

## Patterns of care over 10 years in young breast cancer patients in the Netherlands, a nationwide population-based study

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### ABSTRACT

**Introduction:** Each year, around 600 young (<40 years) breast cancer (BC) patients are registered in the national NABON Breast Cancer Audit (NBCA). The aim of this study is to compare patient and treatment characteristics of young and older age BC patients over time with a focus on outcome of quality indicators (QIs). Furthermore, we analysed whether de-escalation trends of treatment can be recognized to the same degree in both patient groups. **Material and methods:** From October 2011 to October 2020 all patients treated for stage I-III invasive BC were included. Tumour characteristics, treatment variables and outcome of QIs of two age categories young (<40 years) and older patient (≥40 years) were analysed. **Results:** In total 114,700 patients were included: 4.6% young patients and 95.4% older patients. Young patients more often presented with a palpable mass, higher stage, and triple-negative BC. Overall, young patients more often started with neoadjuvant systemic treatment (NST) (54.3% vs. 18.6%) and a greater proportion of the young patients retained their breast contour after surgery (73.5% vs. 69.3%). De-escalation trends such as decrease in axillary lymph node dissections and in the use of boost were observed. The omission of radiation treatment after breast conserving surgery was only observed in older patients. **Conclusion:** Although this study shows that young women more often present with unfavourable tumours, therapeutic procedures are performed with a higher adherence to the QIs than for older patients and young women do benefit from some de-escalation trends to the same extent as older patients.

### 1. Introduction

Breast cancer (BC) is the most common type of cancer in women in the Netherlands and one of the most common cancers in young women (<40 years) [1,2]. Each year, 600 new young patients (4.5% of all new BC patients) are registered in the NABON Breast Cancer Audit (NBCA), a national multidisciplinary audit that started in the Netherlands in 2011 [3]. The main aim of the NBCA is to monitor the quality of BC care by compiling a multidisciplinary set of quality indicators (QIs), drafted by mandated members of all medical associations involved in BC care, patient advocates, The Breast Cancer Patients Association (BVN) [4] and

the Dutch health insurance companies (ZN) [5]. The results of these QIs are reported on hospital level enabling comparison and reflection. Based on the results, this set of QIs is adapted on a yearly basis. All Dutch hospitals participate in the NBCA [3].

Because of the increased complexity of BC care, a multidisciplinary approach is required for optimal disease management. This approach has resulted in improved overall prognosis and local disease control, enabling several de-escalation trends such as breast-conserving therapy (BCT) and performing less extensive axillary surgery [6–10]. Systemic treatment is increasingly being used in the neoadjuvant setting to tailor locoregional treatment and currently new trials are designed to even

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de-escalate systemic treatment [11–13]. De-escalation trends in radiation therapy that are currently being investigated are omission of the boost dose [14] and applying partial breast irradiation [15].

Given the more aggressive tumours found in young BC patients (<40 years of age) [6–9] combined with the more aggressive treatment, it is not known whether younger BC patients benefit to the same extent from these (loco regional) de-escalation trends as older patients.

The aim of the current study is to compare patient and tumour characteristics, and types of treatment over time between the young and older age groups with a focus on the adherence of the NBCA QIs as well as the implementation of treatment de-escalation trends.

### 1.1. Material and methods

#### 1.1.1. Study design

We conducted a retrospective analysis using data from the NBCA [3]. In the NBCA, all surgically treated BC patients above the age of 18 years with primary invasive BC or ductal in situ carcinoma (DCIS) in the Netherlands are registered. Exclusion criteria for the NBCA registration are patients who had any prior breast surgery for BC, patients with Lobular Carcinoma In Situ, Phyllodes tumours, sarcomas and lymphomas.

#### 1.2. Patient selection and collected parameters

Patients with stage I-III (according to the eighth edition of American Journal Committee of Cancer (AJCC)) invasive BC, from all different Dutch hospitals, registered from October 2011 to October 2020 were included. Two age categories were analysed: young group (<40 years) and older group (≥40 years). Data from the NBCA dataset include demographic variables, tumour and treatment variables see Appendix 1. No formal consent from an ethics committee in the Netherlands was required for this retrospective study, which is in accordance with the Central Committee on Research involving Human Subjects.

