Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
KCE

Quality indicators in oncology: breast cancer

KCE reports 150C

Belgian Health Care Knowledge Centre
Federaal Kenniscentrum voor de Gezondheidszorg
Centre fédéral d'expertise des soins de santé
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Executive summary

INTRODUCTION

In 2004, the PROCARE project (PROject on CAncer of the REctum) was launched as a multidisciplinary, profession-driven project with as main objective to reduce diagnostic and therapeutic variability and to improve outcome in patients with rectal cancer. This goal was pursued by means of standardization of practices through guidelines, implementation of these guidelines, and quality assurance through registration and feedback. In 2005, a rectal cancer specific clinical data register was set up at the Belgian Cancer Registry (BCR). In order to allow individual feedback and national/international benchmarking, a quality indicator system was set up in 2008. Up to now, there have been two feedback rounds to the participating centres.

As a preparation to set up a quality system for oncology in Belgium, the Minister commissioned the KCE to apply the lessons learned from the PROCARE project to another frequent cancer, i.e. breast cancer, and a rare cancer, i.e. testicular cancer. The main research questions are:

1. Is it feasible to develop a quality indicator set for breast cancer and testicular cancer, making use of the available administrative databases? And what would be the added value of the Minimal Clinical Dataset (MCD) and the Minimal Financial dataset (MFD)?
2. Which methods/systems/structures are described in the literature to follow up the quality of care in oncology? This research question will be addressed in a subsequent report.

In a first phase, the national guidelines were already updated and published for both cancer types (KCE report 142 and 143). The next step consists in the development of a quality indicator set. The present report presents the elaboration of a quality indicator set for breast cancer. A second report on testicular cancer will be published in parallel.

QUALITY INDICATORS: SELECTION PROCESS AND ELABORATION

METHODS

Both OVID Medline and the grey literature were searched to identify published and validated quality indicators for breast cancer. Various sources were considered to identify grey literature, such as the National Quality Measures Clearinghouse, the Agency for Healthcare Research and Quality, Joint Commission (USA), the Clinical Indicators Support Team (UK) and the National Health Service (UK). Existing CPGs identified during the development of the breast cancer guideline were also evaluated for included quality indicators. The searches were conducted in November and in December 2009. Quality indicators derived from the recommendations of the breast cancer guideline were added to the list of quality indicators resulting from the literature search.

The selection process was done independently by 7 experts. Selection criteria were: reliability, relevance, interpretability and actionability.

RESULTS

Globally, 229 indicators were found in the literature and 47 quality indicators were formulated on the basis of the Belgian CPG. Among the final list of 276 quality indicators, 32 were retained (Table 1).

Table 1. Final selection of breast cancer quality indicators

General indicators: outcomes		**Type of indicator**
BC1	Overall 5-year survival by stage	Outcome
BC2	Disease-specific 5-year survival by stage	Outcome
BC3	Disease-free 5-year survival by stage	Outcome
BC4	5-year local recurrence after curative surgery, by stage	Outcome
General indicators: process		
BC5	Proportion of breast cancer women discussed at the multidisciplinary team (MDT) meeting	Process
BC6	Proportion of women with breast cancer who participate in clinical trials	Process
Diagnosis and staging		
BC7	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	Process
BC8	Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy	Process
BC9	Proportion of newly diagnosed cstage I-III breast cancer women who underwent two-view mammography or breast sonography within 3 months prior to surgery	Process
BC10	Proportion of women who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment	Process
BC11	Proportion of women in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment	Process
BC12	Proportion of women in whom a ER and PgR status assessment were performed before any systemic treatment	Process
BC13	Proportion of breast cancer women with cytological and/or histological assessment before surgery	Process
BC14	Proportion of sentinel lymph nodes biopsy (SNLB) in cN0 women without contraindications	Process
Neoadjuvant treatment		
BC15	Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	Process
Surgery		
BC16	Proportion of breast cancer women who underwent an axillary lymph node dissection (ALND) after positive SNLB > 2 mm	Process
BC17	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)	Outcome
BC18	Proportion of cStage I and II women who undergo breast-conserving surgery (BCS) / mastectomy	Process
BC19	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy	Process
Adjuvant treatment		
BC20	Proportion of women with a breast cancer who are	Process

	receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen	
BC21	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer	Process
BC22	Proportion of women with hormone receptor positive invasive breast cancer or ductal carcinoma in situ (DCIS) who received adjuvant endocrine treatment (Tamoxifen/AI)	Process
BC23	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of ≥50-55% who received chemotherapy and Trastuzumab	Process
BC24	Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months	Process
BC25	Proportion of women who received radiotherapy after breast conserving surgery	Process
BC26	Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND	Process
BC27	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment	Process
BC28	Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment	Process
BC29	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	Process
Follow-up		
BC30	Proportion of women who benefit from an annual mammography after a history of breast cancer	Process
Histopathology		
BC31	Proportion of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the lymphovascular invasion (LVI) and the histologic grade.	Process
BC32	Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed	Process

