	1.24	1.05 - 1.47
	cT1	1248	ref		ref	
	cT2	864	0.61	0.55 - 0.67	0.68	0.61 - 0.76
	cT3	125	0.34	0.28 - 0.41	0.34	0.28 - 0.43
	cT4	11	0.07	0.04 - 0.12	0.10	0.06 - 0.19
Clinical lymph node stadium	cNx / Unknown	108	0.91	0.74 - 1.13	0.72	0.57 - 0.92
	cNo	2098	ref		ref	
	cN1	307	0.40	0.35 - 0.46	0.37	0.32 - 0.43
	cN2	9	0.33	0.17 - 0.65	0.36	0.18 - 0.72
	cN3	14	0.32	0.18 - 0.55	0.33	0.18 - 0.58
Multifocal	No	1681	ref		ref	
	Yes	855	1.38	1.26 - 1.51	1.14	1.03 - 1.26
Histology	Ductal	2025	ref			
	Lobular	265	0.61	0.53 - 0.70	0.71	0.61 - 0.83
	Combination	103	1.20	0.96 - 1.50	1.19	0.93 - 1.52
	Other	143	1.00	0.83 - 1.21	1.12	0.91 - 1.39
Grade	1	513	ref		ref	
	2	1065	0.74	0.66 - 0.83	0.84	0.73 - 0.96
	3	685	0.69	0.61 - 0.78	0.64	0.55 - 0.75
	Unknown	273	0.76	0.64 - 0.89	0.98	0.81 - 1.19
Receptor groups	HR positive, Her2 negative	1608	ref		ref	
	HR positive, Her2 positive	294	1.31	1.14 - 1.50	1.22	1.04 - 1.42
	HR negative, Her2 positive	135	1.00	0.83 - 1.21	1.06	0.85 - 1.31
	Triple negative	292	1.02	0.89 - 1.17	1.15	0.98 - 1.36
	Unknown	207	0.94	0.80 - 1.10	0.92	0.77 - 1.09

CI, Confidence interval; OR, Odds Ratio; HR, Hormone Receptor.

Effect of case-mix adjustment on variation in IBR rates between hospitals

After case-mix correction for tumor and patient factors (age, clinical tumor status, clinical nodal status, multifocality, histology, grade, and receptor status), a slightly narrower but statistically significant variation in the use of IBR between hospitals was observed, ranging from 0% to 43% (**Figure 1**), compared to the initially observed variation.

Ductal carcinoma in situ

Variation in use of immediate breast reconstruction

With an average rate of 42% (786/1881), IBR was more often performed after mastectomy for DCIS than for invasive breast cancer. Nineteen hospitals in 2011 and 17 hospitals in 2013 did not perform IBR for DCIS. IBR rates after mastectomy for DCIS varied largely between hospitals (range 0–83%). The use of IBR slightly increased in 3 years; 41% of the patients received IBR in 2011 (range 0–100%) compared to 45% in 2013 (range 0–83%) using unadjusted data. Most patients diagnosed with DCIS received an implant-based reconstruction (86.1%). Autologous reconstruction and a combination of autologous and implant reconstruction were both performed in 5% of the patients undergoing IBR. The type of reconstruction was unknown in 3.3% of the patients.

Predictive factors for immediate breast reconstruction

Factors potentially affecting the use of IBR following mastectomy for DCIS were age, multifocality, and DCIS grade. Older patients (≥65 years) had an OR of 0.16 compared to patients aged between 50 and 65 years. Patients with multifocal disease had a 1.56-fold higher chance of undergoing IBR than patients with unifocal tumors (95% CI 1.22–1.99). DCIS grade did not have a statistically significant relationship with receiving IBR, and therefore was not included in multivariate analyses. Patient age and multifocality remained statistically significant predictive factors in multivariate analyses. **Table 4** shows univariate and multivariate analyses of factors predicting the use of IBR after mastectomy for DCIS.

Effect of case-mix adjustment on variation in IBR rates between hospitals

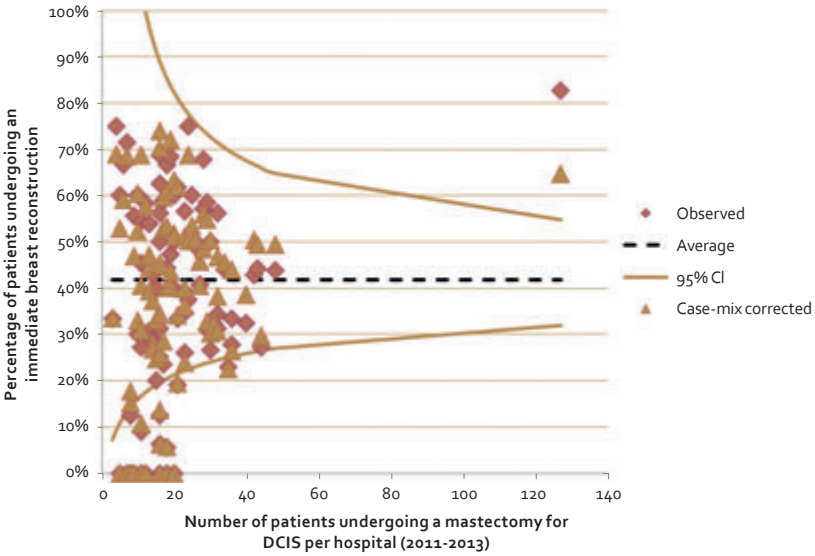
Case-mix adjustment of age and multifocality, enabling comparison between hospitals for IBR rates after mastectomy for DCIS, revealed a similar pattern as that of unadjusted data, with a variation between 0% and 74% (**Figure 2**).

Table 4. Univariate and multivariate analyses of factors determining the use of immediate breast reconstruction after mastectomy in 1,881 patients with ductal carcinoma in situ operated between 2011 and 2013 in the Netherlands.

			Univariate Analysis		Multivariate Analyses	
		n	OR	95% CI	OR	95% CI
Age	Below 50	265	2.29	1.79 - 2.93	2.29	1.79 - 2.94
	50 to 65	452	ref		ref	
	65 or above	69	0.16	0.12 - 0.22	0.17	0.13 - 0.22
Multifocal	No	627	ref		ref	
	Yes	159	1.56	1.22 - 1.99	1.40	1.07 - 1.82
Grade	1	80	ref		n.a.	
	2	271	0.89	0.64 - 1.25	n.a.	
	3	398	0.78	0.56 - 1.07	n.a.	
	Unknown	37	0.83	0.49 - 1.39	n.a.	

CI, Confidence interval; OR, Odds Ratio.

Figure 2. Funnel plot showing hospital differences in percentage of patient with ductal carcinoma in situ treated with mastectomy and immediate breast reconstruction, unadjusted (terra squares) and adjusted for age and multifocality (ocher triangles) (2011 – 2013).



DISCUSSION

This is the first nation-wide study investigating the variation in the use of IBR after mastectomy for invasive breast cancer and DCIS between hospitals in the Netherlands. A large variation was found; IBR was performed on average in 17% of patients with invasive breast cancer (range 0–64%) and in 42% of patients with DCIS (range 0–83%). Although various patient and tumor characteristics were found to have a significant effect, adjustment for these factors using multivariate analyses did not result in less variation between hospitals. Apparently, there are other yet unidentified factors, such as patient preferences, surgeons' beliefs, or hospital organizational factors, which probably affect the use of IBR to a larger extent.

Previous studies have reported on breast reconstruction rates after mastectomy[1,8,11]; however, the results of these studies cannot be compared with our results because immediate and delayed breast reconstructions and invasive breast cancer and DCIS were combined in other studies. Some studies reported mean postmastectomy IBR rates of 21% in the United Kingdom[1] and 24% in the United States[11] when combining invasive breast cancer and DCIS. In our study, we decided to analyze DCIS and invasive breast cancer separately because certain factors such as hormone receptor status are only available and relevant for patients diagnosed with invasive breast cancer. Moreover, the IBR rate for patients with DCIS was more than two-fold higher than that for patients with invasive breast cancer, which is consistent with literature.[2] Furthermore, previous studies often combined immediate and delayed breast reconstruction. A large meta-analysis (n=159,305 cases, 28 studies) showed an average of 16.9% of patients receiving immediate or delayed breast reconstruction. Comparison of the 10 largest population-based studies with a total of 10,000 mastectomy cases resulted in breast reconstruction rates (immediate and delayed) varying between 4.9% and 30.3%.[8] Combining immediate and delayed reconstruction for analysis is not preferred in our opinion because treatment approaches and patient populations may be different. Most importantly, the exact numerator to calculate the delayed breast reconstruction rate in a given time period is unknown because a delayed reconstruction may be performed many years after the initial surgery.

In the present study, we investigated the possible effect of patient and tumor characteristics on the use of IBR. In accordance with other studies, we found that a younger age was significantly related with higher IBR rates.[2,8,12,13] This finding may be explained by both clinician beliefs and patient preferences. Younger patients may be more aware of and more interested in the possibility of IBR, and they may be more assertive to discuss reconstructive options. Clinicians in turn may consider younger patients to be more eligible to undergo a reconstruction. In addition, older patients are more likely to have significant comorbidities leading to the decision to not perform IBR, may more easily accept the loss of their breast(s), or may not want to undergo major surgery.

Patients with an early-stage tumor had a higher likelihood of receiving IBR, which was also consistent with literature.[2,8] Locoregionally advanced tumors require adjuvant therapies such as radiotherapy and chemotherapy more often, even after a mastectomy. Patients with an indication for adjuvant therapies, particularly radiotherapy, have a lower chance of being treated with IBR.[14] There is still much debate on the timing and type of reconstruction in case radiotherapy is needed.[15–17] Particularly in implant-based reconstructions, radiotherapy leads to a significantly higher reconstruction failure rate compared to patients without radiotherapy.[18] In cases where patients require radiotherapy, clinicians may decide not to perform IBR as most reconstructions are implant based. It is recommended to perform an autologous flap technique when radiotherapy is required because radiotherapy-related complications of the autologous flap are less frequent and less severe.[15] In case of adjuvant chemotherapy, it is not the fear of increased chance of IBR complications but the delay IBR may cause to initiate adjuvant chemotherapy. However, a recent review found that IBR does not necessarily delay the start of adjuvant chemotherapy to a clinically relevant extent.[19]

The presence of a multifocal cancer was associated with a higher rate of postmastectomy IBR. Although multifocality may explain the propensity to prefer ablative surgery in these patients because of the size of the involved breast area, the size of the individual lesions will rarely be a reason to abstain from IBR. The observation that IBR was more frequent in patients treated for DCIS than those

treated for invasive breast cancer supports this explanation because DCIS usually involves a larger area of the breast than invasive breast cancer. Similar findings were found in the study by Roder et al.[2]

The uptake and variation of IBR can be only partly explained by the identified patient and tumor factors, suggesting that other factors contributed to the variation to a larger extent. Patient preferences may vary between institutions or regions. For example, the reported percentages of patients deciding not to undergo IBR varied between 17% and 62% in different regions of the United Kingdom.[1] An even more important role could be attributed to the personal perception, preferences, and beliefs of physicians considering patients eligible for IBR.[6,7,13,20]

Hospital-related factors such as location in an urban environment or being a teaching hospital, high-volume breast cancer center, private hospital, or hospital with a plastic surgical department may all affect the rate of IBR.[8,14,21] Other organizational factors such as the length of the operation and availability of a plastic surgeon in the hospital may further challenge the frequency of IBR. Further research should focus on identifying these additional factors that may have contributed to the large variation found.

A strength of the present study is that a national audit with 100% participation of all hospitals in the Netherlands provides a unique insight into the quality of breast cancer care delivered and the areas for improvement. An audit includes patients who are usually not included in clinical trials and reflects practice patterns in daily practice. Moreover, the availability of data at a hospital level enables nationwide hospital comparisons. A limitation of the present study is in the nature of a national audit itself. Registration bias may be present as the data were collected for a national audit. However, high rate of case ascertainment was found when the data was compared with that in the National Cancer Registry. Second, although many case-mix variables were available, there may have been unknown confounding variables that were not available in the data set and may have influenced variation in IBR between hospitals.

CONCLUSION

In conclusion, we found large variation between hospitals in IBR after mastectomy for invasive breast cancer and DCIS. Several factors (e.g., age, tumor status, grade, and receptor status) could be identified as predictive factors but did not exclusively explain the variation between hospitals. Further research is needed to investigate other causes such as patient and surgeon's preferences and hospital-related factors and to increase the percentage of IBR in all eligible patients.

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CHAPTER 5

Hospital organizational factors affect the use of immediate breast reconstruction after mastectomy for breast cancer in the Netherlands

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ABSTRACT

Objectives: Significant hospital variation in the use of immediate breast reconstruction (IBR) after mastectomy exists in the Netherlands. Aims of this study were to identify hospital organizational factors affecting the use of IBR after mastectomy for ductal carcinoma in situ (DCIS) or invasive breast cancer (BC) and to analyze whether these factors explain the variation.

Materials and methods: Patients with DCIS or primary invasive BC treated with mastectomy between 2011 and 2013 were selected from the national NABON Breast Cancer Audit. Hospital and organizational factors were collected with an online web-based survey. Regression analyses were performed to determine whether these factors accounted for the hospital variation.

Results: In total, 78% (n=72) of all Dutch hospitals participated in the survey. In these hospitals 16,471 female patients underwent a mastectomy for DCIS (n=1,980) or invasive BC (n=14,491) between 2011 and 2014. IBR was performed in 41% of patients with DCIS (hospital range 0–80%) and in 17% of patients with invasive BC (hospital range 0–62%). Hospital type, number of plastic surgeons available and attendance of a plastic surgeon at the MDT meeting increased IBR rates. For invasive BC, higher percentage of mastectomies and more weekly MDT meetings also significantly increased IBR rates. Adjusted data demonstrated decreased IBR rates for DCIS (average 35%, hospital range 0–49%) and invasive BC (average 15%, hospital range 0–18%).

Conclusion: Hospital organizational factors affect the use of IBR in the Netherlands. Although only partly explaining hospital variation, optimization of these factors could lead to less variation in IBR rates.

INTRODUCTION

Current surgical treatment of breast cancer patients consists of either breast conserving surgery or mastectomy. A mastectomy is performed in about 40% of invasive breast cancer patients and in approximately 33% of patients with a ductal carcinoma in situ.[1–3] An increasing number of patients desire restoration of their breast contour following mastectomy and consequently breast reconstruction has become an integral part of breast cancer treatment.[4] The breast can be reconstructed during the initial operation following mastectomy (immediate breast reconstruction (IBR)) or at a later time (delayed breast reconstruction).[2]

IBR has proven to be safe in terms of local recurrence and long-term survival rates compared to mastectomy only.[5,6] Moreover, IBR offers women psychological benefits in terms of recovery and improved quality of life and is associated with superior esthetic results compared to delayed breast reconstruction.[5–7] Guidelines emphasize the importance of reconstruction after mastectomy and recommend clinicians to discuss the possibility of IBR with every patient undergoing mastectomy.[2,8,9]

Despite the benefits of IBR, the percentage of patients with DCIS or invasive breast cancer actually undergoing IBR after mastectomy is approximately 20% in the Netherlands. Large hospital variation in the use of IBR was found previously, ranging from 0 to 64% for invasive breast cancer and 0–83% for DCIS.[10] Comparable IBR rates were shown in other international studies; IBR was performed in 21% of the postmastectomy patients in the United Kingdom and 24% in the United States.[2,11,12] Literature has demonstrated that patient and tumor factors such as age, social economic status, multifocality, tumor type, clinical tumor stage, clinical lymph node stage, grade and previous breast surgery are predictors of the use of IBR.[10,11,13–17] However, these patient and tumor factors do not fully explain the large variation between hospitals in the Netherlands.[10]

The aim of the present study was to investigate which hospital and hospital organizational factors affect the use of IBR after mastectomy for DCIS and invasive breast cancer in the Netherlands and whether these factors account for the variation seen.

MATERIAL AND METHODS

Data source

Data of the NABON Breast Cancer Audit (NBCA) was used to obtain information on breast cancer patients in the Netherlands. The NBCA is a national multidisciplinary quality improvement register in which all 92 hospitals in the Netherlands participate and is supported by the Dutch Institute for Clinical Auditing (DICA) and the Netherlands Comprehensive Cancer Organization (IKNL).[18] Information concerning patient, tumor, diagnostics and treatment is continuously collected prospectively either by the hospitals themselves or by data managers of the Netherlands Cancer Registry (NCR).

Study population

All female patients diagnosed with DCIS or invasive breast cancer between January 1st, 2011 and December 31st, 2013 who underwent a mastectomy were selected.

Hospital organizational factors based on data from the NBCA

Hospitals were categorized as district hospital, teaching hospital (despite educational activities, not affiliated with a medical faculty), university hospital (hospitals having a medical faculty) or cancer specific hospital (hospitals only treating cancer patients). According to the number of new breast cancer patients annually diagnosed in a hospital, three groups were identified (group 1: 1–150, group 2: 150–300, group 3: >300 patients per year). The percentage of mastectomies (related to all surgical excisions) were categorized in three groups (group 1: 0–30%, group 2: 30–50% and group 3: >50%).

Survey

All 92 hospitals were invited to complete a web-based survey regarding hospital organization factors. Questions encompassed the number of weekly MDT meetings (1, 2, >2 times per week), the presence of the various disciplines involved in breast cancer care participating in the MDT meeting (e.g., nurse practitioners, pathologists, radiation oncologists, radiologists and medical oncologists), number of plastic surgeons available at the institution per 100 new diagnoses of breast

cancer (0–0.5, 0.5–2.5 and > 2.5), number of breast surgeons available at the institution per 100 new diagnoses of breast cancer (0–1.5, 1.5–2.5 and >2.5) and the presence of a plastic surgeon at the weekly MDT meeting (never/incidental, structural). "Never" refers to hospitals where no plastic surgeon was attending the weekly MDT meetings and "incidental" only incidentally on request. Only patients of hospitals that responded to the survey were included for analyses. In case data were missing, we categorized them as unknown.

Statistical analyses

DCIS and invasive breast cancer were analyzed separately. Factors tested for confounding were age, social economic state (SES), multifocality, clinical tumor stage, clinical lymph node stage, grade and radiation therapy. With use of a logistic regression model hospital organizational factors were related to the prevalence of IBR and were presented as odds ratio's with 95% confidence intervals (95%CIs). Factors that demonstrated to significantly affect IBR rates in univariable analyses ($p < 0.10$) were included in the multivariable analyses.

Hospital performance of IBR was visualized with the use of funnel plots. In the funnel plots the volume is based on the number of mastectomies (and not the total number of breast cancer diagnosis treated per hospital) over 3 years. Actually, in the Netherlands, 60% of the patients are treated with breast conserving surgery, so the actual hospital volume of breast cancer patients is much higher. Data were analyzed unadjusted and adjusted for patient, tumor and hospital organizational factors significantly affecting the use of IBR. Since the data is organized at more than one level and is clustered for the individual hospitals, multilevel analysis was performed. Not all organizational characteristics of the hospitals were known, but with use of a multilevel analysis, all hospital depending factors were taken into account in the adjusted data. All statistical analyses were performed in STATA (version 13.1 2013, Texas).

RESULTS

Study population

Seventy-two hospitals (78.3%) responded to the survey leading to inclusion of 16,471 patients with a mastectomy for DCIS (n=1,980) and invasive breast cancer (n=14,491) (**Table 1**). Almost 90% of the responding hospitals were categorized as a district or teaching hospital and most (85%) of the hospitals had 0–300 diagnosis annually. In most hospitals, one MDT meeting per week was organized and one hospital reported to have a daily MDT meeting (**Table 1**). All disciplines related to breast cancer care (e.g., surgeons, medical oncologists, radiation oncologists, radiologists, pathologists, nurse practitioners) structurally attended the MDT meetings. In 71% of the hospitals a plastic surgeon was structurally attending the MDT meeting. In most hospitals the geneticist, psychologist and palliative care expert were incidentally present. Eighty percent of the hospitals reported to offer plastic surgical care for breast cancer patients. In 83% of the responding hospitals, 0.5–2.5 plastic surgeons per 100 new diagnoses of breast cancer were available. For breast surgeons, most hospitals (49%) reported to have 1.5–2.5 breast surgeons per 100 new diagnoses of breast cancer (**Table 1**).

Table 1. Hospital characteristics of the 72 responding hospitals in the Netherlands.