##### 1.2.1. NBCA quality indicators

Since 2011 the NBCA multidisciplinary QI set, drafted by mandated members of all medical associations involved in BC care, is used by the national health department to monitor the quality of BC care [3]. We have chosen to evaluate the most recent QIs in this study (Table 1).

##### 1.2.2. Statistical analyses

Two age categories were analysed: a young group (<40 years) and an older group (≥40 years). This selection was made because no difference was seen in patient and tumour characteristics under the age of 40 years. By grouping the patients by their tumour stage, it was possible to

**Table 1**  
NABON Breast Cancer Audit quality indicators 2019.

NBCA Quality Indicator 2019	
Indicator Description	Department
Breast MRI in patients treated with NAC	Radiology
Tumour-positive margins after first primary breast conserving surgery for invasive breast cancer	Surgery
Breast contour preserving procedure*	Surgery
Immediate breast reconstruction after first ablative surgery	Surgery
Consultation with radiation oncologist prior to NAC	Radiotherapy
Radiotherapy for locally advanced breast cancer (excluding T3N0) treated with mastectomy	Radiotherapy
Transit time between diagnosis and primary treatment (NAC or primary surgery)	Multidisciplinary

NBCA, NABON Breast Cancer Audit; neoadjuvant chemotherapy, NAC, neoadjuvant chemotherapy \* Since 2015, the quality indicator breast contour preserving procedure is used in the NABON Breast Cancer Audit as a parameter to encompass all strategies to preserve breast contour; 1. primary BCS, 2. BCS after NAC, and 3. mastectomy with IBR [14].

distinguish between diagnosis and treatment in both age groups. To analyse trends in applied treatment, we compared data from 2011 until 2015 with data from 2016 until 2020, considering that the COVID-19 pandemic has affected the patient volume and the treatment of BC patients. Descriptive analyses were used to show patient, tumour, and treatment characteristics for women with stage one to three BC. Categorical variables were analysed using the chi-square test, and continuous variables were analysed using Student's t-test. Because information on adjuvant treatments requires a longer period (~9 months), these data for the year 2020 were not yet available. Analysis on adjuvant treatment (radiation treatment and systemic treatment) were analysed from January 1, 2012 till December 31, 2019. To evaluate treatment trends in the outcome of QIs, the  $\chi^2$  trend test was used. A p-value <0.05 was considered statistically significant. The median was used to represent the time interval between diagnosis and first treatment. All analyses were performed using R studio version 3.6.1 (for Windows, RStudio, Inc).

## 2. Results

Between October 2011 and October 2020, 141,327 patients with BC in 82 Dutch hospitals were registered in the NBCA. Patients with stage IV disease (n = 1524), pure DCIS (n = 18,277), unknown type of operation (n = 317), tumour stage (n = 344) and date of birth (n = 17) were excluded from further analyses. Of the remaining 114,700 included BC patients, 4.6% (n = 5238) were younger than 40 years (mean age 34.7 years) and 95.4% (n = 109,462) were older than 40 years (mean age 62.4 years).

The proportion of patients <40 years stays stable over the years with yearly about 600 young patients (Fig. 1).

### 2.1. Tumour characteristics

As shown in Table 2, BC is detected by screening in 1.3% of young patients versus 39.1% in the older patient group. The majority of the young patients presented with a palpable mass (91.4%) and were diagnosed with a higher tumour grade (42.0% grade III), tumour and nodal stage compared to older patients. Majority of young patients had an invasive BC of no special type (90.5% versus 79.0% in the older patients) whereas invasive lobular cancer was barely observed in the young group; 3.1% versus 12.3% in the older patient group. Young women more frequently had a HER2 positive or triple-negative (TN) tumour compared to older women, although in both age groups hormone receptor positive BC occurred most frequently (47.9% and 75.3%).