QUALITY INDICATORS: MEASURABILITY

METHODS

To analyse the measurability of these indicators, 3 different databases were linked. The primary selection consisted of all women with invasive breast cancer registered in the BCR, with an incidence date cancer between 01/01/2001 – 31/12/2006. For these women, the BCR data were linked to healthcare insurance claims data from the Intermutualistic Agency (IMA) (2001-2006) and the MCD data (2002-2006). An additional selection was done using appropriate ICD-9-CM codes in the MCD-MFD database to check the exhaustiveness of the primary selection.

For each selected quality indicator, the numerator and denominator (and their respective in- and exclusion criteria) were defined and the measurability was evaluated.

For each measurable quality indicator the results per anonymized centre were produced, and the variability between centres was presented graphically by means of funnel plots.

Cox proportional hazard models (PH) were used to assess the relationship between the volume of women treated per centre and the overall 5 year-survival. For these analyses, centres were categorized as small-volume centres (< 100 women per year), medium-volume centres (100-149 women per year) and high-volume centres (≥ 150 women per year). Results were risk-adjusted for age, tumour stage (pStage and if missing, cStage) and tumour differentiation (grade).

RESULTS

Measurability of quality indicators

Of the 32 selected indicators, 13 were found to be measurable, and one was measurable using a proxy indicator. The most important reasons for not being measurable was the absence of administrative or nomenclature codes (N=12) or the absence of the procedure's or test's results in the administrative databases (N=3). Moreover, even if available in the nomenclature, codes are not always specific to a pathology or an organ (e.g. biopsy, medical imaging [CT and MRI]…), and hence, of limited use for the evaluation of diagnostic, staging or follow-up procedures. As long as sufficiently recent national data on causes of death are not available, the disease-specific survival is not measurable as such. Therefore, relative survival (observed survival / expected survival) was used as a proxy indicator.

At a national level, it is physically impossible to consult all medical records to obtain the clinical information needed to assess quality indicators related to the chemotherapy (drug[s] prescribed, dose, and duration), its indications or contraindications. However, a random sample of medical files could be selected (for example 30 in each centre) to be audited in depth at regular intervals. Similar surveys are conducted in France by the National Federation of French Cancer Centres (FNCLCC) and the Institut National du Cancer (INCa), leading to identification of action points and initiation of corrective measures.

One of the aims of the present report was to evaluate the added value of MCD data to increase the measurability of the included indicators. However, many technical problems led to an incomplete linkage of MCD data to linked BCR-IMA data. Linked BCR, IMA and MCD data could only be obtained for the years 2002-2004 and for a limited number of cases (75%). The addition of MCD helped improving measurability of indicators involving lytic bone metastases. The added value of MCD for other indicators was not demonstrated.

Indicator results on the national level

A total of 50 039 women were included in the analyses. This corresponds to 98.4% of the BCR database cases (the remaining could not be linked to IMA database).

From 2001 to 2004, a slight improvement was observed in the 5-year survival for non-metastatic invasive cancers. Positive evolutions were found for diagnostic and staging procedures, surgical procedures (proportion of surgically treated women and proportion of women who underwent breast conserving surgery), adjuvant treatment (systemic treatment and radiotherapy) for invasive breast cancer and follow-up procedures (Table 2).

Table 2. Evolution of measurable quality indicators between 2001 and 2006.

	Indicator	**Result 2001**	**Result 2006**
		N= 7 669	**N= 9 067**
	General indicators: outcomes		
BC1	Overall 5-year survival by stage • pStage I • pStage II • pStage III • pStage IV	 93% 81% 59% 30%	 93% 84% 64% 27% *(2004 results)*
	General indicators: process		
BC5	Proportion of breast cancer women discussed at the multidisciplinary team meeting (MDT)	61.4% *(2003 results)*	80.3%
	Diagnosis and staging		
BC9	Proportion of newly diagnosed cstage I-III breast cancer women who underwent two-view mammography or breast sonography within 3 months prior to surgery	84.9%	86.0%
BC12	Proportion of women in whom a ER and PgR status assessment were performed before any systemic treatment	90.5%	98.0%
BC13	Proportion of breast cancer women with cytological and/or histological assessment before surgery	50.4%	71.5%
	Neoadjuvant treatment		
BC15	Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	5.5%	18.9%
	Surgery		
BC18	Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy • Proportion of operated women • Proportion of women with BCS • Ratio BCS/mastectomy	 93.0% 55.3% 1.46	 95.8% 58.4% 1.56
	Adjuvant treatment		
BC21	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer • Chemotherapy within 4 months after surgery • Endocrine therapy within 9 months after surgery	 38.7% 37.0%	 36.9% 43.8%
BC25	Proportion of women who received radiotherapy after breast conserving surgery	82.0%	89.8%
BC28	Proportion of metastatic breast cancer women who received systemic therapy as 1st and/or 2nd line treatment	86.9%	84.3%
BC29	Proportion of women with metastatic breast cancer	88.0%	93.0%