		Dutch hospitals (n=72)		Number of patients	
		Number	%	DCIS	Invasive breast cancer
Response	Non-responding hospitals	20	21.7		
	Responding hospitals	72	78.3	1,980	14,491
Hospital type	District hospital	27	37.5	499	4,044
	Teaching hospital	37	51.4	1.106	8,624
	University hospital	7	9.7	243	1,299
	Cancer specific hospital	1	1.4	132	524
Volume (# diagnosis annually)	Group 1 (1/150)	24	33.3	420	2,92
	Group 2 (150/300)	37	51.4	1.109	8,023
	Group 3 (>300) ub=436	11	15.3	451	3,548

Table 1. Hospital characteristics of the 72 responding hospitals in the Netherlands. (continued)

		Dutch hospitals (n=72)		Number of patients	
		Number	%	DCIS	Invasive breast cancer
% mastectomies (of all surgical excisions)	Group 1 (0/30)	4	5.6	90	612
	Group 2 (30/50)	49	68.1	1.275	9,505
	Group 3 (50/90)	19	26.4	615	4,374
% referrals for mastectomy	Group 1 (0/2.5)	17	23.6	691	4,532
	Group 2 (2.5/ 5.0)	26	36.1	628	5,054
	Group 3 (>5) ub=31	29	40.3	661	4,905
% referrals mastectomy+ reconstruction	Group 1 (0/2.5)	46	63.9	1.419	10,162
	Group 2 (2.5/ 5.0)	17	23.6	409	3,119
	Group 3 (> 5.0) ub=21	9	12.5	152	1,21
# of weekly MDT	Group 1 (1)	24	33.3	535	4,214
	Group 2 (2)	14	19.4	374	2,661
	Group 3 (>2) ub=7	9	12.5	265	2,217
	Group 4 (unknown)	25	34.7	806	5,399
# of plastic surgeons / 100 diagnoses	Group 1 (0/0.5)	4	5.6	43	453
	Group 2 (0.5/2.5)	60	83.3	1.713	12,791
	Group 3 (>2.5) ub=23	7	9.7	215	1,136
	Group 4 (unknown)	1	1.4	9	111
# of breast-surgeons / 100 diagnoses	Group 1 (0/1.5)	28	38.9	932	7,181
	Group 2 (1.5/2.5)	35	48.6	908	6,32
	Group 3 (>2.5) ub=17	9	12.5	140	990
Attendance plastic surgeon at weekly MDT	Never or incidental	13	18.1	294	2,404
	Yes, structural	51	70.8	1.381	10,145
	Unknown	8	11.1	305	1,942

DCIS, ductal carcinoma in situ; ub, upper boundary; MDT, multidisciplinary team meetings.

On average, 41% (n=809) of the patients underwent IBR after a mastectomy for DCIS. The hospital variation in performing IBR for DCIS varied between 0 and 80%. The average rate of IBR for invasive breast cancer was 17% (n=2,435) with a hospital variation ranging from 0 to 62%.

DCIS

Hospital organizational factors such as hospital type, hospital volume, number of weekly MDT meetings, number of plastic surgeons per 100 new diagnoses and the attendance of a plastic surgeon at weekly MDT meetings significantly affected IBR rates in univariable analyses. Consequently, these variables were included in the multivariable model (**Table 2**). The percentage of mastectomies (related to all surgical excisions), and the number of breast surgeons available at the institution per 100 new diagnoses did not affect IBR rates significantly in univariable analyses and were therefore not included in multivariable analyses.

Because age, SES and grade significantly affected IBR rates (data not shown)[10], these factors were included in the multivariable model to correct for confounding (**Table 2**). The multivariable model demonstrated that patients who underwent a mastectomy for DCIS at the cancer specific hospital had a higher chance of receiving IBR (OR=6.10 95%CI: 3.34–11.13) compared to patients receiving a mastectomy at a district hospital. Patients treated at a teaching (OR=1.33, 95%CI: 0.97–1.83) or university hospital (OR=0.97, 95%CI: 0.47–1.99) did not have a significant higher chance of receiving IBR compared to patients treated at a district hospital. The percentage of patients receiving IBR increased with an increasing number of plastic surgeons practicing in that specific hospital. Hospitals with more than 2.5 plastic surgeons per 100 diagnoses had a more than 3-fold higher IBR rate in comparison to hospitals with no or limited plastic surgeons available (OR=3.26, 95%CI: 1.11–9.59). The structural attendance of a plastic surgeon at the weekly MDT meeting was significantly associated with a higher IBR rate compared to MDTs with no or incidental plastic surgeon attendance (OR=1.52, 95%CI: 1.10–2.10) (**Table 2**).

Table 2. Univariable and multivariable analyses of hospital organization factors affecting the use of immediate breast reconstruction after mastectomy for 1,980 patients with ductal carcinoma in situ (DCIS).

		Immediate breast reconstruction (DCIS) (n=1,980)								
							Univariable		Multivariable*	
		No	%	Yes	%	Total	OR	95% CI	OR	95% CI
Hospital type	District hospital	355	71.14	144	28.86	499	ref		ref	
	Teaching hospital	663	59.95	443	40.05	1106	1.65	1.31-2.07	1.33	0.97-1.83
	University hospital	127	52.26	116	47.74	243	2.25	1.64-3.09	0.97	0.47-1.99
	Cancer specific hospital	26	19.70	106	80.30	132	10.05	6.28-16.09	6.10	3.34-11.13
Volume (# diagnosis annually)	Group 1 (1/150)	278	66.19	142	33.81	420	ref		ref	
	Group 2 (150/300)	627	56.54	482	43.46	1109	1.50	1.19-1.90	1.25	0.88-1.78
	Group 3 (>300) ub=436	266	58.98	185	41.02	451	1.36	1.03-1.79	1.19	0.78-1.82
% mastectomies (of all surgical excisions)	Group 1 (0/30)	52	57.78	38	42.22	90	ref			
	Group 2 (30/50))	731	57.33	544	42.67	1,275	1.02	0.66-1.57		
	Group 3 (50/90)	388	63.09	227	36.91	615	0.80	0.51-1.25		
# of weekly MDT	Group 1 (1)	361	67.84	174	32.52	535	0.59	0.44-0.80	0.69	0.47-1.02
	Group 2 (2)	237	63.37	137	36.63	374	0.71	0.51-0.98	0.67	0.45-0.99
	Group 3 (>2) ub=7	146	55.09	119	44.91	265	ref		ref	
	Group 4 (unknown)	427	52.98	379	47.02	806	1.09	0.82-1.44	0.71	0.48-1.04

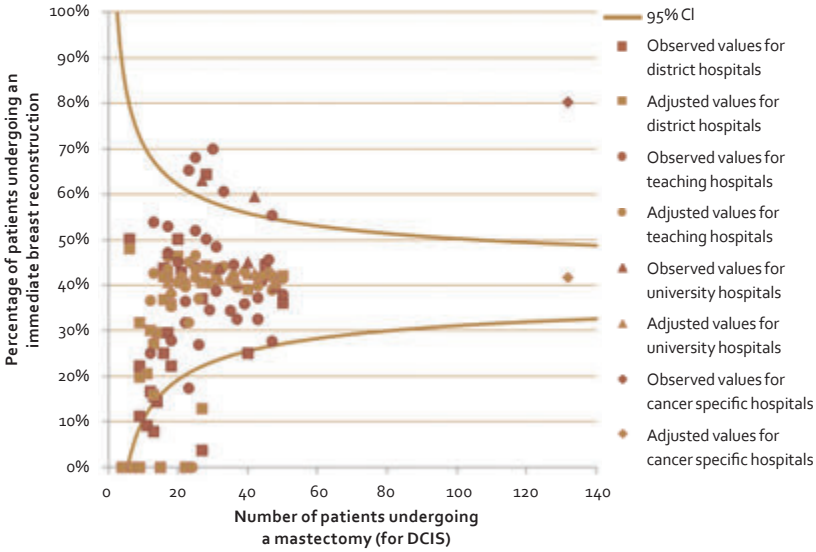
Table 2. Univariable and multivariable analyses of hospital organization factors affecting the use of immediate breast reconstruction after mastectomy for 1,980 patients with ductal carcinoma in situ. (continued)

		Immediate breast reconstruction (DCIS) (n=1,980)								
							Univariable		Multivariable*	
		No	%	Yes	%	Total	OR	95% CI	OR	95% CI
# of plastic surgeons / 100 diagnoses	Group 1 (0/0,5)	33	76.74	10	23.26	43	ref		ref	
	Group 2 (0,5/2,5)	1,021	59.60	692	40.40	1,713	2.24	1.10-4.57	1.56	0.70-3.47
	Group 3 (>2,5) ub=23	108	50.23	107	49.77	215	3.27	1.53-6.97	3.26	1.11-9.59
	Group 4 (unknown)	9	100.00	0	0.00	9	omitted		omitted	
# of breast-surgeons / 100 diagnoses	Group 1 (0/1,5)	532	57.08	400	42.92	932	ref			
	Group 2 (1,5/2,5)	552	60.79	356	39.21	908	0.86	0.71-1.03		
	Group 3 (>2,5) ub=17	87	62.14	53	37.86	140	0.81	0.56-1.17		
Attendance plastic surgeon in weekly MDT	Never or incidental	209	71.09	85	28.91	294	ref		ref	
	Yes, structural	798	57.78	583	42.22	1,381	1.80	1.37-2.36	1.52	1.10-2.10
	Unknown	164	53.77	141	46.23	305	2.11	1.51-2.96	2.15	1.39-3.34
Radiation therapy	No	1,152	59.20	794	40.80	1,946	Ref			
	Yes	19	55.88	15	44.12	34	1.15	0.58-2.27		

CI, Confidence interval; OR, Odds Ratio; Ub, upper boundary; MDT, multidisciplinary team meetings.
* Corrected for age, grade, social economic state, hospital type, hospital volume, % referrals for mastectomy, number of weekly MDT, number of plastic surgeons and attendance of plastic surgeon at weekly MDT.

In **Figure 1**, the variation between hospitals in the use of IBR after mastectomy for DCIS in the Netherlands is demonstrated. Case-mix adjustments for patient and tumor factors significantly affecting the use of IBR were performed. Also, adjustments for hospital organizational factors were performed, due to the characteristics of a multilevel analysis. Adjusted data demonstrated a decrease in hospital variation in the use of IBR from 0–80% to 0–49%.

Figure 1. Funnel plot demonstrating the variation in the use of immediate breast reconstruction for ductal carcinoma in situ between hospitals in the Netherlands with and without case-mix correction for patient and tumor factors, combined with multilevel analyses to adjust for hospital factors.



In the adjusted data; Case-mix correction for age, grade and social economic state combined with mutilevel analysis to correct for hospital organizational factors.

Invasive breast cancer

The hospital organizational factors (hospital type, hospital volume, percentage of mastectomies, number of weekly MDT meetings, number of plastic surgeons per 100 new diagnoses, number of breast surgeons per 100 new diagnoses and the attendance of a plastic surgeon at weekly MDT meeting) demonstrated to significantly affect IBR rates in univariable analyses and were included in the multivariable model (**Table 3**).

Table 3. Univariable and multivariable analyses of hospital organization factors affecting the use of immediate breast reconstruction after mastectomy for 14,491 patients with invasive breast cancer.

		Immediate breast reconstruction (invasive breast cancer) (n=14,491)								
							Univariable		Multivariable*	
		No	%	Yes	%	Total	OR	95% CI	OR	95% CI
Hospital type	District hospital	3,582	88.58	462	11.42	4,044	ref		ref	
	Teaching hospital	7,232	83.86	1,392	16.14	8,624	1.49	1.33-1.67	0.97	0.83-1.14
	University hospital	1,042	80.22	257	19.78	1,299	1.91	1.62-2.26	0.65	0.45-0.95
	Cancer specific hospital	200	38.17	324	61.83	524	12.56	10.27-15.36	13.39	9.76-18.38
Volume (# diagnosis annually)	Group 1 (1/150)	2,579	88.32	341	11.68	2,920	ref		ref	
	Group 2 (150/300)	6,596	82.21	1,427	17.79	8,023	1.64	1.44-1.86	1.20	0.97-1.48
	Group 3 (>300) ub=436	2,881	81.20	667	18.80	3,548	1.75	1.52-2.02	1.29	1.00-1.65
% mastectomies (of all surgical excisions)	Group 1 (0/30)	537	87.75	75	12.25	612	ref		ref	
	Group 2 (30/50))	7,861	82.70	1,644	17.30	9,505	1.50	1.17-1.92	1.15	0.87-1.54
	Group 3 (50/90)	3,658	83.63	716	16.37	4,374	1.40	1.09-1.81	1.50	1.11-2.02
# of weekly MDT	Group 1 (1)	3,550	84.24	664	15.76	4,214	0.65	0.57-0.74	0.74	0.61-0.89
	Group 2 (2)	2,340	87.94	321	12.06	2,661	0.48	0.41-0.56	0.66	0.54-0.82
	Group 3 (>2) ub=7	1,722	77.67	495	22.33	2,217	ref		ref	
	Group 4 (unknown)	4,444	82.31	955	17.69	5,399	0.75	0.66-0.84	0.48	0.39-0.59

Table 3. Univariable and multivariable analyses of hospital organization factors affecting the use of immediate breast reconstruction after mastectomy for 14,491 patients with invasive breast cancer. (continued)

		Immediate breast reconstruction (invasive breast cancer) (n=14,491)								
							Univariable		Multivariable*	
		No	%	Yes	%	Total	OR	95% CI	OR	95% CI
# of plastic surgeons / 100 diagnoses	Group 1 (0/0,5)	441	97.35	12	2.65	453	ref		ref	
	Group 2 (0,5/2,5)	10,606	82.92	2,185	17.08	12,791	7.57	4.26-13.46	5.55	3.04-10.11
	Group 3 (>2,5) ub=23	898	79.05	238	20.95	1,136	9.74	5.39-17.59	12.33	6.03-25.21
	Group 4 (unknown)	111	100.00	0	0	111	omitted		omitted	
# of breast-surgeons / 100 diagnoses	Group 1 (0/1,5)	5,793	80.67	1,388	19.33	7,181	ref			
	Group 2 (1,5/2,5)	5,394	85.35	926	14.65	6,320	0.72	0.65-0.78	0.76	0.65-0.88
	Group 3 (>2,5) ub=17	869	87.78	121	12.22	990	0.58	0.48-0.71	0.64	0.47-0.87
Attendance plastic surgeon in weekly MDT	Never or incidental	2,227	92.64	177	7.36	2,404	ref			
	Yes, structural	8,144	80.28	2,001	19.72	10,145	3.09	2.63-3.63	2.91	2.39-3.54
	Unknown	1,685	86.77	257	13.23	1,942	1.92	1.57-2.35	2.49	1.91-3.24
Radiation therapy	No	8,162	79.96	2,046	20.04	10,208	Ref			
	Yes	3,894	90.92	389	9.08	4,283	0.40	0.36-0.45	0.45	0.39-0.53

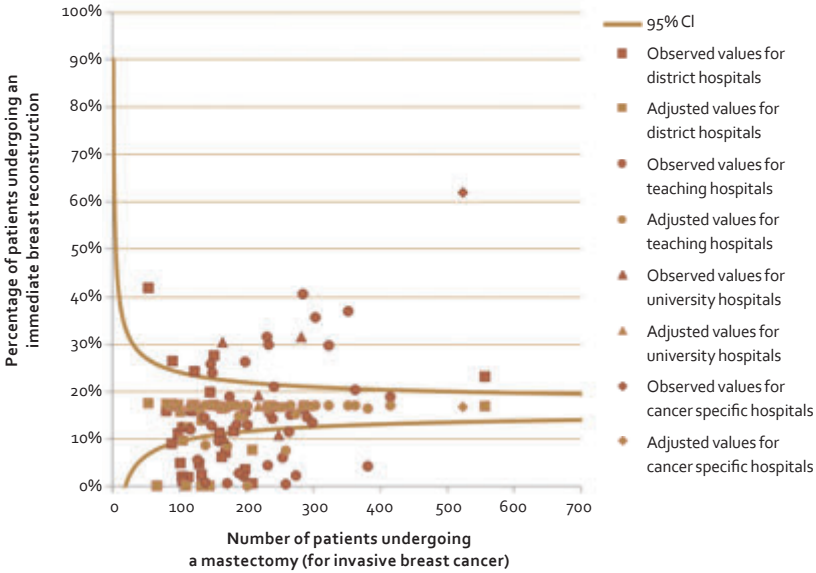
CI, Confidence interval; OR, Odds Ratio; Ub, upper boundary; MDT, multidisciplinary team meetings.
* Corrected for age, tumor type, clinical tumor stage, clinical lymph node stage, grade, multifocality, social economic state, hospital type, hospital volume % mastectomies (of all surgical excisions), % referrals for mastectomy, number of plastic surgeons, # of breast-surgeons / 100 diagnoses, attendance of plastic surgeon at weekly MDT and radiation therapy.

Because patient (age, SES) and tumor factors (tumor and nodal stage, multifocality, grade) significantly affected IBR rates (data not shown)[10], these factors were included in the multivariable model to correct for confounding (**Table 3**). The multivariable model demonstrated that patients who underwent a mastectomy at a cancer specific hospital had a higher chance of receiving IBR (OR=13.39, 95%CI: 9.76–18.38) compared to patients who received a mastectomy at a district hospital. As for DCIS, invasive breast cancer patients who were treated at a teaching hospital did not have a significantly higher chance of receiving IBR (OR=0.97, 95%CI: 0.83–1.14) compared to patients treated at a district hospital. University hospitals demonstrated to perform significantly less IBR compared to district hospitals (OR=0.65, 95% CI: 0.45–0.95).

Also, the number of weekly MDT meetings positively affected the rate of IBR. Hospitals having one or two MDT meetings per week (OR=0.74, 95%CI: 0.61–0.89 and OR=0.66, 95%CI: 0.54–0.82, respectively) performed significantly less IBR compared to hospitals that organized more than two MDT meetings per week. The percentage of patients receiving IBR increased with an increasing number of plastic surgeons practicing in that specific hospital. Hospitals with 0.5–2.5 plastic surgeons per 100 new diagnoses of breast cancer performed 5-fold more IBR (OR=5.55, 95%CI: 3.04–10.11) and hospitals with more than 2.5 plastic surgeons performed almost twelve-fold more IBR (OR=12.33, 95%CI: 6.03–25.21) compared to hospitals with less than 0.5 plastic surgeons per 100 diagnoses of breast cancer. The number of breast surgeons did not affect IBR rates. The structural attendance of a plastic surgeon at the weekly MDT meeting was strongly associated with performing more IBR compared to MDT meetings with no or incidental plastic surgeon attendance (OR=2.91 95%CI: 2.39–3.54).

In **Figure 2**, the variation between hospitals in the use of IBR after mastectomy for invasive breast cancer in the Netherlands is demonstrated. Case-mix adjustments for patient and tumor factors, significantly affecting the use of IBR were performed. Adjustments for hospital organizational factors were performed, due to the characteristics of a multilevel analysis. Adjusted data demonstrated a decrease in hospital variation in the use of IBR from 0–62% to 0–18%.

Figure 2. Funnel plot demonstrating the variation in the use of immediate breast reconstruction for invasive breast cancer between hospitals in the Netherlands with and without case-mix correction for patient and tumor factors, combined with multilevel analyses to adjust for hospital factors.



In the adjusted data; Case-mix correction performed for age, tumor type, clinical tumor stage, clinical lymph node stage, grade, multifocality and social economic state combind with multilevel analysis to correct for hospital organizational factors

DISCUSSION

It is known that various patient and tumor characteristics significantly affect IBR rates.[10] However, these characteristics were not fully responsible for the observed large hospital variation in the use of IBR following mastectomy in the current cohort.[10] Like other studies, we were able to show that hospital organizational factors such as hospital type, patient volume or presence and availability of a plastic surgery facility may additionally explain part of the hospital variation.[8–12] In previous research, Jagsi et al., demonstrated the influence of radiation therapy on the chance of receiving a reconstruction.[16] Although the focus of the current study was hospital characteristic, we performed an analysis to determine the possible influence of radiation therapy. This revealed similar results as demonstrated

by Jagsi et al. Moreover, radiation therapy does not influence the effects of the hospital organizational factors in multivariable analysis.