### 2.2. Treatment characteristics

#### 2.2.1. Systemic treatment

Systemic treatment can be either given prior to locoregional treatment (neoadjuvant chemotherapy (NAC)) or thereafter (adjuvant systemic treatment). Over the ten years' time interval, in total 21.4% (24,546 of 114,700) patients started with NAC. Over the years, we observed a significant increase in the use of NAC in both young and older patients. However, this upward trend was most pronounced in the young patients (Fig. 2).

Fig. 2 shows the shift from adjuvant to NAC (excluding hormone therapy) in BC patients over the years for both young and older patients.

Especially in young women, we saw that the use of NAC, or NAC plus HER2 blockade for patients with a HER2pos subtype of BC increased dramatically over the years for all subtypes: from respectively 36.9% in 2012–2015 to 48.4% in 2016–2020 in HRpos/HER2neg patients, from 25.8% in 2012–2015 to 72.4% in 2016–2020 for HRpos/HER2pos patients; from 37.7% in 2012–2015 to 78.9% in 2016–2020 in HRneg/HER2pos patients and from 44.3% in 2012–2015 to 82.3% in 2016–2020 in TN young patients.

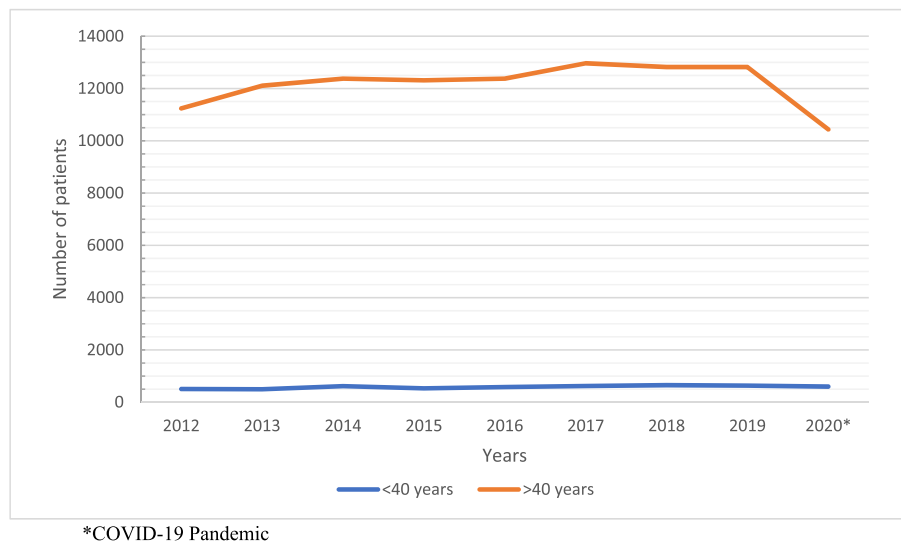


Fig. 1. The number of patients aged <40 years and ≥40 years over the years.

Table 2

Patient and tumour characteristics of 114,700 patients diagnosed with invasive breast cancer in 2012–2020 stratified by age.

		Age 18–39 years		Age ≥40 years		p-value
<b>Patient</b>		n = 5238	4.6%	n = 109,462	95.4%	
<b>Mean age</b>		34.7		62.4		
<b>Gender</b>	Male	10	0.2	785	0.7	<0.001
	Female	5226	99.8	108,666	99.3	
<b>Detected by screening<sup>a</sup></b>	No	5168	98.7	66,655	60.9	<0.001
	Yes	70	1.3	42,807	39.1	
<b>Palpable</b>	No	337	7.3	35,508	35.7	<0.001
	Yes	4248	91.4	62,217	62.6	
<b>Histology</b>	NST	4742	90.5	86,501	79.0	<0.001
	Lobular	161	3.1	13,427	12.3	
	Combination	47	0.9	3017	2.8	
	Unknown	288	5.4	6517	5.9	
<b>Grade</b>	I	467	8.9	25,648	23.4	<0.001
	II	1654	31.6	50,738	46.4	
	III	2208	42.2	25,209	23.0	
	Unknown	909	17.4	7867	7.1	
<b>Clinical tumor stage</b>	cT0	1	0.0	21	0.0	<0.001
	cT1	2152	41.1	65,723	60.0	
	cT2	2396	45.7	35,658	32.6	
	cT3	600	11.5	5972	5.5	
	cT4	87	1.7	2067	1.9	
<b>Clinical nodal stage</b>	cN0	3536	67.5	91,484	83.6	<0.001
	cN1	1376	26.3	15,457	14.1	
	cN2	89	1.7	899	0.8	
	cN3	237	4.5	1622	1.5	
<b>Clinical stage</b>	I	2115	40.4	65,412	59.8	<0.001
	II	2432	46.4	37,399	34.2	
	III	691	13.2	6651	6.1	
<b>Receptor type</b>	HR positive, HER2 negative	2510	47.9	82,386	75.3	<0.001
	HR positive, HER2 positive	872	16.6	8501	7.8	
	HR negative, HER2 positive	380	7.3	4104	3.7	
	Triple negative	1476	28.2	14,471	13.2	