	and lytic bone metastases who received biphosphonates	*(2002 results)*	*(2004 results)*
	Follow-up		
BC30	Proportion of women who benefit from an annual mammography after a history of breast cancer • Mean number of mammograms per patient 1 year after last treatment	1.35	1.73

The following results are discussed in more detail in the scientific report:

- Since breast cancer is a complex cancer and asks for a specialized approach, a discussion of the therapeutic approach in a multidisciplinary setting is necessary. In 2006, MDT was done for 80% of the women.
- While mammography and breast sonography are highly recommended, 14% of women had no record of these exams in the diagnostic work-up (3 months before surgery);
- The assessment of hormonal receptors (ER/PgR) before any systemic treatment, is common practice, as it was done for 98% of women in 2006, but cytological and/or histological assessment still seem to be underused before surgery (71.5% in 2006);
- Whereas European guidelines suggest that breast conservation surgery (BCS) should be achievable in 70-80% of all cases, less than 60% of all surgically treated women underwent BCS in Belgium;
- No information on the number of patients included in clinical trials is available.
- Yearly mammography with or without ultrasound is essential to detect recurrence or second primaries after treatment for breast cancer, but remains underused during follow-up, since 20% of all treated women receiving no mammography in the year following their last treatment. It is possible that physical examination or other imaging procedures, such as X-rays, CT or MRI are performed, although these tests are not recommended in asymptomatic women.

Variability between centres and volume-outcome relationship

The results showed considerable variability between centres, both for process and outcome indicators.

The average number of women per centre was rather low, as half of the hospitals treated less than 50 women per year (based on 2004-2006 data).

The 5-year survival rate was higher in high-volume centres (84%; 14 hospitals treating at least 150 women) than in small-volume centres (77%, 83 hospitals treating less than 100 women per year). When case mix was taken into account (age, tumour stage, tumour grade), women treated in small-volume hospitals had still a 20% higher probability of dying within 5 years after diagnosis than women treated in high-volume centres. Differences in process indicators between small- and high-volume centres were investigated, and the following differences could be outlined: in high-volume centres, there were more MDT consultations, more breast conserving surgery, more adjuvant radiotherapy after breast conserving surgery or after mastectomy, and a better reporting of patients' stage.

CONCLUSIONS

- The present study showed that it is feasible to implement a quality indicator set for breast cancer, covering the whole range of diagnostic and therapeutic options. Based on current nomenclature and cancer registry data, the set contains 14 measurable indicators.
- The added value of the hospital administrative discharge data (MCD) is rather limited for this quality indicator set as it improved the measurability of only one indicator (the identification of lytic bone metastases).
- This analysis, based on 2001-2006 data, shows a positive and improving overall picture of the quality of care for breast cancer women in Belgium. Survival is high for early-advanced stages and progressively decreases for more advanced stages. However, there are indications of underuse of recommended interventions having an impact on survival, recurrence or aesthetics (e.g. breast conserving surgery, radiotherapy after surgery).
- A high rate of unknown cStages and pStages was found. An improvement in the reporting of these data is essential to refine some analyses.
- This analysis also showed a wide variability in diagnostic and therapeutic approaches between centres. A graphical tool allowing an easy identification of outlying centres has been proposed. However, the fact that a centre is an outlier in a funnel plot does not automatically imply suboptimal quality of care. Possible data errors, differences in billing habits, differences in case-mix should be investigated first.
- The annual volume of women per centre is on average low, as half of the centres treated less than 50 women (volume based on period 2004-2006). Lower volume has been shown to be associated with lower survival rates. However, this is not systematically observed in all low-volume centres, a finding which asks for an in-depth evaluation of their organisational and functional characteristics. New regulations, introduced by Royal Decree on July 20th 2007, stipulate that, in order to be recognized as a Breast clinic, a centre should have treated surgically at least 100 new women per year in 2008 and 2009 and 150 new women from 2010 on. In addition, any surgeon treating breast pathology should also reach a volume of 50 surgically treated women per year.