The current population-based study shows that multiple hospital organizational factors affect the use of IBR after mastectomy for DCIS and breast cancer in the Netherlands. Hospital type (cancer specific center), the number of plastic surgeons and the structural attendance of a plastic surgeon at the MDT meeting increased IBR rates significantly for both DCIS and non-metastatic invasive breast cancer. For invasive breast cancer, also the percentage of mastectomies related to all surgical excisions (>50%), >2 weekly MDTs and number of plastic surgeons available at the institution (>0.5 per 100 new diagnoses) significantly increased IBR rates. Therefore, the use of IBR in breast cancer patients could be improved by optimization of these hospital organizational factors. Although the aim of the present study was not to stimulate performing more IBR in clinical practice, we feel that the availability of IBR for eligible patients should be more or less comparable between hospitals and unrelated to hospital organizational factors. However, hospital variation could only be partially explained by hospital organizational factors in the present study.

A large variation was found in the use of IBR for DCIS or invasive breast cancer between hospitals that were included in the current study. The large variation is comparable with other studies; IBR was performed in 21% of the mastectomy patients in the United Kingdom and 24% in the United States.[2,11] Our data demonstrated that some hospitals tended not to perform IBR, however, the referral rates for IBR revealed that there were collaborations between hospitals. Therefore, it is possible that hospitals referred their patients to other hospitals in case IBR was preferred. Like others, we demonstrated that collaboration between hospitals does not significantly affect IBR rates in the hospital of referral. An English national study also reported similar hospital variation in performing IBR after statistically correcting for hospital collaborations.[2]

Different hospital organizational factors were investigated and appeared to be related to the use of IBR in the present study. For example, hospital type (cancer specific hospital) significantly affected IBR rates. Other nationwide studies also demonstrated the relationship between hospital type and IBR rates.[11,17] Alderman

et al. demonstrated that IBR rates were most probably higher in specialized cancer centers, because of high referrals to plastic surgeons.[19] Others revealed that high volume clinical breast hospitals extensively collaborate with plastic surgery departments, which could result in higher IBR rates.[13,19] We were not able to demonstrate a significant association between a higher volume hospital (>150 diagnoses) and higher IBR rates for invasive breast cancer.

In our study a higher number of plastic surgeons working in a hospital positively affected IBR rates. However, the number of breast surgeons working in a hospital did not. Breast surgeons in the Netherlands differ from the breast surgeons in other countries, since Dutch oncologic breast surgeons only perform breast ablative surgery or breast conserving surgery and do not carry out breast reconstructions, which is exclusively performed by plastic surgeons. In addition, the presence of a plastic surgeon at the MDT meeting positively affected the use of IBR. Alderman et al. demonstrated that a large proportion of surgeons did not refer breast cancer patients to a plastic surgeon at the time of surgical decision-making.[19] This implicates the relevance of the attendance of a plastic surgeon at the weekly MDT meeting to timely discuss the possibility of IBR. However, in Dutch clinical practice, it is quite common for patients to visit the plastic surgeon before surgery. Interestingly, Alderman et al. also concluded that surgeons who have a high referral propensity are more likely to be women.[19] Unfortunately we did not have information on gender of the (plastic) surgeon.

Limitations

In total, 72 of the 92 of the Dutch hospitals (78.3%) participated in this study, despite repeated invitations to the non-responding hospitals. However, the included hospitals are a good reflection of all Dutch hospitals, since representative proportions of hospital type and hospital volume were included. Although we were able to demonstrate a significant effect of hospital type on IBR rates, it is important to realize that even within three out of four hospital categories variation in performing IBR existed.

DCIS and invasive breast cancer were analyzed separately, to make testing for confounding (tumor factors such as tumor and nodal stage) possible. However,

due to low numbers of DCIS patients we were not able to demonstrate the same significant effect of hospital organizational factors on IBR rates as for invasive breast cancer.

To investigate the effect of hospital factors explaining variation in performing IBR, a multilevel analysis was performed to obtain the adjusted data for the funnel plot. The demonstrated reduction in variation after case-mix correction for patient and tumor factors was mainly caused by hospital factors. Other undefined hospital related factors could have contributed to this reduction, such as surgeons' attitude towards IBR, gender of the (plastic) surgeon, geographical location, waiting times for plastic surgery, patient preferences and loss of control of patient's management.[11,15] Jeevan et al. demonstrated that 50% of the patients were very satisfied with the options they received about breast reconstruction but preferred no IBR.[2] Further research should identify patient preferences and surgeon's attitudes towards IBR and whether or not these factors can explain the variation in performing IBR completely; such studies are on its way.

CONCLUSION

Large hospital variation in IBR rates was observed between hospitals in the Netherlands. The current study demonstrated that the observed variation in performing IBR was significantly affected by hospital type, but also by organizational factors that could be subject for change and improvement. Although hospital variation could only be partially explained by these factors, optimization of these factors could lead to an increased use of IBR in breast cancer patients and less variation in IBR rates between hospitals.

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CHAPTER 6

Discrepancies between surgical oncologists and plastic surgeons in patient information provision and personal opinions towards immediate breast reconstruction

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ABSTRACT

Background: Immediate breast reconstruction (IBR) may improve quality of life of patients receiving mastectomy. However, a significant hospital variation exists in the use of IBR due to various reasons. To better understand this variation, the present study investigated preoperative information provision to patients and personal opinions of surgical oncologists and plastic surgeons towards potential contra-indications for IBR.

Methods: An online survey (35 questions) was developed including questions on respondent demographics, information provision to the patient about IBR and potential contra-indications by IBR technique.

Results: One-hundred-eighty-nine physicians participated: 118 surgical oncologists and 71 plastic surgeons. All clinicians discussed the possibility of IBR with their patients. Complications (79% versus 100%, P<0.001) and esthetic outcomes (83% versus 99%, P = 0.001) were discussed less frequently by surgical oncologists than by plastic surgeons. Patient age >75 years, breast size >D-cup, BMI >40 kg/m^2, smoking (for implant reconstruction), pulmonary/cardiac comorbidities (for autologous reconstruction) and radiotherapy were considered a contra-indication more frequently by plastic surgeons. In contrast, surgical oncologists reported tumor stage (≥cT3), nodal stage (≥cN2) and chemotherapy more frequently to be a contra-indication for IBR.

Conclusion: We observed that all respondents discussed the possibility of IBR with their patients, whereas patient-tailored information was given more frequently by plastic surgeons. Physicians differed in their opinions towards contra-indications for IBR, with plastic surgeons reporting patient-related risk factors for wound healing problems and surgical oncologists reporting oncological contra-indications more frequently. Consensus between physicians regarding contra-indications for IBR may optimize patient counseling and shared decision-making.

INTRODUCTION

In the Netherlands, about 15,000 new breast cancer patients are diagnosed annually, which makes it the most frequently diagnosed cancer in women.[1] About 40% of all surgically treated patients receive a mastectomy.[2] According to current guidelines, immediate breast reconstruction (IBR) has to be considered in every patient who is planned for mastectomy.[3,4] IBR does not compromise the oncological outcomes,[5] while resulting in improved quality of life with better psychological and functional wellbeing in the majority of patients.[6–9]

In general, breast reconstruction can be performed with an implant, autologous tissue or using a combination of both. However, implant reconstructions are performed most frequently.[10–13] These different techniques vary in complexity and operation time, complication rates, recovery period and esthetic outcomes, making not every technique suitable for every patient, depending on comorbidities, local anatomy and previous surgery or other treatment, and patient preferences.[14–16]

The NABON Breast Cancer Audit (NBCA) is a nationwide multidisciplinary audit measuring quality of breast cancer care in the Netherlands.[17] Current data show that the mean percentage of patients undergoing IBR in the Netherlands is rather low given every patient planned for mastectomy should be considered for IBR; 17% for invasive breast cancer and 43% for ductal carcinoma in situ (DCIS).[2,17] Immediate implant based reconstructions were performed most frequently (89%). Autologous or a combination of autologous and implant reconstructions were both used in less than 5% of the patients who underwent IBR for invasive breast cancer.[11] Moreover, large variation in the use of IBR between hospitals in the Netherlands was previously shown by our group; 0–64% and 0–83% for invasive breast cancer and DCIS, respectively.[11] Numerous factors are considered contra-indications for the use of IBR which may affect its current use. Patient characteristics such as older age, high Body Mass Index (BMI), smoking status, comorbidities have been reported to affect the probability to receive IBR.[18,19] In addition, tumor factors as histology, larger tumor size and lymph node involvement also have an impact on whether or not IBR is performed as well as the need for adjuvant treatments.[6,18,20–22] Furthermore,

differences in care processes between hospitals or physician preferences have been suggested to have a relationship with the use of IBR.[18,23,24]

In the Netherlands, every patient diagnosed with breast cancer is discussed in a multi-disciplinary team prior to treatment. The final decision to perform IBR is predominantly made by surgical oncologists and plastic surgeons together with the patient. The surgical oncologist performs the mastectomy (i.e., oncological resection) and the plastic surgeon performs the breast reconstruction thereafter. Physicians' personal attitudes and the weighing of possible contra-indications may affect this decision-making process. Moreover, the preoperative information given to patients may affect patient preferences.

To better understand the existing large variation in the use of IBR and to ultimately improve breast cancer care, it is important to learn about the various attitudes of physicians in the decision-making process of offering patients IBR. Therefore, the aim of the current study was to investigate the practice of preoperative information provision to patients by surgical oncologists and plastic surgeons and their personal opinion towards potential contra-indications for different types of IBR in patients with breast cancer requiring mastectomy.

MATERIALS AND METHODS

Respondents

Surgical oncologists and plastic surgeons with special interest in breast cancer care were identified through clinical networks of the Netherlands Comprehensive Cancer Organization (IKNL) and were invited to participate in a self-administered survey. The responses were collected over an 8-month period from July 2014 to February 2015. To maximize response rates, five reminders were sent approximately after 1.5 months, 3 months, 5 months, 7 months and 7.5 months.

Questionnaire

The survey consisted of 35 questions divided in three sections. First, the respondents' demographic information was asked. In the second section the provision of preoperative information to patients about IBR or delayed reconstruction, possible complications, expected esthetic outcomes and reconstructive techniques was investigated. Finally, respondents were asked about their personal opinion towards contra-indications such as patient characteristics, tumor characteristics and neo-adjuvant or adjuvant treatments. If one responded positively on a specific contra-indication, a drop-down menu opened asking for which specific reconstruction technique and for which sub-group of patients the contra-indication was applicable (for example, age below 35, age 35–55, age 56–75, age >75). Contra-indications were chosen based on evidence in current literature and expert-based opinions. We decided not to include delayed breast reconstruction in the questionnaire, as we believe that treatment approaches and the patient population may be different compared to patients receiving IBR. Members of the scientific committee of the NBCA reviewed and piloted the survey. The survey was administered anonymously with the use of SurveyMonkey, an online secure web-based database.[25] None of the respondents received an offer for an incentive for completion of the survey.

Statistical analysis

Demographic characteristics of the respondents were analyzed for surgical oncologists and plastic surgical oncologists separately. Next, the information provided to patients by surgical oncologists and plastic surgeons was evaluated. Reconstructive techniques were divided into three categories: implant reconstruction, autologous reconstruction, or combination of both implant and autologous reconstruction. The opinions about potential contra-indications per reconstructive technique reported by the respondents were categorized and results of surgical oncologists and plastic surgeons were compared. All statistical analyses were performed using SPSS 20.0 (IBM-SPSS, Inc., Chicago, IL).

RESULTS

Respondents

In total, 41% (193/466) physicians responded. Four of the 193 surveys (2%) were excluded from analyses due to data incompleteness resulting in 118 surgical oncologists and 71 plastic surgeons participating, representing 82 of the 89 hospitals in the Netherlands. Plastic surgeons were significantly younger and on average had less working experience (**Table 1**).

Table 1. Demographic characteristics of respondents (118 surgical oncologists and 71 plastic surgeons) on questionnaire regarding breast cancer management process.

		Surgical oncologist		Plastic surgeon		Total	
		n=118	%	n=71	%	n=189	%
Gender	Male	59	50%	42	59%	101	53%
	Female	59	50%	29	41%	88	47%
Age, mean in years (range)		48 (35-65)		45 (30-64)		48 (30-65)	
Working experience, mean in years (range)*		13 (2-33)		10 (1-26)		12 (1-33)	
Type of hospital**	District hospital	42	36%	11	15%	53	28%
	Teaching hospital	63	53%	48	68%	111	59%
	University hospital	12	10%	12	17%	24	13%
Breast cancer patients treated per year	0 - 50	20	17%	47	66%	67	35%
	51 - 100	61	52%	19	27%	80	42%
	101 - 150	25	21%	3	4%	28	15%
	>150	12	10%	2	3%	14	7%

* Excluding time as registrar.
** One respondent left the question unanswered.

Preoperative Information Provision

All surgical oncologists discussed the possibility of IBR and delayed reconstruction with patients undergoing a mastectomy. Surgical oncologists significantly less frequently discussed complications (79% versus 100%, P<0.001) and esthetic outcomes (83% versus 99%, P=0.001) compared to plastic surgeons. Information provision to patients regarding the difference between IBR and delayed

reconstruction did not differ significantly between surgical oncologists and plastic surgeons (97% versus 99%, respectively, P=0.594). This was also true regarding advantages and disadvantages of the timing of reconstruction (97% versus 99%, respectively, P=0.589), and consequences of other therapies such as adjuvant therapy (84% versus 91%, respectively, P=0.130). Forty-eight percent of the surgical oncologists discussed all reconstructive techniques with their patients, versus 85% of the plastic surgeons (P<0.001). The remaining surgical oncologists (52%) tended to discuss only techniques offered at their own institution (29%) or reconstructive techniques that they regarded relevant to the specific patient (23%).

Patient related contra-indications

Table 2 provides a general overview of factors considered a contra-indication by surgical oncologists and plastic surgeons. Age was not considered a contra-indication for any of the IBR types except age >75 years. Specifically for autologous reconstructions, a considerable percentage of the plastic surgeons (38%) reported age >75 years as contra-indication compared to 19% of the surgical oncologists. For implant reconstructions, older age was less frequently considered a contra-indication by both surgical oncologists (9%) and plastic surgeons (15%) when compared to autologous reconstructions. Smoking was a contra-indication for IBR for surgical oncologists in 60%, 56% and 41% for autologous, combination autologous-implant and implant reconstructions, respectively. These figures were 48%, 45% and 47%, respectively, for plastic surgeons. About 14–17% of the plastic surgeons, depending of the reconstruction technique, reported large breast size (>D-cup) to be a contra-indication compared to 7–8% of the surgical oncologists. No significant differences between reconstruction techniques were found. Approximately 65% of the plastic surgeons and 40% of the surgical oncologists found BMI >40 kg/m^2 a contra-indication for IBR. A BMI <18.5 kg/m^2 was reported as contra-indication by approximately 13–18% of the plastic surgeons compared to approximately 3% of the surgical oncologists.

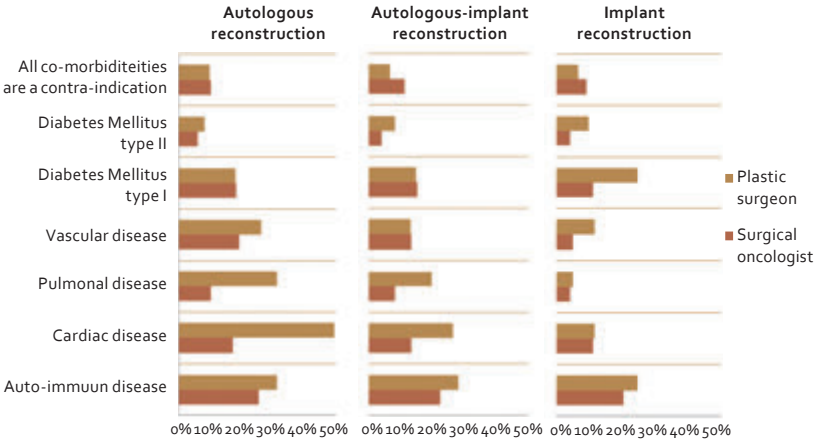
Table 2. Factors affecting the indication for immediate breast reconstruction reported by 189 surgical oncologists (n=118) and plastic surgeons (n=71) involved in breast cancer care.

		Surgical oncologist		Plastic surgeon		Total		
Contra-indication		**n=118**	**%**	**n=71**	**%**	**n=189**	**%**	**P-value***
Age	Yes	24	24%	26	43%	50	31%	0.015
	No	75	76%	35	57%	110	69%	
	Missing	19		10		29		
Smoking	Yes	67	66%	36	58%	103	63%	0.327
	No	35	34%	26	42%	61	37%	
	Missing	16		9		25		
Breast size	Yes	19	19%	26	43%	45	28%	0.001
	No	83	81%	35	57%	118	72%	
	Missing	16		10		26		
Body Mass Index	Yes	63	63%	52	85%	115	71%	0.002
	No	37	37%	9	15%	46	29%	
	Missing	18		10		28		
Co-morbidities	Yes	70	71%	53	87%	123	77%	0.024
	No	28	29%	8	13%	36	23%	
	Missing	20		10		30		
Tumor stage	Yes	65	59%	29	45%	94	54%	0.064
	No	45	41%	36	55%	81	46%	
	Missing	8		6		14		
Nodal stage	Yes	44	75%	18	67%	62	72%	0.448
	No	15	25%	9	33%	24	28%	
	Missing	59		44		103		
Neo-adjuvant or adjuvant treatment	Yes	21	20%	26	42%	47	28%	0.003
	No	82	80%	36	58%	118	72%	
	Missing	15		9		24		

* Using Chi-square tests to calculate differences between surgical oncologists and plastic surgeons.

About 10% of the respondents reported that comorbidities in general should be regarded as a contra-indication for IBR, irrespective of reconstructive technique. Overall, auto-immune diseases were considered to be a contra-indication by both surgical oncologists and plastic surgeons. The most striking differences between surgical oncologists and plastic surgeons were found for autologous reconstructions. Forty-nine percent of the plastic surgeons compared to 17% of the surgical oncologists mentioned cardiac comorbidities as contra-indication for autologous reconstructions. For pulmonary comorbidities this was the case in 31% of the plastic surgeons versus 10% of the surgical oncologists (**Figure 1**).

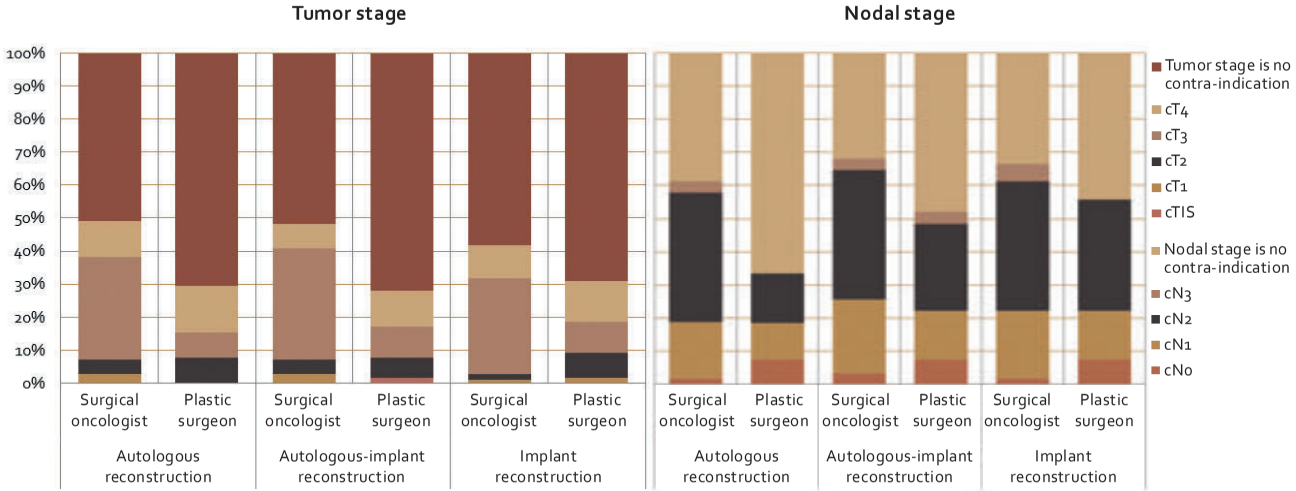
Figure 1. Comorbidities indicated as contra-indication per reconstructive technique, separated for surgical oncologists and plastic surgeons.