NST, no special type a In the Netherlands breast cancer population screening is being performed between the age of 50 and 75 years. In patients younger than 50 years of age screening is only performed in women with a gene mutation. b Data of this item are available till the year 2019.

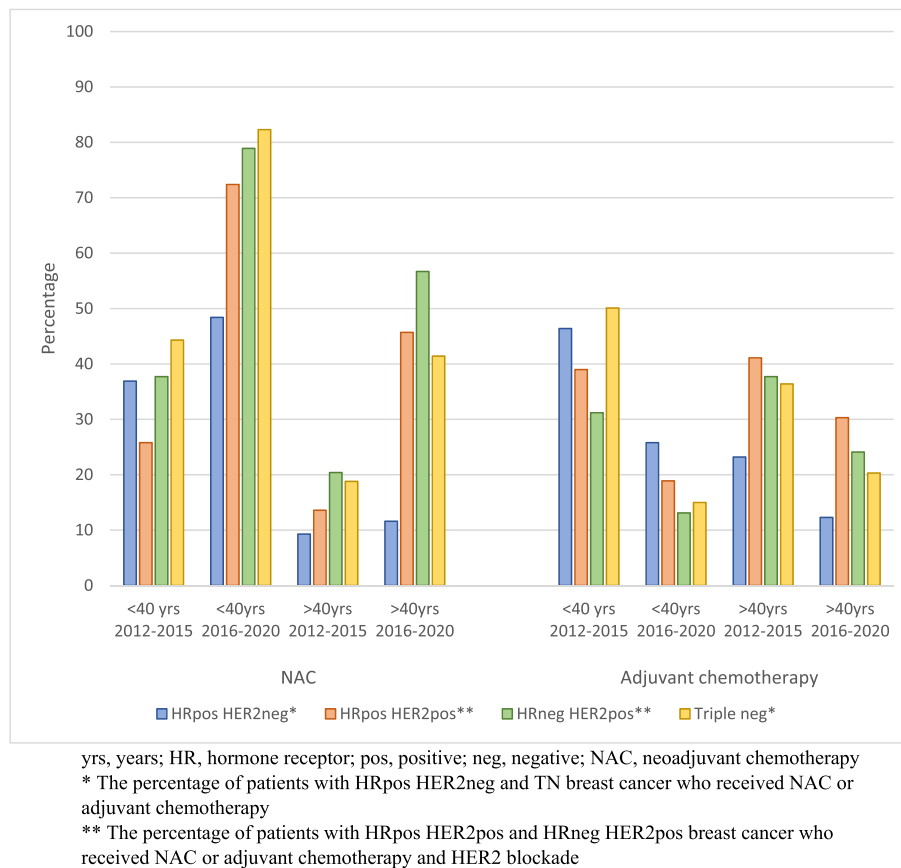
In total 21,755 (=21.0% of the 103,488 fully registered patients) received adjuvant chemotherapy or adjuvant chemotherapy plus HER2 blockade without prior, over the years a decrease was observed (Fig. 3).

When looking at all HRpos patients (n = 85,254) adjuvant hormone therapy was given in 46.2%. Over the years, an increase in the use of adjuvant hormone therapy was observed in both patient groups; in young patients from 39.4% to 77.3% and in the older patients from 28.5% to 60.0%.