RECOMMENDATIONS[a]

Given the large variability observed between centres in the management of breast cancer women, the implementation of the quality indicator set proposed in this study should be considered. To that end, the following actions need to be undertaken:

Data-related actions:

1. Modifications of the nomenclature

- **The nomenclature codes for CT, MRI, percutaneous biopsy and cytological assessment need to be made specific to an anatomic location.**

2. Cancer registration

- **The correct use of the 7th edition of the TNM classification and the complete registration of cTNM and pTNM at the cancer registry should be encouraged from all hospitals;**
- **The delay between the incidence year and the availability of these data for publication and research should be at 2 years or less;**
- **According to European regulation, national data on causes of mortality should be available and be made linkable to the cancer registration data within a delay of 2 years;**
- **Some variables should be added to the current list of variables with mandatory registration at the cancer registry**
  - **Local and distant recurrence: mandatory registration of recurrences should be implemented and modifications should be made to the follow-up MDT form**
  - **Recruitment in clinical trials with diagnostic and therapeutic interventions**
  - **Number of positive lymph nodes**
  - **Resection margins after surgery**
  - **Radiation dose and field (clinical target volume)**
- **Standardisation of the breast pathology report is required.**

3. Regular prospective surveys on selected topics

- **A random sample of medical files could be selected (for example 30 in each centre) to be audited in depth at regular intervals, following the example provided in France by FNCLCC and INCa.**

Research agenda

To allow the correct interpretation of the included quality indicators the following actions need to be undertaken:

1. **For each of the included quality indicators, the need for risk-adjustment should be thoroughly assessed.**
2. **For each quality indicator, appropriate cut-off values should be defined in collaboration with the College of Oncology.**

a The KCE is the only responsible for the recommendations given to the public authorities

Scientific Summary

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ABBREVIATIONS

AHRQ	Agency for Healthcare Research and Quality
ALND	Axillary Lymph Node Dissection
BCR	Belgian Cancer Registry
CNK	Code National(e) Kode
CPG	Clinical practice guideline
CT	Computerized tomography
DCIS	Ductal carcinoma in situ
ER	Estrogen receptor
ESR	European Standardised Ratio
FNCLCC	Fédération Nationale des Centres de Lutte contre le Cancer
HER2	Human epidermal growth factor receptor 2
ICD	International classification of diseases
IMA	Sickness Funds Agency (Intermutualistisch Agentschap/ L'Agence Intermutualiste)
KCE	Belgian Healthcare Knowledge Centre
KM	Kaplan-Meier
MCD	Minimal Clinical Data
MDC	Major Disease Category
MDT	Multidisciplinary team
MeSH	Medical Subject Headings
MFD	Minimal Financial Data
MRI	Magnetic resonance imaging
PET	Positron emission tomography
PgR	Progesterone receptor
PROCARE	PROject on CAncer of the REctum
RCT	Randomized controlled trial
SD	Standard deviation
SEER	Surveillance, Epidemiology, and End Results Program
SNLB	Sentinel Lymph Node Biopsy
US	United States
WLE	Wide Local Excision

1 INTRODUCTION

The instauration of a "personalised care program" for all new cancer patients is one of the initiatives of the National Cancer Plan 2008-2010. The development of these care programs, together with the follow-up of the quality of care, are among the responsibilities of the College of Oncology. To perform this task efficiently, a structure is needed that allows (1) a rapid development and update of clinical practice guidelines (CPGs), (2) the translation of these guidelines into concrete care programs, (3) and the definition and implementation of quality criteria to follow up the quality of care. At present, the College of Oncology and the KCE already collaborate for the development of CPGs. However, no such collaboration exists for the evaluation of the quality of care.

In 2004, the Belgian Section for Colorectal Surgery, a section of the Royal Belgian Society for Surgery, launched the PROCARE project (PROject on CAncer of the REctum) as a multidisciplinary, profession-driven and decentralized project (www.belgiancancerregistry.be). The main objective of this multidisciplinary project was to reduce diagnostic and therapeutic variability and to improve outcome in patients with rectal cancer by means of:

- standardization through guidelines (which were issued in 2007[1]);
- implementation of these guidelines (workshops, meetings, training);
- quality assurance through registration and feedback.

In 2005, a multidisciplinary dataset was elaborated for registration in a rectal cancer specific database at the Belgian Cancer Registry (BCR). Registration started in October 2005. In order to allow individual feedback and national/international benchmarking, a quality indicator system was set up in 2008[2]. At present, two rounds of feedback were already given to the participating centres.

The PROCARE project drew the attention of the Minister of Health. Indeed, in the National Cancer Plan 2008-2010 (http://www.laurette-onkelinx.be/articles_docs/32_initiatieven_N.pdf, accessed on November 16th 2010), initiative 9 aimed at the instauration of a "personalised care program" for all new cancer patients. The development of these care programs, together with the follow-up of the quality of care, are the responsibilities of the College of Oncology. To allow an efficient realisation of this task, a structure is needed that allows a rapid development and update of clinical practice guidelines, the translation of these guidelines into concrete care programs, and the definition and implementation of quality criteria to follow up the quality of care. At present, the College of Oncology and the KCE already collaborate for the development of clinical practice guidelines[3-5]. However, for the subsequent evaluation of the quality of care, no such collaboration exists.