Oncological related contra-indications

In general, surgical oncologists reported tumor T-stage and nodal N-stage more frequently as a contra-indication for IBR compared to plastic surgeons. Surgical oncologists reported tumors clinical T_3 or larger for all three reconstruction techniques as a contra-indication (around 30%). Plastic surgeons had less agreement on T-stage; cT_4 was reported as contra-indication for all reconstruction techniques in 12%, and also T-stages T_2 and T_3 were reported by 8% of the plastic surgeons, see **Figure 2**.

Figure 2. Tumor T-stage and Nodal N-stage reported by clinicians as contra-indication, separated per reconstructive technique.



For the three reconstruction types, 39% of the surgical oncologists reported lymph node involvement ≥cN2 to be a contra-indication. Plastic surgeons showed a similar response for implant reconstructions (34%), although lower percentages were found for autologous and autologous-implant reconstructions (**Figure 2**).

Overall, surgical oncologists differed in their perspective of adjuvant treatments as contra-indication compared to plastic surgeons (**Table 3**). No difference between surgical oncologists and plastic surgeons was found for radiotherapy as contra-indication for immediate autologous reconstruction. However, in case of reconstruction using implants (either autologous-implant or implant reconstruction) radiotherapy was less often reported as contra-indication by surgical oncologists compared to plastic surgeons (**Table 3**).

Chemotherapy, neo-adjuvant and specifically adjuvant chemotherapy were more often considered to be a contra-indication for IBR by surgical oncologists compared to plastic surgeons. Adjuvant hormonal therapy was hardly reported as a contra-indication for IBR by any of the clinicians (≤2%, **Table 3**).

Table 3. Various treatments reported by clinicians as contra-indication, separated per reconstructive technique.

	Autologous reconstruction		Autologous-implant reconstruction		Implant reconstruction	
	Surgical oncologist	Plastic surgeon	Surgical oncologist	Plastic surgeon	Surgical oncologist	Plastic surgeon
Neo-adjuvant therapies are no contra-indication	7%	15%	7%	8%	6%	2%
Neo-adjuvant chemotherapy	4%	6%	4%	2%	4%	0%
Adjuvant therapies are no contra-indication	0%	8%	0%	3%	0%	2%
Adjuvant chemotherapy	7%	3%	7%	2%	5%	2%
Adjuvant hormonal therapy	1%	2%	1%	0%	1%	0%
Adjuvant radiotherapy	11%	10%	13%	23%	15%	36%

DISCUSSION

Hospital variation in IBR after mastectomy can partially be explained by variation in patient and tumor characteristics (i.e., case-mix factors) that cannot be altered.[11] In addition, differences in patient preferences may also be a cause of variation.[6,26] However, variation in IBR due to hospital organizational factors[18,24] or personal opinions towards IBR of individual physicians is undesirable.[26]

As found in the present study, surgical oncologists and plastic surgeons differ in their information provision to patients about IBR. More importantly, personal opinions towards IBR differ between surgical oncologists and plastic surgeons as well. Surgical oncologists more frequently reported cancer related factors to be a contra-indication for IBR compared to plastic surgeons, whereas the latter mentioned factors affecting complications or reconstruction failure more frequently.

Preoperative information provision

The Dutch, evidence-based NABON breast cancer treatment guideline recommends that every patient undergoing mastectomy should be considered for IBR.[3] Interestingly, in the present study all surgical oncologists discussed the possibility of IBR with their patients, while other studies reported lower rates of information provision about IBR, ranging from 23% in Japan[27] to 74% in the United States.[28] It seems justified that surgical oncologists inform patients about the existence and possibility of IBR and delayed reconstruction, while details about the reconstructive procedures, shared decision-making and patient expectations are managed by plastic surgeons, indicating that patients need to be referred to a plastic surgeon for complete and correct information on IBR.

Patient related contra-indications

Surgical oncologists in another study considered age (37%) as a factor affecting the decision to refer patients to the plastic surgeon for IBR.[28] Age has been described in literature as a factor significantly affecting the prevalence of IBR,[11,13–15,19,26] but also as a risk factor (age >55 years) for implant loss after IBR.[29] In the current study, we found that age was not considered as a major contra-indication by both professions,

except for patients aged over 75 years, which was more frequently reported by plastic surgeons compared to surgical oncologists. A possible explanation for this finding may be the assumption that older patients prefer not to undergo IBR. Another reason may be that older patients generally have more comorbidities and are therefore less eligible for IBR, specifically for more complex autologous reconstructions with potentially higher risk of complications. Smoking was considered an important contra-indication for all types of breast reconstruction by all physicians due to associated complications. In case of autologous reconstruction smoking leads to an increased risk of fat necrosis and wound healing problems, also of the donorsite,[30] and in implant reconstruction an increased risk of implant loss due to wound healing problems and infections was found.[29,31] It is therefore recommended to stop smoking 4–6 weeks prior to surgery.[32]

As expected, morbid obesity affected the decision-making process for all reconstructive techniques.[18,19,26] It is well-known from plastic surgery literature that obesity leads to an increased risk of complications of the breast reconstruction itself,[29,31,33] and therefore it was not a surprise plastic surgeons more frequently regarded obesity as a contra-indication compared to surgical oncologists. Besides BMI, plastic surgeons tended to report large breast size (>cup D) more frequently as contra-indication compared to surgical oncologists. Larger breast volume is associated with an increased risk of complications as skin flap morbidity, implant loss and reoperations.[34–36]

Comorbidities have been frequently reported in literature as contra-indications for IBR.[18,19,30,31,37] Plastic surgeons specifically reported cardiac and pulmonary comorbidities as contra-indications for autologous reconstruction because of the lengthy operative procedure with prolonged general anesthesia time leading to an increased risk of postoperative medical complications in these patients. Previous cardiac surgery has been suggested to be a predictor of major surgical complications.[30]

Oncological related contra-indications

Consistent with previous literature,[18] advanced tumor stage (cT3) and tumor positive nodes (cN2) were important contra-indications according to both groups.

However, surgical oncologists reported tumor and nodal stage more frequently as contra-indication compared to plastic surgeons. Potential reason could be that in cT4 tumors the skin is involved and should be excised as well as the need for radiotherapy of the chest wall, as well as in patients diagnosed with a T3N2 tumor. A survey among breast surgical oncologists and plastic surgeons in the UK reported that 26% of the surgical oncologists would not offer IBR in patients with stage IV disease.[38] Reasons were related to poor prognosis (31%), concerns about temporary cessation of systemic treatments (21%) and recovery time (17%).[38]

In the present study, (neo)-adjuvant therapies were not considered major contra-indications while literature suggests that adjuvant therapies such as chemotherapy and radiotherapy may affect IBR rates significantly.[18,22] The question in our survey enquiring about neo-adjuvant and adjuvant therapies may have been phrased not clearly enough, with respondents assuming that only neo-adjuvant therapies were asked for. Surgical oncologists more often regarded adjuvant chemotherapy a contra-indication for IBR compared to plastic surgeons, presumably because of fear of delay in chemotherapy administration.[28] However, a recent systematic review showed no clinically relevant delay in chemotherapy administration if a patient has undergone IBR, irrespective of type of reconstruction.[39]

Of the respondents who reported (neo)-adjuvant therapies as contra-indication, radiotherapy was considered a contra-indication specifically for implant reconstructions. Use of radiotherapy leads to a significantly higher reconstruction failure rate compared to if no radiotherapy is given,[40] reason for plastic surgeons not to perform IBR.[41] Radiotherapy is less detrimental to autologous reconstructions[42] and it is therefore not surprising that in this situation it was considered a less important contra-indication for this type of reconstruction. Another study showed that 19% of surgical oncologists answered they did not refer patients to a plastic surgeon if adjuvant radiotherapy was indicated.[28]

Our study had respondents from nearly all hospitals in the Netherlands, resulting in a large and representative sample of clinicians. Respondent characteristics differed slightly between surgical oncologists and plastic surgeons and may have affected

their opinions on contra-indications. In addition, recall bias may have occurred since the information was based on self-reports. The result that 100% of the surgical oncologists reported to preoperatively discuss the possibility of IBR with their patients may possibly be an overestimation due to socially desirable answers. Other factors that in literature have been suggested to have a relationship with the use of IBR, like socio-economic status and ethnicity, were not investigated in our study. However, we expect that these factors did not have an impact on the considerations of Dutch clinicians to offer a patient IBR. In the Netherlands, all patients have a healthcare insurance plan and postmastectomy IBR is always fully reimbursed.

Lastly, referral patterns and collaboration between disciplines involved in breast cancer care all around the world may differ from the Netherlands. However, we feel our results may be representative for attitudes of clinicians in countries with similar constructions between surgical oncologists performing breast cancer surgery and plastic surgeons performing breast reconstruction. Therefore, this study may be a good starting point to exalt the differences found to inspire further research and enable the development of guidelines for discussion and decision-making relevant to potential candidates for IBR.

Our findings suggest there are multiple opinions on selecting patients for IBR. Information provision to patients and participation in decision-making should not vary considerably between hospitals or clinicians from different specializations and ideally should not affect IBR rates. Patient selection is crucial to achieve favorable esthetic outcomes with improved quality of life and minimal complication rates. For every individual patient a new trade-off should be made based on her patient and oncological tumor characteristics and preferences, with some contra-indications more relevant compared to others. This process could be facilitated by evidence-based guidelines, patient decision aid tools and establishment of multidisciplinary teams, ultimately leading to consistent information provision from every discipline involved and optimization of shared decision-making. An evidence-based, multi-disciplinary breast reconstruction guideline is publicly available in English since 2015 to guide the decision-making process and to provide the information needed, hopefully resulting in a reduction of variation in personal opinions of physicians towards IBR.[41]

CONCLUSIONS

Reasons whether or not to perform IBR are multifactorial, with patient and tumor factors as most examined causes. The results of the current study gained insight into personal opinions of surgical oncologists and plastic surgeons towards IBR. The final decision to offer postmastectomy IBR was affected by multiple factors weighed differently by surgical oncologists and plastic surgeons involved. Oncological characteristics (tumor size and nodal status) were reported more frequently as contra-indication by surgical oncologists, while plastic surgeons mentioned risk factors and wound-associated problems (age >75, smoking in implant reconstructions, large breast size, BMI and comorbidities) more frequently.

Reaching consensus between surgical oncologists and plastic surgeons regarding contra-indications for IBR helps improving patient counseling and optimizing shared decision-making.

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CHAPTER 7

The effect of being informed on receiving immediate breast reconstruction in breast cancer patients

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ABSTRACT

Introduction: In previous research from the NABON breast cancer audit, observed hospital variation in immediate breast reconstruction (IBR) rates in the Netherlands could not be fully explained by tumor, patient, and hospital factors. The process of information provision and decision-making may also contribute to the observed variation; the objective of the current study was to give insight in the underlying decision-making process for IBR and to determine the effect of being informed about IBR on receiving IBR.

Methods: A total of 502 patients with IBR and 716 without IBR treated at twenty-nine hospitals were invited to complete an online questionnaire on obtained information and decision-making regarding IBR. The effect of being informed about IBR on receiving IBR was determined by logistic regression analysis.

Results: Responses from five hundred and ten patients (n=229 IBR, n=281 without IBR) were analyzed. Patients with IBR compared to patients without reconstruction showed a difference in patient, tumor, treatment (including radiotherapy), and hospital characteristics. Patients with IBR were more often informed about IBR as a treatment option (99% vs 73%), they discussed (dis)advantages more often with their physician (86% vs 68%), and they were more often involved in shared decision-making (91% vs 67%) compared to patients without IBR. Multivariate logistic regression analysis, corrected for confounders, showed that being informed about IBR increased the odds for receiving IBR fourteen times ($p<0.001$).

Conclusions: The positive effect of being informed about IBR on receiving IBR stresses the importance of treatment information in the decision-making process for IBR.

INTRODUCTION

In 2014, about 14,500 women were diagnosed with invasive breast cancer and 2300 with ductal carcinoma in situ (DCIS) in the Netherlands.[1] Surgical procedures as mastectomy and breast conserving therapy combined with adjuvant radiotherapy have been shown to offer equivalent survival.[2,3] However, loss of one or both breasts mutilates the female appearance and consequently, mastectomy may negatively impact body image and sexuality, leading to feelings of anxiety and depression.[4,5] These effects may be minimized by restoring the contour of the breast with a breast reconstruction.[6–8] Breast reconstruction may be performed either directly after mastectomy in the same operation, which is known as immediate breast reconstruction (IBR), or in a separate operation, sometime after the mastectomy, which is called a delayed breast reconstruction (DBR).[9] IBR can be safely performed without affecting patient survival[10,11] or hampering detection of local recurrences.[10–12]

Although in the Netherlands the national guideline on breast cancer treatment recommends considering IBR for every patient needing mastectomy[3], the average IBR-rate of about 20% was rather low in 2014[13], albeit comparable to other countries.[14] In the NABON ("National Breast Cancer Consultation the Netherlands") Breast Cancer Audit (NBCA)[15] we previously demonstrated varying IBR-rates between Dutch hospitals from 0 to 83% (DCIS) and 0–64% (invasive breast cancer), which could not be fully explained by tumor, patient, and hospital factors.[13,16] However, it could well be that other reasons for this observed variation exist, such as preoperative information provision about IBR, shared decision-making (SDM), and patient or physician preferences.

Aside from the recommendation to consider IBR in every mastectomy patient, the guideline also recommends physicians to provide sufficient and timely information to patients.[3] In the Netherlands, IBR is performed by plastic surgeons; therefore, consultation between surgeon and plastic surgeon and referral of patients for a consultation with a plastic surgeon is recommended.[17] Although information facilitates SDM[18], current information provision about IBR may be insufficient.[19–21]

Considering the positive effects of both IBR and SDM (for instance about treatment decisions) on the quality of life[7,22–24], psychosocial functioning[25–28], and patient satisfaction[29-31] of mastectomy patients, breast reconstruction should ideally be performed whenever feasible[22] and more importantly, pre-operatively discussed with patients in a process of SDM. Therefore, the objective of the present study was to investigate the underlying decision-making processes patients experienced during the preoperative consultations for their breast cancer surgery with or without IBR in the Netherlands. The second aim was to determine the effect of being informed about IBR on actually receiving IBR.

METHODS

Study population

Twenty-nine hospitals (1/3rd of the total number of hospitals in the Netherlands) volunteered to participate in the study. These hospitals were general (n=15), teaching (n=10), academic hospitals (n=4, including a cancer-specific hospital), and all offered IBR in-house or referring to IBR-performing hospitals based on the national guideline as mentioned in the introduction. All patients that fit the inclusion criteria (female, aged 18 years, diagnosed with DCIS or invasive breast cancer, treated with mastectomy between January 2013 and October 2014, no distant metastases) were selected from the Netherlands Cancer Registry (NCR), a national registry in which all newly diagnosed cancer patients are registered annually. Based on our power calculation (**Supplementary Appendix 1**), fifty patients (25 with IBR and 25 without IBR) were randomly selected from every participating hospital by assigning them a random value between 0 and 1 and including those with the lowest values. In consultation with each hospital, we then excluded patients with recent recurrent disease (we did not want to bother patients currently receiving treatment) and patients who were unfit to fill in a questionnaire (due to psychological difficulties (dementia, depression) or language limitations). Since information about DBR is not collected in the NCR, we could not exclude patients with DBR on beforehand. The survey was hosted in PROFILES ("Patient-Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship"), an online secured environment which facilitates data collection on patient-reported

outcome measures (PROMs) from cancer survivors.[32] Paper questionnaires were provided on request. Invitations were sent out to selected patients from January 8th to May 29th, 2015; responses were collected until July 30th, 2015. Respondents gave consent for processing their completed questionnaires and to merge them with the clinical data available in the NCR and NBCA. According to the Central Committee on Research involving Human Subjects (CCMO), this type of study does not require approval from an ethics committee in the Netherlands. This study was approved by the Privacy Review Board of the NCR.

Questionnaire

The questionnaire was specifically developed for this study and included items on patient characteristics, general health, breast cancer treatment, and breast reconstruction (**Supplementary Appendix 2**). In addition, questions about SDM were categorized according to the definition of SDM: acknowledging a decision is required by knowing that IBR is an option, understanding and weighing all available information about the treatment options, and incorporating the patients' preferences in the final decision.[18] The questionnaire was tested for readability and comprehensibility by a panel of former breast cancer patients (members of the Dutch Breast Cancer Patient Association, "Borstkankervereniging Nederland") before deployment.

Analysis

Patients who reported they had had DBR were excluded. Statistical analyses were performed in three steps. First, characteristics of respondents with IBR versus without IBR were compared using Pearson Chi-square tests. Second, patient responses regarding information provision and decision-making items were described and compared using Chi-square tests. In the third step, a multivariate logistic regression analysis was performed to determine the effect of being informed about IBR on receiving IBR, controlled for patient, tumor, and treatment characteristics that appeared to have a statistically significant relation with IBR in univariate analyses (relaxed significance level $p<0.10$); the significance level within the multivariate analyses was $p<0.05$. The following variables were included in the univariate analysis: age, body mass index (BMI), number of comorbidities, highest

completed education, stage of disease (clinical), multifocality, unilateral or bilateral mastectomy, axillary dissection, neo-adjuvant chemotherapy, radiotherapy, and IBR hospital volume. Variables were selected based on our previous research[13,17] and literature on factors affecting the use of IBR.[32]
All statistical analyses were performed using STATA (STATA Version 14).[33]

RESULTS

Respondents

Five hundred and two patients with IBR and 716 without IBR received an invitation. Two hundred and fifty-three patients who had received IBR and 305 patients without IBR responded, giving a total of 558 responses (46%). Twenty-four patients were excluded due to incomplete questionnaires, leading to valid data from 534 patients (n=229 IBR, n=305 without IBR). Twenty-four patients who reported they had had DBR were excluded for the analyses, leaving 281 patients without IBR. No statistically significant differences between respondents and non-respondent groups were found in baseline characteristics (tumor morphology, year of surgery, IBR hospital volume) other than that respondents were younger than non-respondents ($p<0.001$). The respondent group consisted of relatively more patients who had received IBR compared to the non-respondent group ($p=0.027$; data not shown). Respondents with IBR compared to respondents without IBR significantly differed in patient (age, education, socioeconomic status, comorbidities, BMI), tumor (stage, grade, lymph node status, multifocality), and treatment characteristics (unilateral or bilateral (prophylactic) mastectomy, radiotherapy), as well as hospital factors (IBR hospital volume, hospital type; all p-values<0.05). Both groups were equally treated with chemo-therapy (46% vs 51%, $p=0.301$) and equally received neo-adjuvant treatment (11% vs 17%, borderline significance: $p=0.085$; **Table 1**).

The majority of patients with IBR either had received a tissue expander followed by a definite implant (55%) or a direct-to-implant (32%) reconstruction; other reconstruction types were latissimus dorsi flap (4%), DIEP flap (5%), or Superior Gluteal Artery Perforator (SGAP) flap (1%; 3% unknown; data not shown in **Table 1**).

Table 1. Patient, tumor, treatment, and hospital characteristics.