2.2.2. Surgery of the breast

Of all the included patients, data of surgery was present in 112,965 (98.5%) patients. In total 79.8% of these patients (n = 90,102; n = 2750 < 40 years of age and n = 20,113 ≥ 40 years of age) underwent primary surgery and 20.2% of patients (n = 22,863; n = 2312 < 40 years of age and n = 87,790 ≥ 40 years of age) underwent surgery after neoadjuvant systemic treatment (NST).

Trends in surgery are shown in Fig. 3. In the young patient group primary surgery BCS rates increased from 43.2% to 47.2% and mastectomy with immediate breast reconstruction (IBR) rates from 26.3% to



**Fig. 2.** Trends in the use of NAC and the use of adjuvant chemotherapy, in breast cancer patients, separated by receptor type, age (<40years vs ≥ 40years) and time periods 2012–2015 vs 2016–2020.

35.0% whereas the number of mastectomies without IBR decreased from 30.5% to 17.8%.

In the older patient group primary surgery BCS rates increased from 62.0% to 69.0%, mastectomy with IBR from 6.1% to 7.2% and a decrease in the number of mastectomies without IBR from 31.9% to 23.8% was observed.

The same trends were observed in the different types of surgery after NST; both in young and older patients.

### 2.2.3. Axillary surgery

Over the years, we saw an impressive decline in axillary lymph node dissections (ALND) in both age groups in all clinical axillary lymph node stages. Of the young patients who underwent primary surgery 27.1% received ALND in 2012–2015 and 8.7% in 2016–2020. Of the young patients who had surgery after NST 39.0% had ALND in 2012–2015 and 32.6% in 2016–2020. In the older patients overall decline over time in ALND's in primary surgery was seen from 17.6% to 6.9% and after NST from 42.5% to 21.7% (Table 3). Decline in ALND was most pronounced in cN1 disease where in 2012–2015 still 67% of young patient underwent ALND compared to only 29.7% in 2016–2020.

### 2.2.4. Radiotherapy

Of all registered surgically treated BC patients 72.2% patients received RT (n = 74,760). Among the patients who underwent BCS 94.0% (n = 61,119) received RT. The results show an increase in the use of RT after BCS over the years from 92.8% in 2012–2015 to 95.5% in 2016–2019 in patients <40 years, while a decrease was visible in patients >40 years from 96.1% to 93.5%.

The proportion of patients receiving a boost decreased in both patient groups, although this trend was more pronounced in the older patients; in patients <40 years from 66.5% in 2012–2015 to 62.6% in

2016–2019 and in patients >40 years from 36.9% to 27.1%.

### 2.3. Quality indicators

An overview of the NBCA QIs per year is shown in Table 4. The outcome of most indicators was better in the young patient group compared to the older patient group. And, there was a trend towards improvement of performance on all indicators over time especially in the indicators related to preservation of the breast contour after surgery.