As a preparation to set up a quality system for oncology in Belgium, the Minister asked the KCE to repeat the PROCARE project for a frequent cancer, i.e. breast cancer, and a rare cancer, i.e. testicular cancer. The main research questions are:

1. Is it feasible to set up a quality indicator set for breast cancer and testicular cancer using the available administrative data? More specifically, the added value of the Minimal Clinical Dataset (MCD) and the Minimal Financial dataset (MFD) will be evaluated.
2. Which methods/systems/structures are described in the literature to follow up the quality of care in oncology? This research question will be addressed in a subsequent report.

In a first phase, the national guidelines for both cancer types were updated and published earlier[6, 7]. In a second phase, a quality indicator set was developed for both cancer types. In the present report, the development of a quality indicator set for breast cancer will be discussed. The report on testicular cancer will be published in parallel.

Based on the results from the 3 exercises (PROCARE included) and the experiences in other countries, recommendations will be formulated to set up a quality system for oncology. These will be discussed in a subsequent report to be published early 2011.

2 SELECTION PROCESS OF QUALITY INDICATORS

2.1 METHODOLOGY

2.1.1 Literature search

Both OVID Medline (see appendix 7.1. for search strategy) and the grey literature were searched to identify published and validated quality indicators for breast cancer. The following sources were considered to identify grey literature:

- National Quality Measures Clearinghouse: http://qualitymeasures.ahrq.gov/
- Agency for Healthcare Research and Quality: http://www.ahrq.gov/
- Joint Commission: http://www.jointcommission.org/
- Clinical Indicators Support Team: http://www.indicators.scot.nhs.uk/
- National Health Service: http://www.nhs.uk/

Furthermore, the CPGs identified during the development of the breast cancer guideline[6] were evaluated for included quality indicators.

The main searches were conducted in November 2009. An additional Medline search for 'pattern of care' studies was done in December 2009.

2.1.2 Addition of guideline-based quality indicators

The list of quality indicators resulting from the literature search was complemented by quality indicators derived from the recommendations of the breast cancer guideline[6]. To this end, most individual recommendations were translated in at least one quality indicator.

2.1.3 Selection process

The long list of indicators, resulting from the literature search and addition of guideline-based indicators, was subjected to a formal assessment based on 4 criteria:

- Reliability: the extent to which the measure provides stable results across various populations and circumstances;
- Relevance: the extent to which important health conditions accounting for a major share of the burden of disease, the cost of care, or policymakers' priorities are reflected;
- Interpretability: the extent to which clear conclusions are possible;
- Actionability: the extent to which action can be taken by individuals, organised groups and public and private agencies to meaningfully address this issue.