Item		IBR (n=229)	%	No IBR (n=281)	%	P-value*
Patient characteristics						
Age in years (at diagnosis)	<40	31	14%	9	3%	<0.001
	40-59	163	71%	118	42%	
	60+	35	15%	154	55%	
Highest completed education[a,b]	Secondary school intermediate level or less	60	26%	135	48%	<0.001
	Medium vocational training (MBO), secondary school high level	81	36%	77	28%	
	Higher vocational training (HBO)/ university	87	38%	68	24%	
Marital status[b]	Married/living together	180	79%	202	72%	0.082
	Divorced/partner deceased	49	21%	79	28%	
Socio-economic status (SES)[c]	Low	58	25%	105	37%	0.014
	Medium	93	41%	99	35%	
	High	77	34%	78	28%	
Comorbidities[b]	Yes	61	27%	102	36%	0.020
BMI[a,b,d]	Healthy weight (BMI<25)	153	67%	123	44%	<0.001
	Overweight (25<=BMI >30)	59	26%	100	36%	
	Obese (BMI>30)	15	7%	57	20%	
Smoking[b]	Yes	43	19%	42	15%	0.248
Tumor characteristics						
Stage (clinical)[b]	0	70	31%	62	22%	<0.001
	I	85	37%	61	22%	
	II	64	28%	118	42%	
	III	3	1%	28	10%	
Receptor status[a]	Triple negative	12	5%	21	7%	0.347
	Hormone-negative, Her2-positive	10	4%	20	7%	
	Hormone-positive, Her2-positive	120	52%	129	46%	
	Hormone-positive, Her2-negative	84	37%	104	37%	
	Unknown	3	1%	7	2%	
Grade[b]	Grade I	34	15%	32	11%	0.012
	Grade II	98	43%	129	46%	
	Grade III	83	36%	81	29%	
Lymph node status	No / unknown	171	75%	163	58%	<0.001
	>No	58	25%	118	42%	
Multifocality	Yes	78	34%	63	22%	0.010

Table 1. Patient, tumor, treatment, and hospital characteristics. (continued)

Item		IBR (n=229)	%	No IBR (n=281)	%	P-value*
Treatment characteristics						
Mastectomy[b]	Bilateral therapeutic mastectomy	14	6%	14	5%	<0.001
	Therapeutic and contralateral prophylactic mastectomy	41	18%	11	4%	
	Unilateral therapeutic mastectomy	174	76%	256	91%	
Radiotherapy	Yes	39	17%	95	34%	<0.001
Hormone therapy	Yes	106	46%	149	53%	0.130
Chemotherapy	Yes	106	46%	143	51%	0.301
Neo-adjuvant chemotherapy	Yes	26	11%	47	17%	0.085
Hospital characteristics						
IBR hospital volume[e]	Low	22	10%	51	18%	0.001
	Medium	70	31%	106	38%	
	High	137	60%	124	44%	
Breast cancer surgery hospital volume[f]	Low	74	32%	114	40%	0.125
	Medium	88	38%	101	36%	
	High	67	30%	66	24%	
Hospital type[g]	General hospital	84	37%	135	48%	0.002
	Top clinical hospital	111	48%	127	45%	
	Academic hospital (including breast cancer-specialized hospital)	34	15%	19	7%	

IBR, mastectomy with immediate breast reconstruction; No IBR, mastectomy without IBR; BMI, body mass index.
* Chi-square tested
[a] Totals do not match up due to missing values
[b] self-reported
[c] Socio-economic status (SES) of the patients was based on four-digit postal code at time of surgery. SES-scores are provided by the Netherlands Institute for Social Research (Sociaal Cultureel Planbureau) and divided into three groups based on the delivered rank numbers: low (1st-3rd deciles), intermediate (4th-7th) and high (8th-10th) SES.
[d] Body Mass Index (BMI) based on body length and weight, according to WHO-definition.
[e] Percentage of annual IBR for mastectomy patients per hospital, categorized as low (0% IBR), middle (1-15%) or high volume (>15%).
[f] Number of surgical treated breast cancer patients per year (average over 2012-2014), categorized as low (<150), middle (150-249), and high (>250) volume.
[g] Hospitals were categorized as either general, teaching, or academic hospitals (including breast cancer-specialized hospital).

Shared decision-making for patients who had received IBR versus no IBR

Patients with IBR compared to patients without IBR were more often preoperatively informed about the opportunity for IBR (99% vs 75%; p<0.001), were just as often informed about DBR (77% vs 73%; p=0.534), and they were less often informed about the possibility of an external breast prosthesis to conceal the missing breast when dressed (64% vs 81%; p<0.001).

Of all patients who had received preoperative information about IBR, 86% of the patients with IBR versus 68% of the patients without IBR had discussed the advantages and disadvantages of IBR with their physician (p<0.001). Moreover, patients with IBR more often reported that the information about breast reconstruction had been comprehensible (p<0.001) and they felt more often than patients without IBR they had had the opportunity to ask questions about breast reconstruction issues (p<0.001). More patients with IBR (91%) than patients without IBR (67%) felt they had shared the decision-making with their physicians (p<0.001; **Table 2**).

Most patients reported they had chosen their treatment based on their preferences (IBR: 53%, without IBR 68%) or their physician had recommended the received treatment (IBR: 41%, without IBR: 10%; **Figure 1**).

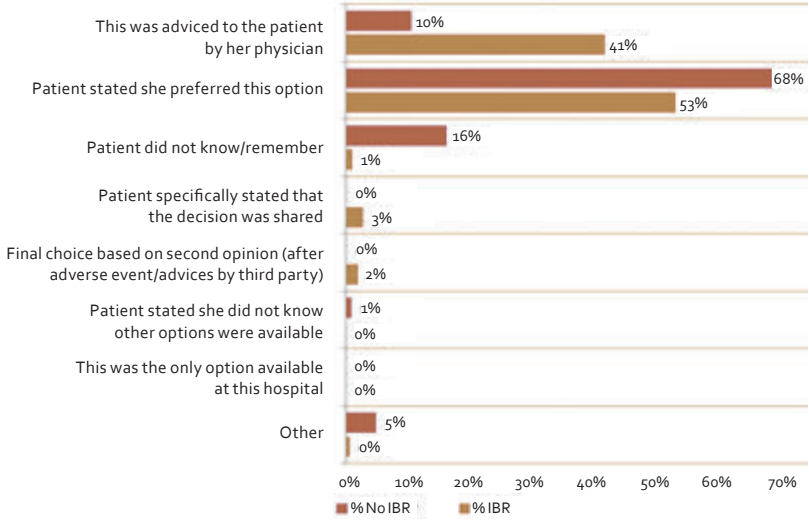
For both patients with IBR and without IBR, 41% of patients who had been treated with radiotherapy had received a preoperative consultation with a radiation oncologist. Furthermore, for patients who were treated with radiotherapy and had received information about IBR, 63% of patients with IBR and 51% without IBR had been informed about the effects of radiotherapy on breast reconstruction (p=0.082, **Table 2**).

Table 2. Patient-reported experience with information provision on treatment options, on advantages and disadvantages of treatment options, and shared decision-making about immediate breast reconstruction.

	IBR		No IBR		
Item in questionnaire	**(n=229)**	**%**	**(n=281)**	**%**	**P-value***
Information on available treatment options					
Patient was preoperatively informed about possible treatment with:					
- IBR	226	99%	204	73%	<0.001
- DBR	176	77%	204	73%	0.534
- External breast prosthesis	147	64%	228	81%	<0.001
Patient received information on pros and cons of reconstruction					
Pros and cons of IBR were discussed between patient and physician (if received information on IBR)	n=226 194	86%	n=204 139	68%	<0.001
Patient regarded information about BR was comprehensible (if information received about IBR)	n=224 224	100%	n=227 191	85%	<0.001
Patient had opportunity to ask questions about BR (if information received about IBR)	n=226 226	100%	n=204 189	84%	<0.001
Discussing effects of radiotherapy on breast reconstructive surgery					
Patient had a preoperative consultation with radiation oncologist (if treated with radiotherapy)	n=39 16	41%	n=95 39	41%	0.784
Patient received information on effect of radiotherapy on BR (if information received about IBR and treated with radiotherapy)	n=38 24	63%	n=74 38	51%	0.082
Experienced shared decision-making					
Patient felt she could share the decision regarding BR	208	91%	187	67%	<0.001

IBR, mastectomy with immediate breast reconstruction; No IBR, mastectomy without IBR; BR, breast reconstructive surgery; DBR, delayed breast reconstruction.
*Chi-square tested.

Figure 1. Patient-reported reasons for the choice for immediate breast reconstruction (IBR), patients with IBR (n=229) versus no IBR (n=281).



IBR: immediate breast reconstruction. No IBR: mastectomy without IBR.

Factors affecting receiving IBR

The following variables were significantly related to having undergone IBR in univariate analyses and were therefore included in the multivariate analysis: informed about IBR, age, BMI 25, highest completed education, two or more comorbidities, stage II or III tumor, multifocal tumor, bilateral mastectomy, neoadjuvant chemotherapy, radiotherapy, and IBR hospital volume.

In the multivariate logistic regression analyses, receiving IBR was significantly and positively affected by preoperatively being informed about IBR: these women had a 14-fold higher chance of receiving IBR (OR 13.87, CI: 3.75–51.30). Other significant factors were age over 60, BMI over 25, stage II and III, multifocality, bilateral mastectomy, radiotherapy, and IBR hospital volume (**Table 3**).

Table 3. Effect of information provision about immediate breast reconstruction (IBR) on receiving IBR, corrected for patient, tumor, and treatment characteristics.

			Univariable		Multivariable		
		n	OR	95% CI	OR	95% CI	P-value[b]
Information about IBR							
Patient received information about IBR[a]	No/don't know	90	ref		ref		
	Yes	444	28.43	8.84 – 91.51	13.87	3.75 – 51.30	<0.001
Patient characteristics							
Age[a]	<40	44	2.49	1.14 – 5.43	1.84	0.66 – 5.19	0.246
	40-59	295	ref		Ref		
	60+	195	0.16	0.11 – 0.25	0.21	0.12 – 0.36	<0.001
BMI[a]	Healthy weight (BMI<25)	286	Ref		Ref		
	Overweight (25<=BMI >30)	171	0.47	0.32 – 0.71	0.59	0.35 – 1.01	0.055
	Obese (BMI>30)	74	0.21	0.11 – 0.39	0.22	0.10 – 0.48	<0.001
Comorbidities[a]	None	351	Ref		Ref		
	One	139	0.67	0.44 – 1.01	1.11	0.64 – 1.95	0.708
	Two or more	33	0.42	0.19 – 0.94	0.91	0.29 – 2.90	0.879
Highest completed education[a]	Secondary school intermediate level or less	203	Ref		Ref		
	Medium vocational training (MBO), secondary school high level	168	2.37	1.53 – 3.66	1.54	0.86 – 2.78	0.149
	Higher vocational training (HBO) or university	160	2.88	1.85 – 4.47	1.62	0.88 – 2.97	0.123
Tumor characteristics							
Stage (clinical)	Stage 0 (DCIS)	135	Ref		Ref		
	Stage I	155	1.23	0.77 – 1.98	1.17	0.64 – 2.14	0.613
	Stage II	189	0.48	0.30 – 0.76	0.39	0.20 – 0.75	0.005
	Stage III	34	0.09	0.03 – 0.33	0.08	0.01 – 0.41	0.003

Table 3. Effect of information provision about immediate breast reconstruction (IBR) on receiving IBR, corrected for patient, tumor, and treatment characteristics. (continued)

			Univariable		Multivariable		
		n	OR	95% CI	OR	95% CI	P-value[b]
Multifocality	No	386	Ref		Ref		
	Yes	148	1.79	1.21 – 2.64	2.52	1.43 – 4.42	0.001
Treatment characteristics							
Mastectomy[a]	Unilateral mastectomy	448	Ref		Ref		
	Bilateral mastectomy	86	3.24	1.94 – 5.39	2.22	1.08 – 4.55	0.029
Axillary dissection	No	128	Ref		-	-	-
	Yes	406	Omitted	omitted	-	-	-
Neo-adjuvant chemotherapy	No	460	Ref		Ref		
	Yes	74	0.63	0.37 – 1.07	0.99	0.41 – 2.40	0.994
Radiotherapy	No	394	Ref		Ref		
	Yes	140	0.40	0.26 – 0.61	0.52	0.28 – 0.98	0.045
Hospital factors							
IBR hospital volume[c]	Low	76	0.39	0.22 – 0.68	0.43	0.20 – 0.94	0.035
	Middle	186	0.60	0.41 – 0.88	0.41	0.24 – 0.69	0.001
	high	272	Ref		Ref		

IBR, immediate breast reconstruction.
[a] Self-reported.
[b] Chi-square tested.
[c] Hospital volume (%IBR) was based on percentage of annual IBR for mastectomy patients, and categorized as low (0% IBR), middle (0-15%) or high volume (>15%).

DISCUSSION

The objectives of the current study were to gain insight into the underlying decision-making process of IBR and to determine the effect of preoperative information provision about IBR on receiving IBR.

Based on more than five hundred completed questionnaires, we found that patients treated with IBR had been better informed about IBR, more often had weighed the advantages and disadvantages of IBR in discussion with their physician, and more often had experienced shared decision-making regarding IBR compared to patients without IBR. Furthermore, our multivariate logistic regression showed that being informed about IBR increased the probability for receiving IBR fourteen-fold. Because of our large sample, we were able to statistically control this relation for patient, tumor, treatment, and hospital factors.

Since we found that being informed about IBR had a large effect on receiving IBR, it may well be that the uninformed mastectomy patients would have opted for IBR if they had received information about IBR. A prospective study by Ananian et al. reported that patients who opted for breast reconstruction more frequently recognized the importance of discussing breast reconstruction with their surgeon, and women who had benefitted more frequently from discussions with their physician in general tended to prefer IBR over DBR.[34] Other factors that significantly reduced the chance of receiving IBR in the multivariate regression analysis, mainly were risk-factors for postoperative complications after IBR (age over 55, BMI over 30, radiotherapy), as stated in the national guideline.[17]

We found that patients without IBR were less often informed about IBR as a treatment option and its advantages and disadvantages than patients with IBR. However, it is the preoperative information discussed between patient and physician that is particularly considered carefully when making a choice[34,35] and not so much the information the patient collects herself from other resources. Guidelines, including the Dutch guideline on breast reconstruction published in 2015, already stress the importance of starting the discussion on different breast

reconstructive possibilities at the same time when mastectomy is offered to the patient by the surgeon.[17,36]

It has already been found that low satisfaction with preoperative information is associated with an increased likelihood of decisional regret.[37] However, in our questionnaire almost 70% of patients without IBR stated they preferred not to have IBR, and 10% indicated their physician advised this. After analyzing the free text field in the survey of the latter patients, it became evident the advice to postpone breast reconstruction was based on severity of tumor characteristics or the increased risk of surgical complications. This suggests that mainly those patients with strong contra-indications for IBR were recommended mastectomy without IBR by their physician; therefore, we would be jumping to conclusions by merely stating that patients without IBR were not informed about IBR. Patients knowing about IBR as a treatment option, could have rejected this option immediately, therefore not receiving any further information. Contradictory to this, patients without IBR less often felt they shared the decision with their physician. Since patients without IBR in our study were older and lower educated, it could well be these patients did not want to share the decision, which was found in patients with these characteristics before.[38,39] A previous study reported that surgeons tend to predict their patients' preferences fairly accurately.[34] For one fifth of the mastectomy patients in our study, the choice had not been based on their preferences or on a medical necessity; these patients possibly may have missed their chance of receiving IBR. As women vary in information seeking behaviour[40] tailoring information to individual patients[41] may be helpful here. Furthermore, we suggest that it should be documented in every patient's file whether and which breast reconstruction options were discussed; this is already recommended in the national guideline on breast reconstruction as well.[17] Often, this documentation is lacking, while it could help the physician in revealing unmet needs in patient information as well as education.[42]

Harcourt et al. reported that only 15% of respondents searched for further information before making a decision, while 82% made "instant" decisions (during the consultation where the reconstruction was first discussed).[35] Opting

for DBR creates a time span for patients in which they can explore their possibilities considering different breast reconstruction types and which provides professionals with the ability to assess whether patients are fully prepared for the outcomes.[43] Neo-adjuvant therapy creates a time span to surgery as well.[43] Based on our selection, we did not know on beforehand who had DBR or was considering this; it turned out 24 patients had had DBR. Thirty-eight respondents that had mastectomy without IBR in our study stated they were currently considering DBR; twenty-five of these patients (70%) were informed about IBR before receiving mastectomy. Since time between diagnosis and completing the questionnaire was short for some patients, we presume that more mastectomy patients in our sample eventually will receive DBR.

We found that patients with IBR more often felt the decision-making had been shared between themselves and their physician compared to patients without IBR. Several studies have reported variation between actual and preferred involvement in decision-making for breast cancer treatment.[31,44,45] As described above, some mastectomy patients were denied IBR based on tumor or treatment characteristics. Therefore, they might feel they did not have a choice. However, involving patients in the decision-making process should always be promoted, because of its positive effects on quality of life[24] and patient satisfaction.[29–31] Although we did not measure SDM-preferences, we expect that a majority of patients would have wanted to participate in decision-making.[30,31] Besides, Lee et al. reported that the majority of patients in their study felt involved in decision-making, while their knowledge on the procedure of IBR could be improved[46]; shared decision-making is therefore not the sole result of providing information.

Radiotherapy is an accepted reason to omit IBR[20,47], as it has been shown to increase the risk of implant loss, complications, poorer esthetic results and less satisfied patients.[48] However, these increased complication and failure rates did not seem to apply for immediate autologous reconstructions, with comparable (partly unpublished) results for pre-reconstructive and post-reconstructive exposure to radiation therapy.[49,50] Since implant-based reconstruction is the most applied form of breast reconstruction[48], which was applicable for our respondents as well, a

majority of patients will face the trade-off between choosing IBR with a hazard of experiencing the negative effects of radiotherapy, or omitting IBR and therefore omitting its positive effects on quality of life and psychosocial functioning. Therefore, patients should be fully aware of these effects in order to make an informed decision. Interestingly, Flitcroft et al. reported that when patients (two-stage with tissue expander) were informed about potential negative esthetic side-effects of post-mastectomy radiotherapy on IBR, 63% still opted for IBR.[51] In our study, 39% of patients who had been informed about the effects of radiotherapy had undergone IBR.

Strengths and limitations

With a response of over five hundred patients from a large geographically diverse and randomly selected nationwide sample, we believe that we accurately reflected reconstructive care for mastectomy patients in the Netherlands. This was confirmed by our analysis of the characteristics of respondents versus non-respondents. Furthermore, patient experiences and clinical data were combined, therefore creating a broad dataset for each patient.

However, also some limitations in the design of our study can be identified. Because patients had undergone mastectomy in 2013 or 2014, whereas our survey was conducted in 2015, potential bias lies in the patients' ability to properly recall the exact process of decision-making and information provision.[52] In addition, there may have been a reduction of inconsistencies between current beliefs and previous decisions ("cognitive dissonance reduction").[53] Finally, inherent to an online survey, and despite the possibility to provide paper based questionnaires, respondents were younger than non-respondents, leading to a slightly lower response rate in the group without IBR. Since we used a non-validated questionnaire, not all invited patients responded, respondents' characteristics were not equal over both groups, which are limitations inherent to patient-reported data, and therefore interpretation of the results should be done with caution.

We recommend that every woman who faces mastectomy is informed about all relevant options for breast reconstruction.[54] She consequently also should receive

this information, even if this means that she has to be referred to another hospital to undergo the type of IBR she desires. Only after knowing and understanding all options, a well-informed decision can be made by the patient. Ideally, all patients should be referred to a plastic surgeon for a completely balanced weighing of the decision whether or not to perform IBR, because another study recently conducted in the Netherlands revealed surgeons informed patients differently compared to plastic surgeons.[50] Physician education is important to accomplish continuity of care and proper referral. Furthermore, more implant IBR than autologous IBR can be performed within the same amount of time; thus, financial incentives made performing implant IBR more attractive for hospitals than autologous IBR[55], explaining the relative low number of respondents with autologous reconstruction. As IBR is covered by every patients' health insurance (except for the obligatory deductible excess of Euro 385, - (2017))[56], this does not hinder access.

CONCLUSIONS

Patients who received IBR had been better informed about IBR as a treatment option, more often had discussed advantages and disadvantages of IBR, and felt significantly more involved in SDM than patients without IBR. After correction for patient, tumor, treatment, and hospital factors, being informed about IBR significantly increased the odds of receiving IBR fourteen-fold. Our results highlight the importance of providing sufficient information on all relevant treatment options.

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SUPPLEMENTARY APPENDIX 1: POWER CALCULATION

The power calculation for this questionnaire was based on the Breast-Q modules that were included in our questionnaire, since the questions for these modules have been validated. The analysis for these questions however will be conducted in a separate manuscript.

Based on Zhong et al (2011)[1], an SD of about 20 was found for separate Breast-Q subscales. A difference of 10 points on each scale (0-100) was considered clinically relevant.

With an alpha of 0.05 (double sided) and a power of 0.85, we needed 32 respondents in each group. Since we estimated we could invite a lot more patients, we chose a lower difference in points:

h = 0,50 → n = 32 (difference of 10 points)
h = 0,40 → n = 49 (difference of 6 points)
h = 0,25 → n = 126 (difference of 5 points)
h = 0,20 → n = 197 (difference of 4 points)

Furthermore, we expected a response of about 25%. Therefore, we decided to invited 500 patients per group (500*0,25=125). Since we wanted a sample of patients that were treated in all types of hospitals and all regions in the Netherlands, we decided to include at least 20 different hospitals. This meant that 50 patients had to be selected per participating hospital.