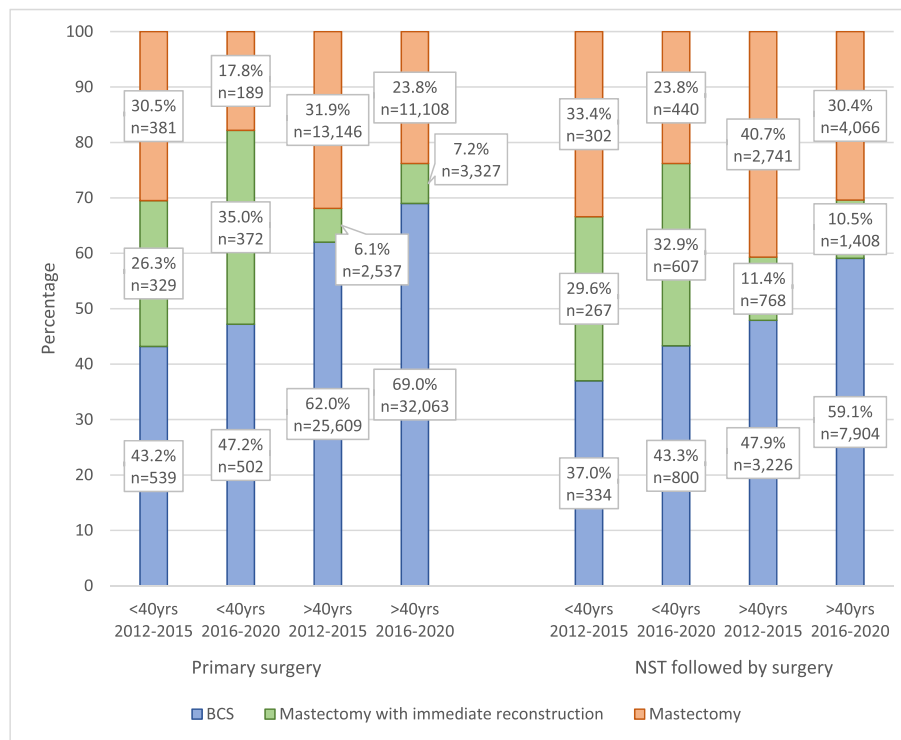
No improvement was seen in the indicator showing the percentage of involved margins after BCS. This percentage remained stable over the years: <5% in both patients groups.

Furthermore, for both age groups the transit time between biopsy and start of first treatment increased over the years; from 24 to 27 days for young patients and from 23 to 27 days in the older patients. A sub analysis shows that the increase in IBR after mastectomy requiring an additional consultation with the plastic surgeon has the greatest influence on this (data not shown).

### 3. Discussion

From this analysis of the Dutch data of all surgically treated patients with BC we now know that the number BC patients younger than 40 years remained stable over the last decade while reports in several other countries (e.g. United States) describe an increase in the number of young BC patients [16,17]. In the Netherland we treat around 600 young patients per year. This corresponds with 4.5% of the total group of newly diagnosed BC patients which is in accordance with the international literature [17–20].

Young patients are more often diagnosed with a palpable mass and a higher tumour grade and tumour and nodal stage. This can be partly



yr, years; NST, neoadjuvant systemic therapy; BCS, breast conserving surgery

**Fig. 3.** Multiple surgical treatment modalities in invasive breast cancer patients separated for age groups (<40 years vs ≥ 40 years) and time periods 2012–2015 and 2016–2020.

**Table 3**

Axilla lymph node dissection in cN0, cN1, cN2 and cN3 breast cancer patients who received primary surgery and neoadjuvant systemic therapy before surgery, separated for age groups (<40 years vs ≥ 40 years) and time periods (2012–2015 and 2016–2020).

Primary surgery												
	<40yrs 2012–2015			<40yrs 2016–2020			≥40yrs 2012–2015			≥40yrs 2016–2020		
	ALND	Total	%	ALND	Total	%	ALND	Total	%	ALND	Total	%
N0	167	1053	15.9	41	982	4.2	3735	37,292	10.0	1123	43,853	2.6
N1	165	185	89.2	49	77	63.6	3393	3818	88.9	1952	2460	79.3
N2	4	5	80.0	1	2	50.0	86	113	76.1	85	103	82.5
N3	3	6	50.0	1	2	50.0	56	64	87.5	71	82	86.6
Total	339	1249	27.1	92	1063	8.7	7270	41,287	17.6	3231	46,498	6.9
Surgery after NST												
	<40yrs 2012–2015			<40yrs 2016–2020			≥40yrs 2012–2015			≥40yrs 2016–2020		
	ALND	Total	%	ALND	Total	%	ALND	Total	%	ALND	Total	%
N0	29	413	7.0	27	100	2.7	291	2843	10.2	195	6649	2.9
N1	276	412	67.0	192	647	29.7	2148	3318	64.7	1924	5306	36.3
N2	11	18	61.1	32	59	54.2	134	168	79.8	272	474	57.4
N3	36	60	60.0	58	141	41.1	289	406	71.2	513	949	54.1
Total	352	903	39.0	309	947	32.6	2862	6735	42.5	2904	13,378	21.7

yr, years; ALND, axillary lymph node dissection; NST, neoadjuvant systemic therapy.