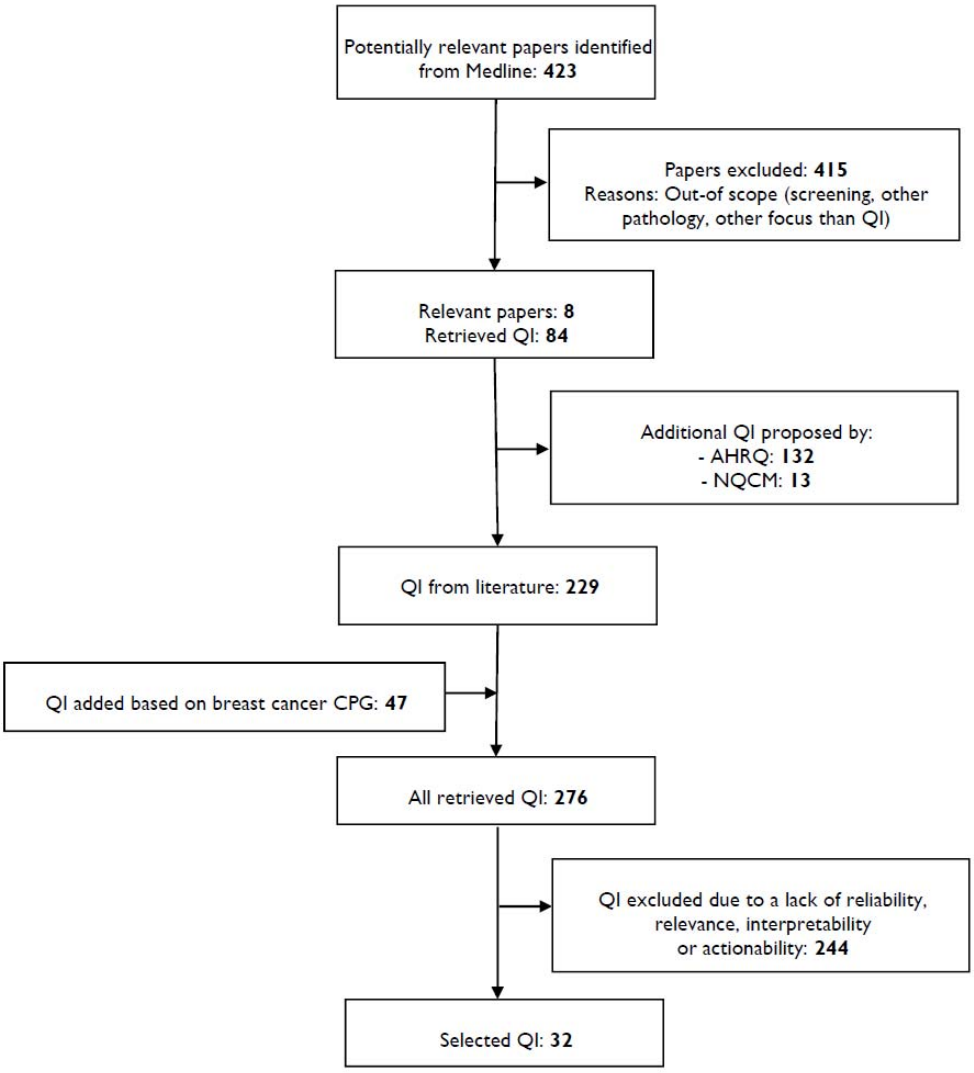
Six clinical experts and one KCE expert independently scored each indicator on these 4 criteria using a scale from 1 (strongly disagree) to 5 (strongly agree). For each indicator and per criterion, the scores were summarized in a median score, minimum score, maximum score and the percentage of '4' and '5' scores. Finally, these summary scores were used during a plenary meeting to guide the final selection of indicators.

2.2 RESULTS

The Medline search yielded 285 (November 2009) and 138 (December 2009) hits respectively. From these 423 papers, 415 were not selected since their focus was out-of-scope (quality indicators for breast cancer screening, other pathology than breast cancer, other scope than quality indicators). Eight relevant articles were retrieved that proposed 84 quality indicators[8-15]. The search in the grey literature identified 132 additional indicators proposed by AHRQ[16] and 13 additional indicators proposed by NQCM (retrieved on http://www.qualitymeasures.ahrq.gov/search/; accessed on 10th December 2009).

Based on the breast cancer guideline, 47 additional quality indicators were proposed resulting in a long list of 276 indicators (Appendix 7.2 'Overview of all identified quality indicators').

Figure 1. Selection process of breast cancer quality indicators



The evaluation scores of the 276 retrieved indicators are provided in appendix (Appendix 7.3. 'Evaluation of the long list of 276 quality indicators'). During the plenary meeting and based on these scores, the list of indicators was reduced to a final selection of 32 quality indicators (Figure 1 and Table 1). The most important criterion during this selection was relevance.

Table 1. Final selection of breast cancer quality indicators

General indicators: outcomes		Type of indicator
BC1	Overall 5-year survival rate by stage	Outcome
BC2	Disease specific 5-year survival by stage	Outcome
BC3	Disease-free 5-year survival rate by stage	Outcome
BC4	5-year local recurrence rate after curative surgery, by stage	Outcome
General indicators: process		
BC5	Proportion of breast cancer women discussed at the multidisciplinary team meeting	Process
BC6	Proportion of women with breast cancer who participate in clinical trials	Process
Diagnosis and staging		
BC7	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	Process
BC8	Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy	Process
BC9	Proportion of newly diagnosed cstage I-III breast cancer women who underwent two-view mammography or breast sonography within 3 months prior to surgery	Process
BC10	Proportion of women who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment	Process
BC11	Proportion of women in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment	Process
BC12	Proportion of women in whom a ER and PgR status assessment were performed before any systemic treatment	Process
BC13	Proportion of breast cancer women with cytological and/or histological assessment before surgery	Process
BC14	Proportion of sentinel lymph nodes biopsy in cN0 patients without contraindications	Process
Neo-adjuvant treatment		
BC15	Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	Process
Surgery		
BC16	Proportion of breast cancer women who underwent an ALND after positive SNLB > 2 mm	Process
BC17	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)	Outcome
BC18	Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy	Process
BC19	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy	Process
Adjuvant treatment		
BC20	Proportion of women with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen	Process
BC21	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer	Process
BC22	Proportion of women with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI)	Process

BC23	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of > or= 50-55% who received chemotherapy and Trastuzumab	Process
BC24	Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months	Process
BC25	Proportion of women who received radiotherapy after breast conserving surgery	Process
BC26	Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND	Process
BC27	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment	Process
BC28	Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment	Process
BC29	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	Process
Follow-up		
BC30	Proportion of women who benefit from an annual mammography after a history of breast cancer	Process
Histopathology		
BC31	Proportion of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade.	Process
BC32	Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed	Process

3 DATA SELECTION

Since this report is part of a larger project, that also includes the development of a quality indicator set for testis cancer, the data selection was done for both tumours at the same time. Therefore, the description of the data selection process also includes data on testis cancer.