We hypothesize that selecting 50 patients per hospital leaves the required workload per hospital acceptable, since all patients are selected in deliberation with the physician and each hospital has to prepare letters for all selected patients, without receiving a financial incentive.

Since more than 20 hospitals committed to our study, we decided to include these hospitals as well; therefore, we were able to indicate differences of 4 points on the Breast-Q subscales.

SUPPLEMENTARY APPENDIX 2: QUESTIONNAIRE

The following questions are covering understated aspects:

Questions on health and treatment:

- general health: Q1, Q2.
- breast cancer treatment: Q3 – Q5
- breast reconstruction: Q17 – 21

Shared decision-making aspects:

- both patient and physician acknowledge a decision is required (by knowing that IBR is an option): Q7 – 9, Q16
- understanding and weighing all available information about the treatment options: Q10, Q12, Q13; Q6, Q15
- incorporating the patient's preferences in the final decision: Q11, Q22 – 24

Questions on patient's background:

- date of birth, nationality, educational level, working status, relationship status, breast size, body length and weight, and menopausal status: Q46 – 57

1. **How was, in your own perception, your physical health over the past three months?**
   Excellent – very well – well – moderate – bad

2. **How was, in your own perception, your mental health over the past three months?**
   Excellent – very well – well – moderate – bad

3. **What kind of surgery did you receive?**
   Amputation – amputation including axillary lymph node dissection – other

4. **When did you receive this surgical procedure?**
   [fill in date DD/MM/YYYY]

5. **Did you receive surgery on one or both breasts?**
   Both breasts (double-sided) because of cancer in both breasts – both breasts (double-sided) because of cancer in a single breast while other side preventive – single breast (single-sided)

6. **Did you have a consultation with a radiotherapist prior to your surgery?**
   Yes – no – can't remember – not applicable since I did not receive radiotherapy

7. **Where you informed on possible treatment with an immediate breast reconstruction prior to receiving your surgical treatment?**
   Yes – no – can't remember

8. **Where you informed on possible treatment with a delayed breast reconstruction prior to receiving your surgical treatment?**
   Yes – no – can't remember

9. **Where you informed on the possibility of breast prosthesis prior to receiving your surgical treatment (when not opting for breast reconstruction)?**
   Yes – no – can't remember

10. **Did you and your physician discuss the advantages and disadvantages of an immediate breast reconstruction?**
Yes – no – not applicable: did not receive any information on immediate breast reconstruction – can't remember

11. **Do you feel you had a choice in choosing for either an immediate breast reconstruction, a delayed breast reconstruction, or no breast reconstruction at all?**
Yes – no – not applicable: did not receive any information on immediate breast reconstruction – can't remember

12. **Do you feel the information you received on breast reconstruction was comprehensible?**
Yes – no – not applicable: did not receive any information on breast reconstruction – can't remember

13. **Do you feel you got the opportunity to ask your physician questions on breast reconstruction?**
Yes – no – not applicable: did not receive any information on breast reconstruction – can't remember

14. **Are you familiar with the 'B-bewust checklist', developed by the Dutch Breast Cancer Patient Association, and did you use this checklist when informing yourself on breast reconstruction?**
Yes, and applied this as well – yes, but did not apply this checklist – no – can't remember

15. **Were you informed on the possible effects of irradiation on the possibility of receiving (any kind of) breast reconstruction?**
Yes – no – not applicable: did not receive any information on breast reconstruction – can't remember

16. **Were you redirected to another hospital in order to receive a breast reconstruction?**
Not applicable, breast reconstruction was offered in my treating hospital – no, I was not redirected and did not receive breast reconstructive surgery – no, I was not redirected but informed myself and eventually rejected breast reconstruction – no, I was not redirected but informed myself and eventually opted for breast reconstruction – yes, I was redirected and received breast reconstructive surgery – yes, I was redirected but rejected breast reconstructive surgery – I can't remember – other

17. **Did you receive a breast reconstruction, and if so, when did you receive this procedure?**
I did not receive breast reconstructive surgery – I did not receive breast reconstructive surgery, but consider having this procedure in de (nearby) future – I did not receive breast reconstructive surgery, but a delayed breast reconstruction is currently planned on [date DD/MM/YYYY] – yes, I received a delayed reconstruction on [date DD/MM/YYYY] – yes, I received an immediate breast reconstruction

18. **Which type of immediate breast reconstruction did you receive?**
Tissue expander, followed by final prosthesis – immediate final prosthesis without use of a tissue expander – tissue from the back (latissimus dorsi) combined with final prosthesis, whether or not with use of tissue expander – tissue from the abdomen (TRAM, DIEP, SIEA) – tissue from thigh (TMG, SGAP, IGAP of PAP) – I don't know – other

19. **Which type of delayed breast reconstruction did you receive?**
Tissue expander, followed by final prosthesis – immediate final prosthesis without use of a tissue expander – tissue from the back (latissimus dorsi) combined with final prosthesis, whether or not with use of tissue expander – tissue from the abdomen (TRAM, DIEP, SIEA) – tissue from thigh (TMG, SGAP, IGAP of PAP) – I don't know – other

20. Did you receive a nipple reconstruction?
Yes, a nipple reconstruction including medical tattooing of the areola – yes, solely a nipple reconstruction – yes, solely medical tattooing of the areola – no, neither a nipple reconstruction nor medical tattooing of the areola – no, because my nipple was saved during amputation (autologous use for breast reconstruction)

21. Did you receive additional surgical procedures in order to accomplish an optimal result of your breast reconstruction?
No, I did not receive additional surgical procedures – yes, I received additional surgical procedures for my reconstructed breast – yes, I received additional surgical procedures for my preserved breast – yes, I received additional surgical procedures for both breasts – other

22. Why did you opt for an immediate breast reconstruction?
My physician recommended this, without specifically stating why – my physician recommended this, because [open text field] – by own choice, because [open text field] – I did not know there were other options than an immediate breast reconstruction – I don't know – other

23. Why did you opt for a delayed breast reconstruction?
My physician recommended this, because an immediate breast reconstruction was too risky – my physician recommended this, because an immediate breast reconstruction was not a possibility since [open text field] – my physician recommended this, without specifically stating why – my physician recommended this, because [open text field] – I did not know there were other options than an delayed breast reconstructive surgery – my treating hospital did only offer delayed breast reconstructive surgery – by own choice, because immediate reconstruction gave a high risk on complications – by own choice, since there was a waitlist to receive an immediate reconstructive surgery – by own choice, since I wanted to focus on getting better first – by own choice, since [open text field] – I don't know – other

24. Why did you reject breast reconstruction?
My physician recommended this, because a breast reconstruction gave too high risk on complications – my physician recommended this, without specifically stating why – my physician recommended this, because [open text field] – by own choice, because a reconstruction gave a high risk on complications – by own choice, because I think a breast reconstructive surgery is unnecessary – by own choice, because I think receiving breast reconstructive surgery is a too lengthy procedure – by own choice, because I think a breast reconstructive surgery is too invasive – by own choice, because I think a breast reconstructive surgery leads to a lengthy and intensive recovery – by own choice, since [open text field] – I did not know there were options for breast reconstructive surgery – I don't know – other

BREAST-Q MODULES
25 to 39: BREAST-Q Postoperative reconstruction module
40 to 45: BREAST-Q Postoperative mastectomy module

46. What is your date of birth?
..-..-19..

47. At time of your breast cancer treatment, what were the four digits of your postal code?
____

48. What is your highest completed education? (completed with diploma or certificate)
No education – lower education – middle education – higher education – other

49. **What is currently your marital status?**
Married/relationship – divorced/separated – widow/widower/partner diseased – single

50. **Which description is most applicable to you at this moment?**
Attending school/education – paid employment – unemployed/seeking work – incapacitated – housewife – retired

51. **What is your nationality?**
Dutch – Moroccan – Surinamese – Turkish – German – Belgian – Other

52. **At time of your breast cancer surgery, how tall were you and how much did you weigh?**
[height in cm] [weight in kg]

53. **At time of your breast cancer diagnosis, did you smoke?**
Yes – no

54. **At time of your treatment for breast cancer, did you suffer from one or more of undermentioned diseases?**
Any other type of cancer – lung disease – cardiovascular disease – gastrointestinal disease – illness of urinary or reproductive system – musculoskeletal disease – central nerve system – illness of metabolism or coagulopathy – infectious disease – none – other

55. **What was your breast size at the time of your breast cancer diagnosis?**
AA – A – B – C – D – E – F – G – other

56. **Were you menopausal at time of your treatment with chemotherapy?**
Premenopausal – perimenopausal – postmenopausal – I don't know – not applicable

57. **Are you an active member of a patient association for breast cancer or breast disease?**
No – yes, but not very active – yes, active member

Do you have any questions/remarks?

CHAPTER 8

The added value of immediate breast reconstruction to health-related quality of life of breast cancer patients

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ABSTRACT

Background: Postmastectomy immediate breast reconstruction (IBR) may improve the quality of life (QoL) of breast cancer patients. Guidelines recommend to discuss the option IBR with all patients undergoing mastectomy. However, substantial hospital variation in IBR-rates was previously observed in the Netherlands, influenced by patient, tumor and hospital factors and clinicians believes. Information provision about IBR may have a positive effect on receiving IBR and therefore QoL. This study investigated patient-reported QoL of patients treated with mastectomy with and without IBR.

Methods: An online survey, encompassing the validated BREAST-Q questionnaire, was distributed to a representative sample of 1218 breast cancer patients treated with mastectomy. BREAST-Q scores were compared between patients who had undergone mastectomy either with or without IBR.

Results: A total of 445 patients were included for analyses: 281 patients with and 164 without IBR. Patients who had received IBR showed significantly higher BREAST-Q scores on "psychosocial well-being" (75 versus 67, $p<0.001$), "sexual well-being" (62 versus 52, $p<0.001$) and "physical well-being" (77 versus 74, $p=0.021$) compared to patients without IBR. No statistically significant difference was found for "satisfaction with breasts" (64 versus 62, $p=0.21$). Similar results were found after multivariate regression analyses, revealing IBR to be an independent factor for a better patient-reported QoL.

Conclusions: Patients diagnosed with breast cancer with IBR following mastectomy report a better QoL on important psychosocial, sexual and physical well-being domains. This further supports the recommendation to discuss the option of IBR with all patients with an indication for mastectomy and to enable shared decision-making.

INTRODUCTION

Against the background of good prognosis and limited local treatment associated morbidity for primary breast cancer patients who undergo curative treatment[1], attention shifts to maintaining quality of life as an important goal of care. Quality of life can be objectified through patient-reported outcome measures (PROMs). PROMs aim to assess the actual feelings and thoughts of a patient and help clinicians and patients to measure, interpret, and understand quality of life as perceived by the patient.[2] As such, it may enhance communication between clinicians and patients in shared decision-making. In addition, PROMs may be used for comparative effectiveness analyses and to monitor quality of care.[3,4]

Approximately 40% of patients with invasive breast cancer and 30% of patients with ductal carcinoma in situ (DCIS) undergo mastectomy in the Netherlands.[5] To restore the breast contour, breast reconstruction may be performed either at the time of initial breast cancer surgery (immediate breast reconstruction, IBR) or as a delayed procedure some time later.[6] IBR has positive effects on body image and psychosocial well-being[7,8] and current guidelines recommend to offer IBR to every patient with an indication for mastectomy.[9,10,11] Nonetheless, a rather low mean IBR rate of 18% for patients undergoing mastectomy for invasive breast cancer was observed in the Netherlands and IBR-rates varied substantially between Dutch hospitals.[12,13] In previous studies, case-mix variation[12], hospital organizational factors[14], attitudes of clinicians towards IBR[15], and information provision about IBR were identified as possible causes of this hospital variation[16]. Even after adjustment for tumor, patient and hospital variables, IBR rates varied from 0% to 64% between hospitals in the Netherlands.[12,14]

To investigate the clinical significance of the observed variation of IBR rates in terms of patient-reported quality of life, the aim of the present study was to compare health-related quality of life of breast cancer patients treated with mastectomy with IBR versus mastectomy without IBR.

MATERIALS AND METHODS

Study population

Twenty-nine hospitals (1/3rd of the total number of hospitals in the Netherlands), serving varying patient volumes and proportions of patients undergoing IBR, were selected from the Netherlands Cancer Registry (NCR) to participate in the survey.[16,17] The selection of patients eligible for the present study consisted of female breast cancer patients from the age of 18 years and surgically treated for primary breast cancer or DCIS by mastectomy either with or without IBR between January 2013 and October 2014. Patients with distant metastases were excluded. From January 8th 2015, the identified patients were invited to participate in an anonymous, self-administered survey and consented to the use of the data for the purpose of this study. Responses were collected until July 30th 2015. Approval from the Committee of Privacy of the NCR was obtained for this study. The Medical Ethical Committee of the University Medical Center Groningen (METc2014/473) declared the Medical Research (Human Subjects) Act was not applicable for this study.

Questionnaire

Health-related quality of life was assessed using the BREAST-Q. This validated PROM is available in Dutch. Patients without IBR completed the postoperative BREAST-Q mastectomy module and patients who had received IBR completed the postoperative BREAST-Q reconstruction module.[18] Both modules have multiple domains examining health related health-related quality of life (perceived psychosocial, physical and sexual well-being) and patient satisfaction with the treatment result (satisfaction with breasts) in common. Every domain of the BREAST-Q has 4 to 16 items and the raw domain scores expressing the extent of satisfaction or well-being are transformed to Q-scores ranging from 0 (low) to 100 (high).[19] In addition, patient characteristics (age, educational level, marital/relationship status, working status, nationality, length and weight, comorbidities, breast size and menopausal state) were asked. Information on breast reconstruction (no reconstruction, immediate reconstruction, delayed reconstruction), type of reconstruction, nipple reconstruction and additional procedures to achieve a favorable result were included as treatment characteristics.

The questionnaire was tested and approved by a panel of patient representatives before distribution. Patients responded via PROFILES, an online secured web-based environment[20], or received the questionnaire on paper on request.

Statistical analysis

First, clinical characteristics of respondents and non-respondents were analyzed. Baseline characteristics of the respondents were presented for patients treated with mastectomy and IBR and for those without IBR. BREAST-Q domain scores were calculated with the Q-Score scoring software system to transform the raw BREAST-Q data.[19] The BREAST-Q outcomes were compared between patients with mastectomy and IBR and patients without IBR. Sub-analyses were performed for the various reconstructive techniques. Chi-square tests were used for categorical data and Student's T-tests were used for comparison of continuous BREAST-Q scores. Finally, a multivariate linear regression analysis was performed to investigate the impact of IBR on the different domain outcomes, adjusted for confounding factors. Factors included in the model were chosen on their possible relevance. Two-sided p-values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS (SPSS for MAC Version 20.0; SPSS Inc., Chicago, Il).

RESULTS

Study population

Questionnaires were sent to a total of 1218 patients: 502 who had undergone mastectomy with IBR and 716 who had not received IBR after mastectomy. The overall response rate was 46% (558/1218). No statistically significant differences between responders and non-responders were found for most patient characteristics, except that older patients and patients without IBR were slightly underrepresented in the respondent group compared to the non-respondent group (**Supplementary Table**). A total of forty-seven patients without IBR were excluded; 25 patients because they had received delayed breast reconstruction and 22 patients who returned incomplete BREAST-Q modules (defined as completion of less than one outcome domain in one of the two modules), leading to 511 patients available for analyses.

Fifty-five percent of the responders (n=281) had undergone a mastectomy without IBR, 45% (n=230) had received mastectomy with IBR. Of these latter, 66 patients were still waiting for at least one additional reconstructive breast procedure and were therefore excluded for further analyses, resulting in a total of 164 patients in the mastectomy with IBR group.

Patients undergoing IBR were significantly younger, were more often employed, had a lower Body Mass Index (BMI), a lower disease stage and received less frequently radiotherapy compared to patients without IBR (**Table 1**). In the IBR group, two-stage tissue expander-implant reconstruction (57%) and direct-to-implant reconstruction (32%) were the most often performed breast reconstruction methods. Most patients had not (yet) received a nipple reconstruction when the questionnaire was completed (66%).

Table 1. Baseline respondents' characteristics (n=511) categorized by surgical treatment (mastectomy without immediate breast reconstruction, n=281; mastectomy with immediate breast reconstruction, n=164).

		Mastectomy (n=281)		Mastectomy with IBR (n=164)		Total (n=445)		
		n	%	n	%	n	%	P-value
Patient characteristics								
Age	<50	47	17%	51	31%	98	22%	<0.001
	50-65	126	45%	98	60%	224	50%	
	>=65	108	38%	15	9%	123	28%	
SES*	Low	102	36%	43	26%	145	33%	0.086
	Mediate	100	36%	70	43%	170	38%	
	High	79	28%	51	31%	130	29%	
Employment status[1]	Student / Unemployed / Disabled	71	25%	39	24%	110	25%	<0.001
	Employed	93	33%	105	65%	198	45%	
	Retired	116	41%	18	11%	134	30%	
Partner[1]	Married / Partner	202	72%	134	82%	336	76%	0.020
	Single / Divorced / Widow	79	28%	30	18%	109	25%	
Comorbidities[1]	No other disease	173	62%	120	73%	293	66%	0.043
	1 other disease	78	28%	33	20%	111	25%	
	2 or more diseases	30	11%	11	7%	41	9%	
Body Mass Index[1]	<=25 kg/m²	126	45%	118	72%	244	55%	<0.001
	>25 kg/m²	155	55%	46	28%	201	45%	
Breast size[1]	AA - B	123	44%	82	50%	205	46%	0.436
	C	71	25%	38	23%	109	25%	
	≥D	87	31%	44	27%	131	29%	
Tumor characteristics								
Type of breast cancer	Ductal carcinoma in situ	55	20%	42	26%	97	22%	0.137
	Invasive breast cancer	226	80%	122	74%	348	78%	
Stage**	0	55	20%	42	26%	97	22%	<0.001
	I	61	22%	68	42%	129	29%	

Table 1. Baseline respondents' characteristics (n=511) categorized by surgical treatment (mastectomy without immediate breast reconstruction, n=281; mastectomy with immediate breast reconstruction, n=164). (continued)

		Mastectomy (n=281)		Mastectomy with IBR (n=164)		Total (n=445)		
		n	%	n	%	n	%	P-value
	II	103	37%	50	31%	153	34%	
	III	62	22%	4	2%	66	15%	
Treatment characteristics								
Type of breast reconstruction[1]	Tissue expander or immediate implant			146	89%	146	89%	
	Latissimus dorsi flap with implant			9	6%	9	6%	
	Autologous reconstruction			9	6%	9	6%	
Nipple reconstruction[1]	No reconstruction			94	57%	94	57%	
	Nipple reconstruction***			47	29%	47	29%	
	Nipple sparing surgery			23	14%	23	14%	
Radiotherapy	Yes	95	34%	25	15%	120	27%	<0.001
Chemotherapy	Yes	143	51%	71	43%	214	48%	0.122
Hospital characteristics								
Hospital	General	133	47%	60	37%	193	43%	0.120
	Educational	128	46%	80	49%	208	47%	
	Academic	20	7%	24	15%	44	10%	
Hospital volume**	Low	50	18%	19	12%	69	16%	0.001
	Intermediate	106	38%	43	26%	149	34%	
	High	125	45%	102	62%	227	51%	

[1.] Self-reported data from the patient survey
* Socio-economic status (SES) of the patients was based on four-digit postal code at time of surgery. SES-scores are provided by the Netherlands Institute for Social Research (Sociaal Cultureel Planbureau) and divided into three groups based on the delivered rank numbers: low (1st-3rd deciles), intermediate (4th-7th) and high (8th-10th) SES.
** Stage according to American Joint Commission on Cancer TNM classification.
*** Nipple reconstruction, either tattooing of the nipple-areola complex, nipple reconstruction or a combination of the two techniques.
**** Hospital volume was calculated by number of mastectomies: number of surgical treated breast cancer patients per year (average over 2012-2014), categorized as low (<150), middle (150-249), and high (>250) volume.