\* It should be taken into account that the number of N-plus patients is small, especially in the group <40 years.

explained by the fact that young patients are more likely to be diagnosed with more aggressive biological subtypes. In line with previous literature our study also showed that patients <40 years more often have BC with a TN and HER2+ subtype, although HR + tumours are relatively more common in both age groups [20–25]. Another factor that could influence higher tumour grade and tumour and nodal stage is time to diagnosis for young women. The National Breast Cancer Screening Programme does not start until the age of 50 [20]. Population based screening in patients <40 years of age is not recommended, due to the low incidence of sporadic breast cancer and the suboptimal performance

of diagnostic modalities in these patients group [26,27]. In the Netherlands, women under 50 years of age are only being screened annually when a BRCA1 or 2 gene mutation is present. Unfortunately, because gene mutations are often still missing in the NBCA data, therefore the proportion of patients with a gene mutation is not known. There is still a lot of debate whether it would be worthy to start population based breast cancer screening at an earlier age than 50, so for example at the age of 45 [28,29].

The trend analyses show that both young and older patients are increasingly treated with NST followed by locoregional treatment which



**Table 4**

Quality indicators for breast cancer health care in the NABON Breast Cancer Audit and mean percentages per year from 2012 to 2020, separate for age groups <40 years vs ≥ 40 years.

Indicator	Age group	2012–2015	2016–2020	P-value <sup>a</sup>
Breast MRI in patients treated with NAC	<40	89.0	93.6	<0.001
	≥40	85.5	90.3	<0.001
Tumour-positive margins after first BCS for invasive BC <sup>b</sup>	<40	3.3	2.7	0.663
	≥40	3.2	2.7	<0.001
Breast contour was preserved (BCPP) in pt with invasive BC	<40	68.1	77.6	<0.001
	≥40	65.7	72.2	<0.001
Breast contour was preserved by BCS as primary treatment	<40	24.5	16.7	<0.001
	≥40	52.8	53.1	<0.001
Breast contour was preserved BCS following NST	<40	14.8	26.2	<0.001
	≥40	5.6	10.7	<0.001
Breast contour was preserved by mastectomy with IBR	<40	28.9	34.7	<0.001
	≥40	7.4	8.4	<0.001
IBR with first ablative surgery	<40	53.1	62.4	<0.001
	≥40	20.5	25.5	<0.001
Prior to NST seen by radiation oncologist <sup>c</sup>	<40	62.0	70.0	<0.001
	≥40	60.3	74.3	<0.001
RT for locally advanced BC treated with mastectomy <sup>c</sup>	<40	80.6	85.6	0.139
	≥40	70.8	76.7	<0.001
Transit time between diagnosis and primary treatment (NST and surgery)	<40	24	27	<0.001
	≥40	23	27	<0.001

NAC, neoadjuvant chemotherapy therapy; NST, neoadjuvant chemotherapy and immune therapy; BCS, breast conserving surgery; BC, breast cancer; IBR, immediate breast reconstruction; RT, radiotherapy.

<sup>a</sup> Using X<sup>2</sup> test.

<sup>b</sup> Tumour positive margins defined as more than focally involved margins according to the Dutch guidelines (=tumour cells in surgical resection over an area of >4 mm, requiring re-excision).

<sup>c</sup> Analyses from one year previously, for adjuvant indicators there are no results yet available from 2020 (periods: 2012–2015 and 2016–2019).

is according to earlier reports [30–33]. In our analyses the most pronounced increase in the use of NST was seen in young patients with TN and HER2 positive tumours.

Previous studies described that young patients are more likely to undergo mastectomy [20,22]. In our study mastectomy percentages in young patients declined a few percent over time. More importantly we showed that an increasing proportion of these young patients received IBR after their mastectomy, thereby allowing these young patients to retain their breast contour.

Results from the United States using The National Cancer Database showed that young patients treated with breast conserving surgery more often received a boost than older patients, with a decrease in receiving a boost over the years in both age groups [34]. In line with the current guidelines we also found that the boost dose was more frequently given in the younger patients. And we did observe a decline in the use of the boost dose, especially in the older patient group.