3.1 PRIMARY SELECTION

From the cancer registry database (BCR), the following records were selected:

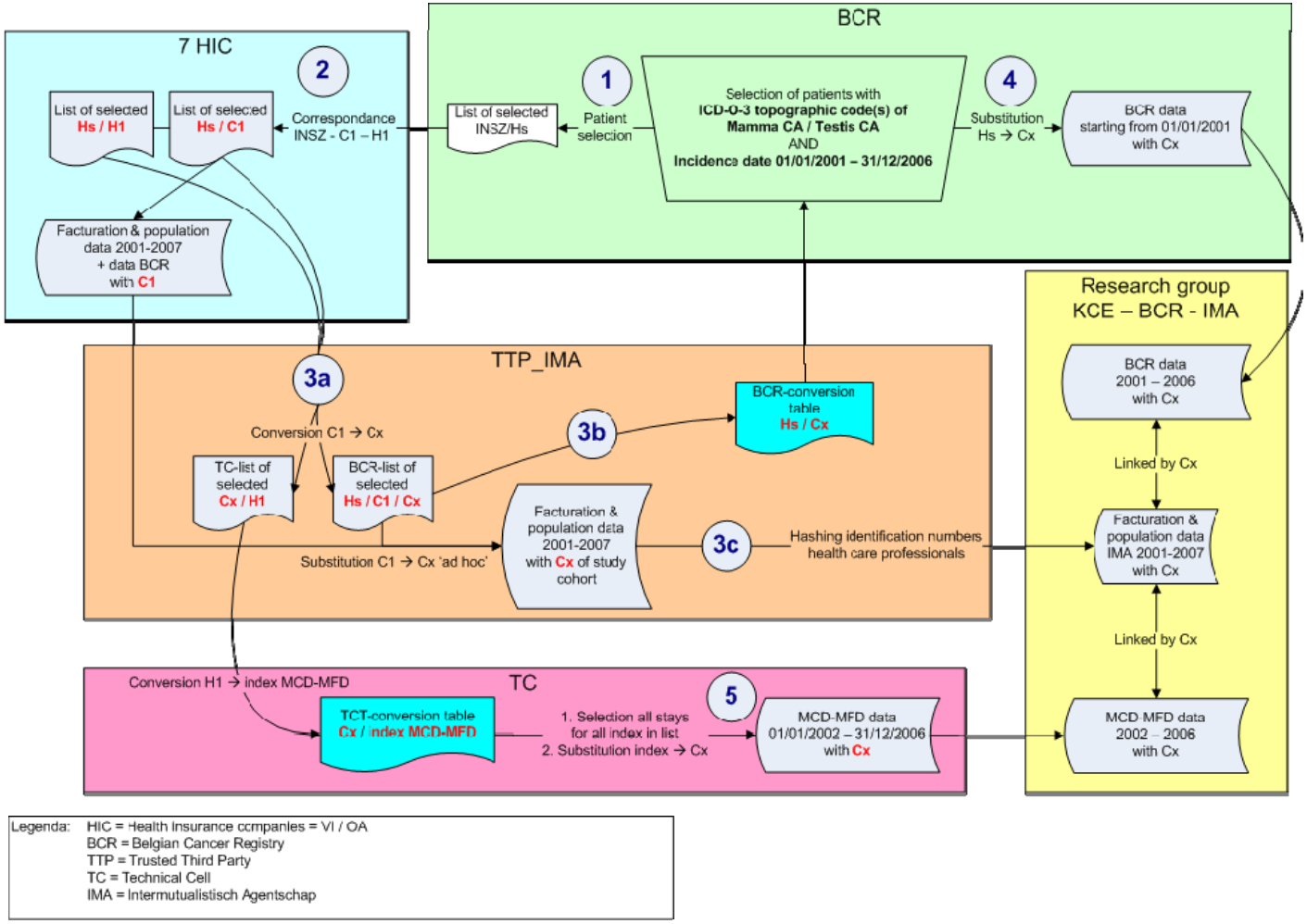
- All breast and testicular cancers with incidence date between 01/01/2001 – 31/12/2006:
  - ICD-10 breast: C50. (only invasive tumours)[a]
  - ICD-10 testis: C62. (only invasive tumours)
- For each selected patient, records related to other tumours (including in situ) were added

The primary selection resulted in 60 765 records, distributed amongst 54 173 patients. These data were sent to IMA and the Technical Cell for linkage (see Figure 2).[b]

[a] Breast carcinoma in situ (D05.) was not selected from the BCR data, because in the initial development of the project, only the quality of care for invasive tumours was considered. Because in a later phase also quality of care indicators (QCIs) for ductal carcinoma in situ (DCIS) were considered, Minimal Clinical Data (MCD) were used in order to estimate these indicators.