Patient-reported outcomes (BREAST-Q scores)

BREAST-Q outcomes per domain are presented in **Table 2**. Patients who had received IBR reported significantly better mean "psychosocial well-being" scores (mean, 75 versus 67, p<0.001) and "sexual well-being" scores (mean, 62 versus 52, p<0.001) than patients who had not undergone IBR. Similar results were found for "physical well-being" scores (mean, 77 versus 74, p=0.021). On the domain "satisfaction with breasts" patients with IBR reported similar mean scores compared to patients without IBR (mean, 64 versus 62, respectively, p=0.21). Due to small numbers of autologous reconstruction (n=9) and latissimus dorsi combined with implant reconstruction (n=9), no meaningful comparisons between these breast reconstruction techniques could be made. Patients with direct-to-implant breast reconstruction had similar BREAST-Q subscale scores compared to patients with two-stage tissue expander-implant reconstruction (data not shown).

Table 2. Mean BREAST-Q domain scores categorized by surgical treatment (Mastectomy without immediate breast reconstruction, n=281; Mastectomy with immediate breast reconstruction, n=164).

	Mastectomy (n=281)		Mastectomy with IBR (n=164)		
BREAST-Q DOMAINS	**Mean**	**SD**	**Mean**	**SD**	**P-value**
Satisfaction with breasts	62	18.46	64	18.08	0.21
Psychosocial well-being	67	18.97	75	18.76	<0.001
Sexual well-being	52	24.28	62	20.70	<0.001
Physical well-being: chest	74	16.44	77	16.08	0.021
Satisfaction with outcome			71	21.15	
Satisfaction with nipples*			67	22.51	
Physical well-being: Abdominal Region**			62	30.46	

IBR, Immediate Breast Reconstruction; SD, Standard Deviation.

* Patients with a nipple reconstruction, either by tattooing of the nipple-areola complex, a nipple reconstruction or a combination of the two techniques.

**Only patients who had a reconstruction with tissue from the abdomen such as Transverse Rectus Abdominis Myocutaneous (TRAM)-flap or Deep Inferior Epigastric Artery Perforator (DIEP)-flap or Superficial Inferior Epigastric Artery Perforator (SIEA)-flap.

Multivariate analyses of patient-reported outcomes in patients with and without IBR

All BREAST-Q outcomes showed a normal distribution with the mean and median closely related, enabling linear regression modeling. Confounding factors included in the multivariate model were age, socio-economic status, employment status, comorbidities, BMI, breast cancer stage and radiotherapy.

IBR proved to be independently associated ($p<0.001$) with favorable "psychosocial" and "sexual well-being" BREAST-Q domain scores and showed a borderline association with "physical well-being" ($p=0.049$). IBR did not appear to be significantly associated with the BREAST-Q domain "satisfaction with breasts" ($p=0.483$). For "psychosocial well-being" and "sexual well-being", no other independently associated factors were found in multivariate linear regression analyses. Younger age and a higher tumor stage were independently associated with "satisfaction with breasts" and the presence of multiple comorbidities was independently associated with "physical functioning".

DISCUSSION

The present study investigated health-related quality of life of patients with and without IBR following mastectomy. After adjusting for confounding factors, IBR was associated with significantly better BREAST-Q outcomes for "psychosocial functioning", "sexual functioning" and "physical functioning" compared to patients without IBR. Interestingly, no statistically significant differences were found for the BREAST-Q domain "satisfaction with breasts". Overall, the results of this reasonably large, and representative sample of more than 400 breast cancer patients in the Netherlands underscore the importance that all patients with an indication for mastectomy should be offered the possibility of IBR in order to achieve favorable quality of life outcomes and to enable shared decision-making. Ultimately, it is up to the patient, together with her clinician, to decide whether or not IBR is preferred or feasible.

Breast cancer survival rates are high, enabling and demanding a shift of focus towards quality of life after cancer treatment. Mastectomy still has a prominent

place to achieve locoregional control of breast cancer. Learning from patient preferences and outcomes of breast cancer surgery guides us through a better understanding of the actual care given. PROMs as the BREAST-Q enable us to understand outcomes beyond mortality and survival rates and to identify outcomes that also matter to patients.

Several other studies have examined health-related quality of life in patient populations following mastectomy with versus without IBR using the BREAST-Q.[21,22,23] Most studies showed similar results for psychosocial and sexual functioning favoring IBR. They also demonstrated a less apparent difference in physical functioning using multivariate regression analyses.[21,22,23] A common finding of these previous and our current study was that patients consistently reported lowest scores for sexual well-being. However, these low scores were also reported in a general population of women without breast cancer treatment, indicating that the low sexual well-being scores may also reflect an overall satisfaction of sexual well-being at a certain age instead of alterations due to breast cancer treatment only.[24]

Unexpectedly, the present study did not show a significant difference in the BREAST-Q domain "satisfaction with breasts" and both patient groups had similar scores compared to normative data.[24] However, this finding is contradictory to the results of previous studies.[21,22,23] An explanation might be that patients without IBR accept the esthetic consequences for the chest area. This is supported by the additional comments found in the survey where 16 patients stated they deliberately decided not to undergo IBR. Patient satisfaction with their breasts is also significantly associated with preoperative information provision by and shared decision-making with the reconstructive surgeon, which highlights the importance of adequate preoperative information provision.[25]

Only the outcome domain "physical well-being" was lower compared to normative data which are used internationally.[24] Patients who had received either mastectomy or IBR scored around 75 compared to the normative score of 93.[24] A recent single center study in the Netherlands investigating a breast cancer population showed mean data of around 70.[23] Surgery in general, including reconstructive surgery,

leads to altered anatomy and scarring, which may lead to pain and discomfort and therefore decreased physical well-being.

A strength of the current study is that it included a representative sample of the breast cancer population in the Netherlands. Limitations are the possibility of recall bias, due to the retrospective design, and response bias, which is inherent to the use of questionnaires. Also, our response rate of 46% was lower compared to other studies, which varied from 56% to 74% [21,22,23,26,27] possibly because we did not send any reminders. The mean time between mastectomy and the questionnaire was approximately 17.5 months (range 3 – 34 months), which is relatively short, however, we excluded patients still in the process of reconstruction. Unfortunately, no preoperative information on the outcome domains was available in our study, similar to most breast cancer surgery studies using the BREAST-Q.[28] The difference in baseline characteristics (younger, employed, more healthy patients and patients with lower stage tumors without radiotherapy have a higher change of receiving IBR) might have resulted in treatment indication bias. A multivariate linear regression analysis was performed to adjust for patient characteristics when comparing mastectomy with IBR versus without IBR. Nevertheless, other (unknown) factors may have contributed to health-related quality of life and may therefore limit the conclusions drawn from this research.

Patients with an indication for mastectomy should receive sufficient preoperative information enabling informed shared decision-making about IBR. It may be seen as a challenge to inform patients about all available and relevant surgical options for breast cancer, including their advantages and disadvantages, enabling a patient to make her own informed decision. In a study previously reported by our group, patients who had received IBR had been better informed about IBR and felt more involved in shared decision-making compared to patients without IBR. Moreover, patients being preoperatively informed about IBR had a 14-fold higher chance of receiving IBR.[16] Others reported that one third of the patients who underwent a mastectomy felt they had not received sufficient information about breast reconstruction, or were dissatisfied with the reconstruction decision-making process (13%).[29]

Understanding health-related quality of life and the effects of breast cancer surgery by longitudinally using PROMs is essential to guide patients in the future, since outcomes may alter over years.[27,30] Recommendations for future practice should involve implementation of these outcome measures in every day practice in the complete care path for breast cancer patients, as advocated by Michael Porter and the International Consortium for Health Outcomes Measurement[31,32] who defined an international standard set of outcomes to track for all breast cancer patients.[33] Fortunately, first implementation efforts are on their way.[34]

CONCLUSION

A significantly better health-related quality of life on various outcome domains including psychosocial, sexual and physical well-being was reported by patients with IBR compared to patient without IBR. It is therefore justified to discuss the possibility of IBR with all patients with an indication for mastectomy. More importantly, this enables shared decision-making in an era where the patient herself, after having received all relevant information including advantages and risks, decides whether or not she wants to undergo IBR.

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SUPPLEMENTARY TABLE

Characteristics of respondents (n=558) versus non-respondents (n=660) to the questionnaire about quality of life after mastectomy or immediate breast reconstruction.

		Respondents		Non-respondents		Total	
		n=558	%	n=660	%	n=1218	P-value
Age at time of mastectomy	Mean	54.59		54.43			
	<50	182	33%	245	37%	427	
	50 - 65	246	44%	208	32%	454	
	65 or above	130	23%	207	31%	337	<0.001
Type of cancer	Invasive breast cancer	434	78%	497	75%	931	
	DCIS	124	22%	163	25%	287	0.311
Year of surgery	2013	313	56%	391	59%	704	
	2014	245	44%	269	41%	514	0.268
Breast reconstruction	Immediate breast reconstruction	253	45%	248	38%	501	
	No reconstruction / delayed breast reconstruction*	305	55%	412	62%	717	0.006
Volume of hospital**	High	316	57%	332	50%	648	
	Middle	193	35%	259	39%	452	
	Low	49	9%	69	10%	118	0.086

DCIS: ductal carcinoma in situ

* Delayed breast reconstruction (25 patients) are excluded from future analyses.

** Volume calculated by number of mastectomies: number of surgical treated breast cancer patients per year (average over 2012-2014), categorized as low (<150), middle (150e249), and high (>250) volume.

CHAPTER 9

General discussion and future perspectives

GENERAL DISCUSSION AND FUTURE PERSPECTIVES

This thesis describes the constitution and results of the first four years of the Dutch Breast Cancer Audit (NBCA), together with factors that may optimize the use of breast reconstructive surgery.

In the years preceding the NBCA, the National Health Care Inspectorate had started to query individual hospitals regarding the possible relationship between volume and outcomes of provided care for patients with various oncologic conditions.[1,2] The results were published in national media and presented as "rankings" that assumedly reflected the quality of care.

In 2011, the endeavors of many clinicians resulted in the constitution of a nationwide breast cancer audit.[3] The joined effort of these clinicians originating from all involved specialties and stakeholders (patients, insurance companies, government) led to a set of 32 quality indicators to gain insight in all aspects of the multidisciplinary care for patients diagnosed with breast cancer (**Chapter 2**). Full participation of the 92 Dutch hospitals was accomplished within two years, resulting in NBCA data of the breast cancer work-up and treatment of 56,927 patients who had been treated between 2011 and 2014. Many indicators showed improvements within the first four years of auditing: the proportion of individual patient cases being discussed in pre-and postoperative multidisciplinary team meetings (from 83% to 98%), the guideline-directed use of BI-RADS (Breast Imaging-Reporting and Data System) classification in the radiological assessment of breast imaging (from 97% to 99%), the proportion of pathology reports containing all clinically relevant items (from 83% to 97%) as well as the rate of tumor-positive margins after first primary breast conserving surgery for invasive breast cancer (from 5.9% to 4.6%).

The percentage of patients treated by breast conserving surgery remained stable during these four years. Hypothesizing that the mere breast conserving surgery rate does not adequately represent the esthetic outcome of local treatment, the rate of undergoing a breast-contour-preserving procedure (BCPP) was coined as an alternative local outcome parameter (**Chapter 3**). The definition of BCPP

encompasses multiple treatment strategies that preserve or restore the contour of the breast, i.e. upfront breast conserving surgery, breast conserving surgery following neo-adjuvant chemotherapy and mastectomy followed by immediate breast reconstruction (IBR). While the rate of breast conserving surgery as primary treatment for breast cancer remained stable over time, the proportion of patients undergoing BCPP increased from 63% in 2011 to 71% in 2015: both the rates of breast conserving surgery following neo-adjuvant chemotherapy and mastectomy combined with IBR increased. The BCPP rate was similar for most age groups, but the means by which the breast contour was maintained varied largely between these groups. An increased use of primary breast conserving surgery in the elderly, and a concomitant decrease in older patients treated with neo-adjuvant chemotherapy or postmastectomy IBR was found.

On average, IBR was performed in 17% of all patients who underwent a mastectomy and this proportion ranged between 0% and 64% in the 92 hospitals. This observed hospital variation in the use of IBR was the basis for the research in **Chapters 4, 5 and 6** into possible patient, tumor, hospital and physicians' factors explaining this variation. Following case-mix correction (for patient and tumor factors that were associated with a higher rate of IBR such as young age, multifocality, small tumor size, low malignancy grade, absence of lymph node involvement), large variation remained between the hospitals (0% to 43%; **Chapter 4**). Hence, hospital organizational factors were collected and compared for all hospitals in the Netherlands (**Chapter 5**). Factors favoring the uptake of IBR related to the observed variation in the institutional IBR rate were: hospital type (district hospitals more frequently performed IBR compared to university hospitals), more plastic surgeons involved in reconstructive breast surgery, attendance of a plastic surgeon at the preoperative multidisciplinary team meeting and a higher institutional rate of performing mastectomies. Next, the potential effect of the involved medical specialties was studied. Since the final decision to undergo/perform IBR is made by patients and their surgical oncologists and plastic surgeons, personal opinions and attitudes of surgical oncologists and reconstructive plastic surgeons towards the decision to undergo IBR were studied. These professional opinions may vary or even differ and therefore questionnaires were sent to the clinicians in a nationwide survey (**Chapter 6**). Plastic surgeons more frequently

reported patient-related risk factors for wound healing problems as an important contra-indication towards advising IBR, while surgical oncologists more frequently underscored oncological contra-indications as reasons to advise against it. The strive for consensus between physicians regarding indications and contra-indications for IBR may optimize patient counseling and shared decision-making. Moreover, being informed about IBR resulted in a 14 times higher chance to undergo IBR and this stresses the importance for clinicians to inform patients about this treatment option to optimize the decision-making process for surgical breast cancer treatment and IBR (**Chapter 7**). In addition to the medical and technical considerations, knowledge about the self-perceived quality of life of patients who underwent IBR is important to take into account for both patients and surgeons in their respective decision and advice for or against reconstructive surgery. From a patient perspective, the self-perceived quality of life in relation to IBR was investigated using patient-reported outcome measures (PROMs). A nationwide quality of life survey was conducted in patients who had undergone mastectomy with or without IBR (**Chapter 8**). Patients who had undergone IBR following mastectomy reported a better quality of life on important psychosocial, sexual and physical well-being domains than patients who had received a conventional mastectomy.

Clinical auditing of breast cancer care in the Netherlands: structuring the outer circle

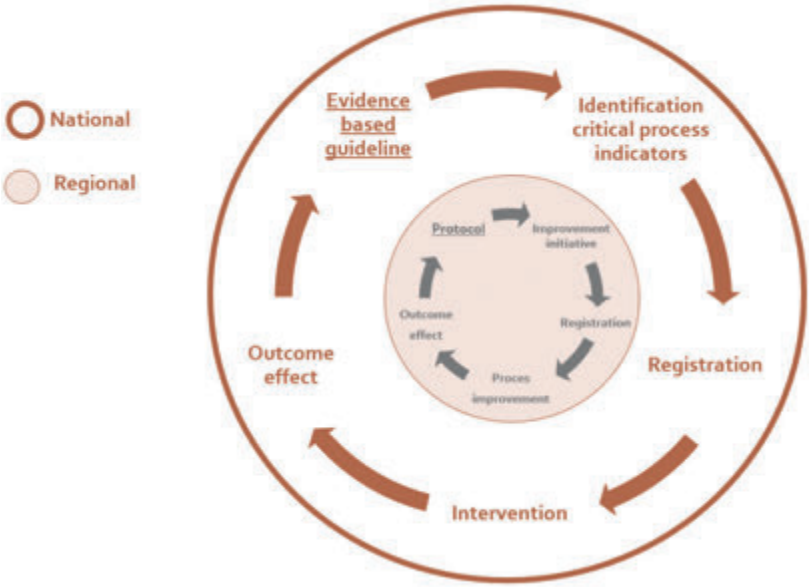
The prelude to the institution of the NBCA was the initiative of the National Health Care Inspectorate to query individual hospitals about the rate of tumor positive margins following breast conserving surgery. The publication of the raw data led to much confusion and it proved to be a poor indicator, because the definition of positive margins turned out to be interpreted very differently by the respective institutions.[4]

After the first year following the initiation of the NBCA and with the introduction of a clear definition of a tumor positive margin, the rate of tumor positive margins following breast conserving surgery proved to be very low and for all participating hospitals well within the confidence interval of the predefined norm. The subsequent publication of the annual results of this indicator and other parameters objectively improved quality of diagnostic work-up and local treatment of breast cancer patients.

From the start of the NBCA in 2011, quality indicators have been adjusted and refined, new ones developed and others abolished, aiming for clearer definitions of process and outcome indicators. Quality parameters should be unambiguous and meaningless indicators should be abandoned. The rate of BCPP, a multidisciplinary indicator of local outcome and an alternative to the mere breast conserving surgery rate well illustrates the continuing adjustment of the Audit's quality parameters. The development of other surgical and non-surgical indicators (e.g. indicators for side-effects related to radiotherapy or chemotherapy) remains "work in progress". Ideally, locoregional recurrence and survival data should become accessible in relation to NBCA data as well. Linking the NBCA data with data in the Netherlands Cancer Registry (NCR) may achieve this without the additional work of collecting more long-term follow-up data.

Measuring quality of care is in itself not a unique concept. Breast cancer audits also exist in other countries like Sweden[5], Australia[6], New Zealand[6] and the United Kingdom[7]. In the United States of America, other databases are used to investigate quality of care to a certain extent.[8] In our country, the NCR has been collecting information regarding treatment and outcomes of breast cancer since 1989 by specially trained data-managers who periodically visit all hospitals in the Netherlands.[9] The NBCA is a result of the collaboration between the Comprehensive Cancer Organization the Netherlands (IKNL), which facilitates the NCR, and the Dutch Institute for Clinical Auditing[10], which facilitates the NBCA. The NBCA has the strength of being initiated by clinicians themselves with drive to improve outcomes of care. It has led to a multidisciplinary, nationwide audit which annually delivers public reports of patient, treatment, and outcome data. Moreover, feedback in the context of benchmark results is provided to individual hospitals and their clinicians treating breast cancer patients, and also an update of the quality parameters. The ongoing process of structuring and restructuring this "outer circle" (**Figure 1**) of the NBCA serves as a quality monitor on a national level and provides a basis to conduct a "Plan Do Check Act" cycle in individual hospitals for the "inner circle".

Figure 1. Outer circle; the Plan Do Check Act cycle on a national level using clinical audit data for improvement of breast cancer care.



The interplay between clinicians and the other stakeholders in the management of the NBCA comes with challenges inherent to the differing perspectives of all participants. The common goal of quality assurance through consistent measurement is evidently acknowledged by all. Yet, while most clinicians strive for optimal outcomes in their individual institutions and acknowledge a reduction in undesirable hospital variation is an important goal, patients and insurance companies at the same time may assign value to observed differences between institutions. They seek discriminative information to identify best practices for their treatment or purchasing for contracting institutions. This "constructive friction" has hitherto strengthened the NBCA.

Interpreting NBCA results

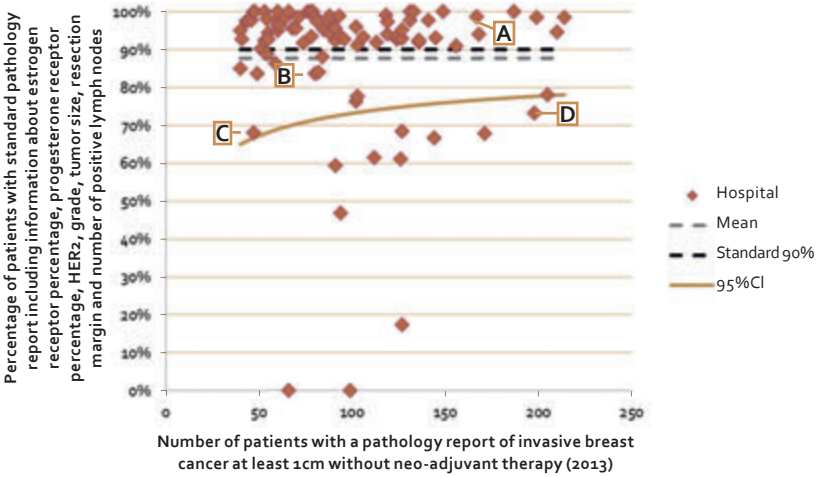
Once quality is unambiguously defined, and a standard of care is translated into a quality indicator with a norm, NBCA results reflect valid and valuable time trends in the delivered breast cancer care in the Netherlands and identify those

institutions that adhere to a predefined quality level. The NBCA has proven its merit by objectifying improvements in the complete tumor excision rates of breast conserving surgery and in radiological and pathological work-up, which underscore the current quality of breast cancer care.[11] Furthermore, a more consistent use of radiotherapy boost was objectivated following publication of national guidelines[12] as well as a decrease in axillary surgery since 2011.[13]

With respect to the identification of true outliers, reality is rather unruly. First, the NBCA usually publishes its annual quality indicator results in funnel plots that depict the indicator for every individual hospital with a certain patient volume within a funnel of 95% confidence intervals corresponding to the number of patients. In a country with approximately 90 hospitals, it is a statistical certainty that two or three hospitals will have divergent results suggesting underperformance, while their results are based on mere coincidence. To overcome this risk of incorrectly identifying underperformers as well as erroneously pointing out best practices, annual benchmark results can be merged by presenting institutional results over a longer time period. This results in tapering of the confidence interval which will enhance interpretation of an institution's audit result. Second, the funnel shaped confident intervals remain at times difficult to explain in particular to the external stakeholders. **Figure 2** shows the quality indicator "percentage of standardized pathology reports for patients with invasive breast cancer". Hospital A (98%) has an unequivocal satisfactory outcome compared to the standard of 90%. Hospital B (83%) is below the standard, but still within the corresponding 95% confidence interval. But for the general public it is less evident that the performance of hospital D (73%) is worse than the performance of hospital C (68%). The provision of quality indicators with funnel plots gives a comprehensive view compared to percentages alone, but also demonstrate that the number of patients should be sufficient.