The most pronounced de-escalation trend in locoregional treatment we saw in our study was the impressive decline in the percentage of ALND's that we performed in both age groups and especially in young patients with cN1 treated with NST where ALND was only still performed in 29.7% patients during 2016 and 2020 whereas in the earlier years still in 67.0% of these patients an ALND was performed. This trend is also seen in other countries [35–37].

In the Netherlands, the central government is responsible for the content and scope of the statutory health insurance package, which is available to every inhabitant of The Netherlands. The government is advised by the independent National Health Care Institute (ZiNL). The basic health insurance package includes most of the essential medical care, medications and medical devices. In this way, every citizen in the Netherlands has access to the same reimbursed care. In the Netherlands

you have many health insurances and it is up to the citizen to choose one. In this system, patients, health insurers and healthcare providers all have an important role in guaranteeing and monitoring the quality of care [38].

The NBCA, a multidisciplinary clinical audit involving BVN and ZN [4,5], it becomes possible to measure quality of breast cancer care by analysing the results of the quality indicators [3].

In the present study we looked at quality of care; over time we saw an improvement in almost all NBCA QIs, with improvements being most pronounced in the young patients. The results suggest that QIs are more strictly adhered to in young patients. This could also be attributed to the motivation of the doctor to use all available means for the younger patient. These substantial improvements in QIs within a relatively short time period, suggest that benchmarked feedback and the use of audit results can lead to new insights and catalyse quality improvement at national level.

In the era of improved prognosis, quality of life is becoming increasingly important [39–41]. In our study we looked at the NBCA QI breast contour preservation, an important aspect of retaining quality of life, especially in young women [41] and saw an upward trend in preserving the breast contour by increased numbers of breast conserving surgery and use of IBR after mastectomy in both age groups and in both primary surgery setting as well as in the groups of patients that underwent surgery after NST. This upward trend seems to be consistent with research results from the United Kingdom, although the study results do not distinguish between age and type of BC [42]. However, these results are in contrast with a national study from the United States. From, 1988 to 2016 there was a decline in breast-conserving therapy in young early-stage BC patients (from 60% to 35%) [43].

Strength of the present study is the use of population-based, externally validated data of a large number of BC patients reflecting daily practice. This study has shown that the data is suitable for observing trends over time. But there are also some limitations. The NBCA lacks information regarding type of chemotherapy which cause a significant escalation for young patients. For example introduction of dose-dense principle, adding Carboplatin in TN BC, and continuing post NAC treatment with Capecitabine in case of an incomplete remission after NST [44,45]. Also, patient and tumour characteristics that are of importance with the emergence of shared decision making and individualized BC treatment. We were unable to evaluate the patient preference and missed patients' characteristics such as family history and genetic mutations. Furthermore, the NBCA does not provide information about delayed reconstruction after mastectomy, recurrence, and survival.

**4. Conclusion**

Although this study shows that young women more often present with unfavourable BC with higher stage of disease, diagnostic and therapeutic procedures are performed with a higher adherence to the QIs than for older patients. Young women are more likely to receive NST and retain their breast-contour after surgery. Young women do benefit from de-escalation trends like fewer performed ALNDs.

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**Statement of ethics**

The Dutch Institute for Clinical Auditing (DICA) is one of the leading organizations that facilitates clinical auditing in the Netherlands. DICA offers participants in its clinical audits the possibility of submitting an application to receive data from clinical audits for the purpose of scientific research under strict conditions. These applications are assessed

at several levels.

In the participation agreement between DICA and the participants in clinical audits, to which the DICA Regulations also apply, further conditions are set for the use of data for scientific research. These conditions include that only pseudonymised or anonymised data that cannot (directly) be traced back to individual patients may be made available. The parties also agree that, in accordance with the applicable laws and regulations, the participants will set up a system of no-objection that offers the patient the possibility to explicitly object to the use of his/her data for scientific research in advance. In this way, the patient's privacy will be protected as much as possible.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.breast.2022.11.002>.

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