A standardized pathology report addresses estrogen receptor-, progesterone receptor-, and HER2-status, malignancy grade, tumor size, margin involvement and number of positive lymph nodes (when sentinel node procedure or axillary node dissection was performed)

Figure 2. Funnel plot of variation between hospitals in the percentage of patients diagnosed with invasive breast cancer and with a standardized pathology report. The 95% confidence intervals are displayed around the standard (90%).



In close cooperation with the stakeholders, proper definitions of standards, statistical limitations of data analysis, thorough exploration and interpretation of results are responsibilities of the Clinical Audit Board that accompany its task to publish annual NBCA results.

Within the NBCA, not only quality indicators with clear standards are monitored, but also data are collected regarding the care of all involved disciplines. Much variation is observed in this data and the observed variation may reflect better or innovative care. In many cases the reasons of this variation and a possible association with quality of care are unclear. In that perspective, variation of IBR was extensively investigated in this thesis while others have studied the use of neo-adjuvant chemotherapy[14], radiotherapy[12] and the use of Magnetic Resonance Imaging (MRI)-scanning in the work-up of breast cancer. Current guidelines advise to use MRI-scanning in case of discrepancy between clinical examination and radiology results in patients with lobular carcinoma or high grade ductal carcinoma in situ (DCIS) with an indication for breast conserving surgery,[15] but there is not a clear standard for its use and this lack of consensus is reflected in the observed use of MRI-scanning. Evaluation of NBCA

data revealed that MRI-scanning increased the number of mastectomies for ductal carcinomas, but decreased the mastectomy rate for lobular cancers.[16] The opposite was found after neo-adjuvant chemotherapy, with decreased mastectomy rates for ductal carcinomas, but not for lobular carcinomas.[17] With evidence-based medicine as cornerstone for initiation of guidelines, this practice-based evidence of observed variation provides feedback on actual performances and strengthens the national guidelines (structuring the outer circle, **Figure 1**).

These results show the delicate balance and weighing of audit results in terms of addressing quality of care, and demonstrate the importance of clear and uniform guidelines. Then again, it is not a goal in itself to eradicate all variation and set norms, because variation may also help us to explore new practice patterns and to learn from each other.

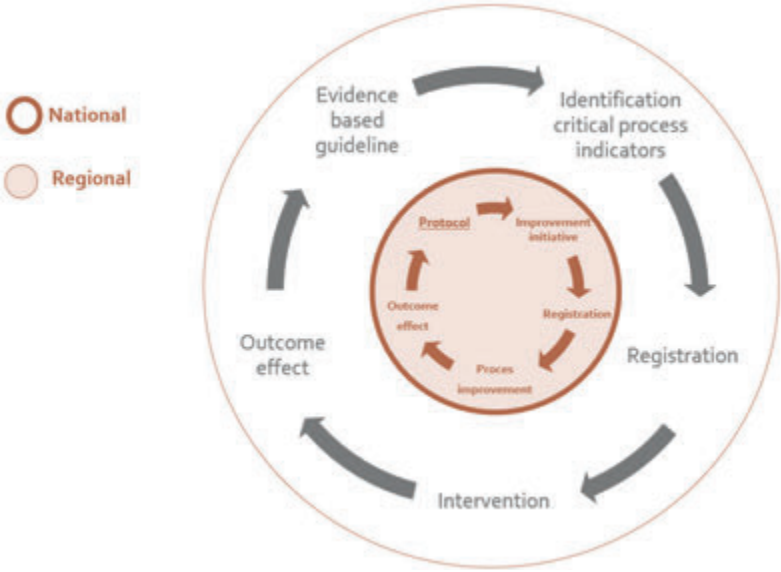
Strengthening the inner circle: the role of Patient-Reported Outcomes Measures (PROMs)

The need for incorporating PROMs in multidisciplinary registries such as the NBCA was called for by patients shortly after the initiation of the NBCA. Adding items that reflect the effects of their disease and its treatment on quality of life enhances the quality overview that the NBCA can deliver for an institution. In addition, the consequences of side-effects of local and systemic treatment, re-interventions, and complications such as breast implant removal or revision due to infection or capsular contracture on patients' psychosocial or sexual well-being, body-image and other quality of life domains may be evaluated.

The additional value of registering PROMs within the context of the NBCA speaks for itself. More important than assessing outcomes using PROMs on a national level is their use in the intimacy of the doctors' office where information regarding other patients' experiences with certain treatments and self-perceived quality of life may better guide shared treatment decisions for the individual patient. Also, PROMs may be used during a patient journey or treatment to compare their quality of life with earlier evaluation moments or with other patients within a similar time frame during an identical treatment. By doing so, this information leads to a greater insight in the effect of the

disease or treatment on perceived quality of life. Some hospitals have started using these PROMs and questionnaires which patients periodically fill out to give them tools when they have to make decisions regarding their treatment. As such, adding results from PROMs have the potency to enhance the inner circle of auditing, i.e. the PDCA cycle in which patients and doctors reflect on the results of and experience with the care that is provided in the institution where the patient is treated (**Figure 3**). By strengthening this inner Audit circle, we will truly live up to the legacy of Ernest A. Codman.

Figure 3. Inner circle; the Plan Do Check Act cycle on a regional and individual hospital level using clinical audit data for improvement of breast cancer care.



With the constitution of a multidisciplinary nationwide audit such as the NBCA, real-world data is disclosed, not only for clinicians, but also for other stakeholders and most importantly for patients. The audit data reveal a good quality of current breast cancer care and areas for improvement with the potential to learn from best practices. With the implementation of PROMs, steps are being made to use these data for personalized medicine, where the data could be used for treatment decisions and self-monitoring of recovery; steps that are essential in achieving an ever-higher level of quality of received care.

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CHAPTER 10

Samenvatting

SAMENVATTING

Meer dan een eeuw geleden werd het systematisch evalueren van medische behandelresultaten voor het eerst beschreven door Ernest A. Codman.[1] In zijn tijd was het evalueren en verbeteren van de gezondheidszorg door zorgprocessen te meten een vooruitstrevende gedachte.

Dat is heden ten dage anders. Tegenwoordig zijn velen van mening dat het analyseren van gegevens van behandelde patiënten een belangrijk onderdeel is in de "Plan Do Check Act (PDCA)-cyclus", waarmee de kwaliteit van zorg kan worden verbeterd.[2] Terwijl clinici en ziekenhuizen hun eigen prestaties ten opzichte van collegae willen evalueren en verbeteren, pleit de samenleving voor transparantie van de kwaliteit van de zorg, zodat patiënten op basis van betrouwbare informatie een zorgaanbieder kunnen kiezen. Ook andere belanghebbenden zoals zorgverzekeraars en de Inspectie Gezondheidszorg en Jeugd (IGJ) vragen om transparantie van de kwaliteit van de zorg in ziekenhuizen.

In Nederland werd de behoefte aan het meten van kwaliteit van zorg actueel vanwege een door de IGJ geïnitieerd onderzoek aan het begin van deze eeuw naar een mogelijke relatie tussen het aantal behandelde patiënten met een oncologische aandoening en de resultaten van de verleende zorg.[3] Mede om die reden werd voor verschillende chirurgisch oncologische aandoeningen een landelijke kwaliteitsregistratie, Clinical Audit genaamd, geïmplementeerd.

In 2011 resulteerden de inspanningen van een aantal clinici in de oprichting van een landelijke borstkankeraudit; de NABON Breast Cancer Audit (NBCA). De audit kenmerkt zich door zijn multidisciplinaire karakter met vertegenwoordigers van alle betrokken specialismen en belanghebbenden (patiënten, verzekeringsmaatschappijen, IGJ). Om inzicht te krijgen in alle aspecten van multidisciplinaire zorg voor borstkankerpatiënten werden initieel 32 kwaliteitsindicatoren ontwikkeld (**Hoofdstuk 2**). Deelname van alle Nederlandse ziekenhuizen werd binnen twee jaar bereikt. Dit resulteerde in NBCA-gegevens van in totaal 56.927 patiënten die tussen 2011 en 2014 behandeld werden

vanwege de diagnose borstkanker. Veel indicatoren toonden verbeteringen in de eerste vier jaar van de registratie: het percentage patiënten dat werd besproken in een multidisciplinair teamoverleg steeg van 83% naar 98%, het gebruik van de radiologische BI-RADS (Breast Imaging-Reporting and Data System)-classificatie bij beeldvormend onderzoek bij patiënten met borstkanker steeg van 97% naar 99%, een toename werd gezien van het percentage patiënten waarbij het pathologieverslag alle klinisch relevante items bevat (van 83% naar 97%), evenals een afname van het percentage tumor-positieve marges na een eerste borstsparende operatie voor borstkanker van 5,9% naar 4,6%.

Het percentage patiënten dat borstsparende chirurgie onderging bleef stabiel gedurende deze vier jaar. Het idee leefde dat alleen het percentage borstsparende operaties onvoldoende representatief was als maat voor het esthetische resultaat van de lokale borstkanker behandeling. De uitkomstparameter "breast-contour-preserving procedure" (BCPP) werd gedefinieerd als een alternatieve lokale uitkomstparameter (**Hoofdstuk 3**). BCPP omvat meerdere behandelstrategieën die de contour van de borst behouden of herstellen. Naast borstsparende chirurgie als eerste behandeling, betrof dat ook borstsparende chirurgie na neo-adjuvante chemotherapie en borstamputatie gecombineerd met een directe borstreconstructie. Hoewel het percentage patiënten dat borstsparende chirurgie als eerste behandeling voor borstkanker onderging in de loop van de tijd stabiel bleef, steeg het percentage patiënten dat een BCPP onderging van 63% in 2011 naar 71% in 2015. Deze stijging was gerelateerd aan een stijging van het aantal borstsparende operaties na neo-adjuvante chemotherapie en van het aantal directe borstreconstructies na borstamputatie. Het BCPP-percentage was vergelijkbaar voor de meeste leeftijdscategorieën, maar binnen die categorieën verschilden de verhoudingen wel. Borstsparende behandeling na neo-adjuvante chemotherapie en een borstamputatie gecombineerd met een directe reconstructie werden vaak op jonge leeftijd uitgevoerd en de percentages van deze strategieën namen af met het toenemen van de leeftijd. Op oudere leeftijd werd vaker een 'klassieke' borstsparende operatie uitgevoerd.

Uit de gegevens van de NBCA kwam naar voren dat een directe borstreconstructie gemiddeld werd uitgevoerd bij 17% van alle patiënten die een borstamputatie ondergingen. Dit percentage varieerde in de 92 ziekenhuizen tussen 0% en 64%. Deze variatie in het uitvoeren van een directe borstreconstructie was de aanleiding voor het onderzoek in de **Hoofdstukken 4, 5** en **6**. Er werd in deze hoofdstukken gekeken naar kenmerken van de behandelde patiëntenpopulatie, kenmerken van de tumor, kenmerken van het ziekenhuis en de ideeën van artsen als potentiele factoren die deze variatie zouden kunnen verklaren.

Case-mix correctie is een statistische methode om behandelingen in ziekenhuizen te kunnen vergelijken indien ziekenhuizen een verschillende patiëntenpopulatie hebben. Indien in ziekenhuis A veelal patiënten komen met grotere, agressievere tumoren in de borst of indien er veel meer oude patiënten worden behandeld ten opzichte van de patiënten die in ziekenhuis B een behandeling krijgen, dan kan het zo zijn dat in ziekenhuis A vaker een borstamputatie verricht wordt. Met case-mix correctie wordt dit effect gecorrigeerd. Na correctie van de zogenoemde case-mix voor patiënt- en tumorfactoren die geassocieerd zijn met een hoger percentage directe borstreconstructies (zoals jonge leeftijd, multifocale tumor, kleine tumorgrootte, lage graad van maligniteit, geen betrokkenheid van lymfeklieren), was er nog steeds grote variatie tussen de ziekenhuizen (0% tot 43%; **Hoofdstuk 4**). Een vervolgstap was daarom om organisatorische factoren van ziekenhuizen te vergelijken voor alle ziekenhuizen in Nederland (**Hoofdstuk 5**). Factoren die het gebruik van directe borstreconstructies bevorderen waren: het ziekenhuistype (in perifere ziekenhuizen werd vaker een directe borstreconstructie uitgevoerd in vergelijking met universitaire ziekenhuizen), de aanwezigheid van meer plastisch chirurgen in een ziekenhuis die betrokken werden bij reconstructieve borstchirurgie, het aansluiten van een plastisch chirurg bij het preoperatieve multidisciplinaire teamoverleg en het percentage borstamputaties dat in het ziekenhuis werd uitgevoerd (in een ziekenhuis waar meer borstamputaties werden verricht werd ook vaker een directe borstreconstructie verricht).

Vervolgens werd de invloed van de betrokken medisch specialismen bestudeerd op de kans dat een borstreconstructie werd uitgevoerd. Aangezien de beslissing om

een directe borstreconstructie te ondergaan wordt genomen door patiënten naar aanleiding van gesprekken met een oncologisch chirurg en plastisch chirurg, werden meningen en attitudes van deze behandelaars over directe borstreconstructie onderzocht in een enquête-onderzoek (**Hoofdstuk 6**). Plastisch chirurgen meldden vaker patiëntgerelateerde risicofactoren voor wondgenezingsproblemen als een belangrijke contra-indicatie voor het uitvoeren van een directe borstreconstructie, terwijl oncologisch chirurgen vaker oncologische contra-indicaties rapporteerden als reden om een directe borstreconstructie af te raden. Overeenstemming tussen de verschillende artsen over indicaties en contra-indicaties voor directe borstreconstructie kan de patiëntvoorlichting en gedeelde besluitvorming (shared decision-making) verbeteren.

Ook patiënten werden bevraagd naar hun ervaringen in de aanloop naar een borstamputatie al dan niet gecombineerd met een directe reconstructie. Hieruit kwam naar voren dat het informeren van patiënten over een directe borstreconstructie resulteerde in een 14 keer hogere kans om ook daadwerkelijk een reconstructie van de borst na borstamputatie te ondergaan. Dit benadrukt het belang voor artsen om patiënten 'first and foremost' te informeren over deze behandelingsoptie tijdens het besluitvormingsproces rondom de chirurgische borstkankerbehandeling (**Hoofdstuk 7**).

Naast de medische en technische overwegingen is kennis over de kwaliteit van leven van patiënten die een directe borstreconstructie hebben ondergaan belangrijk voor zowel patiënten als chirurgen bij de afweging om wel of niet reconstructieve chirurgie te ondergaan of aan te bieden. Vanuit een patiëntperspectief werd de kwaliteit van leven in relatie tot het ondergaan van een directe borstreconstructie onderzocht met behulp van patiënt gerapporteerde uitkomstmaten (patient-reported outcome measures; PROMs). Een landelijk onderzoek naar de kwaliteit van leven werd uitgevoerd bij patiënten die een borstamputatie hadden ondergaan met of zonder directe borstreconstructie (**Hoofdstuk 8**). Patiënten bij wie een directe borstreconstructie werd uitgevoerd meldden een betere kwaliteit van leven op belangrijke psychosociale, seksuele en fysieke welzijnsdomeinen vergeleken met patiënten die een borstamputatie zonder reconstructie hadden ondergaan.

Met de oprichting van een multidisciplinaire landelijke audit zoals de NBCA worden de diverse zorgprocessen die deel uitmaken van een complexe multidisciplinaire behandeling inzichtelijk gemaakt. Dit is niet alleen relevant voor clinici en patiënten, maar ook voor andere belanghebbenden, zoals ziekenhuisorganisaties, verzekeraars en de overheid. De gegevens van de NBCA tonen een goede en nog altijd verbeterende kwaliteit van de huidige zorg voor patiënten die zijn gediagnosticeerd met borstkanker. Daarnaast geeft de registratie inzicht in deelgebieden waar nog steeds ruimte voor verbetering is. Met de implementatie van PROMs worden verdere stappen gezet om ook de resultaten van de behandeling en de door de patiënt ervaren kwaliteit van leven te meten. Deze PROMs kunnen worden gebruikt voor beslissingen over een gewenste behandeling in de spreekkamer, waarmee het begrip shared decision-making verder gestalte wordt gegeven, alsmede bij het zelf-evalueren van herstel.

Door het continue meten, terugkoppelen en acteren op de gevonden data op zowel nationaal niveau alsmede in de spreekkamer zal het erfgoed van Ernest A. Codman zeker worden waargemaakt.

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CHAPTER 11

Curriculum Vitae
Author's list of publications
Dankwoord

CURRICULUM VITAE

Annelotte van Bommel was born on November 17, 1986 in Rotterdam, the Netherlands. In 2005 she graduated from Erasmiaans Gymnasium, Rotterdam. She went to medical school at Utrecht University. Her passion for traveling through Africa was realized in 2009, when she was able to go to Malawi with a good friend for a rotation in gynecology at the Queen Elizabeth Hospital in Blantyre and the Holy Family Mission Hospital in Phalombe.

With a special interest in plastic surgery, she wrote her first case report under the supervision of dr. P.P.A. Schellekens, University Medical Center, Utrecht. She continued with various research projects at Birmingham Children's Hospital, United Kingdom, under the supervision of dr. A. Jester (plastic and hand surgeon).

Annelotte graduated from medical school in 2012. After a short period as resident not in training at the department of surgery of the Diakonessenhuis Utrecht (dr. T. van Dalen), she embarked on a new phase; her PhD research that led to this thesis at the Leiden University Medical Center. Under the supervision of prof. dr. R.A.E.M. Tollenaar (surgeon at Leiden University Medical Center), dr. T. van Dalen and prof. dr. M.A.M. Mureau (plastic surgeon at Erasmus Medical Center, Rotterdam), she combined scientific research using the data of the NABON Breast Cancer Audit (NBCA) with coordination of the NBCA and several other national audits initiated by the Dutch Institute for Clinical Auditing (DICA).

One step further in measuring quality of care was defining the outcomes that matter most to patients, a step so logical, but until that moment not yet taken. In 2014, Annelotte had the opportunity to work as a project leader at the International Consortium for Health Outcomes Measurement (ICHOM) in Boston, United States of America. She developed the Advanced Prostate Cancer and Lung Cancer standard sets and she counseled the Breast Cancer and Colorectal Cancer standard sets. The drive to inform other young clinicians about Value Based Healthcare led to the organization of a two-day masterclass.

Returning to the Netherlands at DICA, Annelotte trained with four colleagues (close friends now) to cycle 1,400 kilometers across the Alps from Italy to Rotterdam in the Tour for Life in 2015 to raise money for cancer research.

In 2016, Annelotte started her postgraduate training in plastic surgery with two years of general surgical training at the Diakonessenhuis Utrecht. Continuation of her training in plastic surgery followed at the plastic and reconstructive surgery department of the University Medical Center in Utrecht.

She is able to stay involved with measuring and improving quality of care by participating in the scientific committee of the Dutch Breast Implant Registry. Also, together with five other trainees, she continues to organize conferences for the non-profit foundation "Kortjakje".

Currently, she is working as a trainee in plastic surgery at the plastic and reconstructive surgery department of the St. Antonius Hospital in Nieuwegein.

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