[b] The delivery of the BCR data to the IMA was done in two steps. First, the data of 2001-2004 were delivered; later on, the data of 2001-2006 were delivered. The present results all refer to the last data delivery.

Figure 2. Primary selection of breast and testicular cancer population.



Legenda: HIC = Health Insurance companies = VI / OA
BCR = Belgian Cancer Registry
TTP = Trusted Third Party
TC = Technical Cell
IMA = Intermutualistisch Agentschap

3.2 ADDITIONAL SELECTION

From the MCD-MFD database (for the years 2002 – 2006), the selection of records was based on the following ICD-9-CM codes (see Figure 3):

Breast:

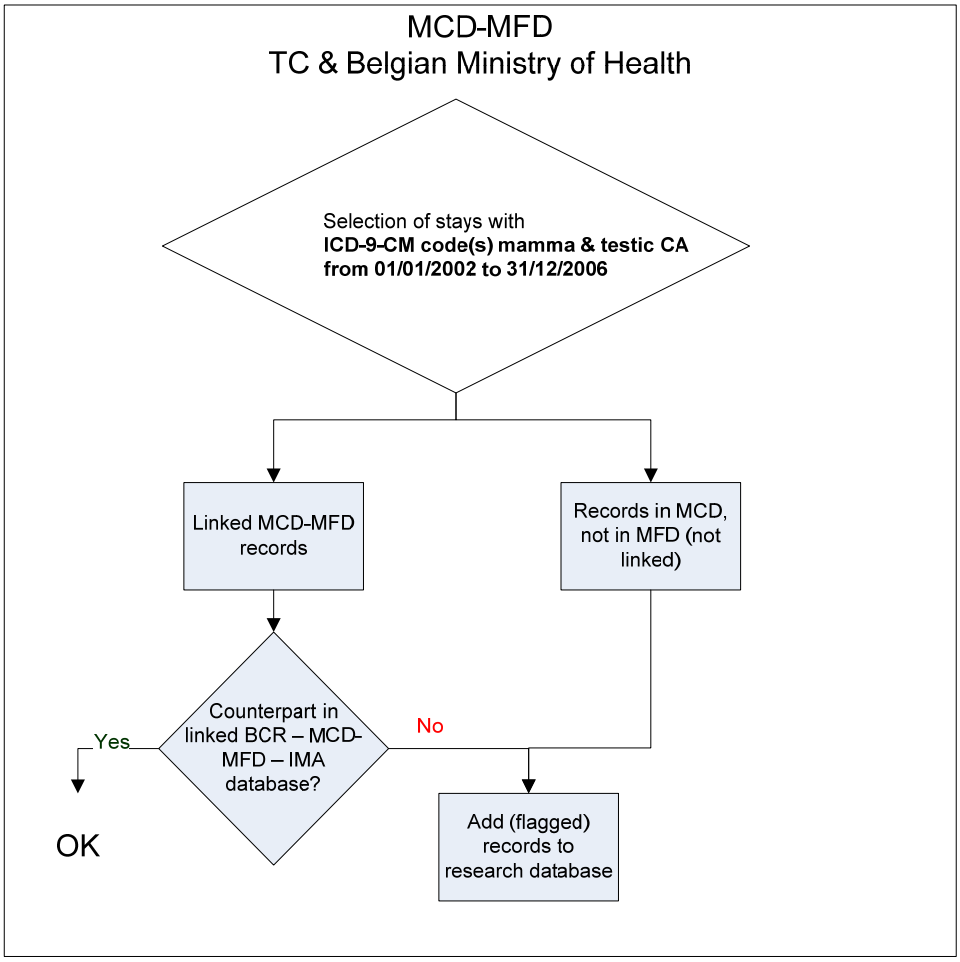
- 174.1 - 174.9: Malignant neoplasm of the breast
- 233.0: Carcinoma in situ of the breast

Testis:

- 86.0 and 86.9: Malignant neoplasm of the testis
- 36.4: Neoplasm with uncertain behavior of the testis

As an exhaustiveness check of the primary selection, the MCD records without an MFD-link and the MCD-MFD records without a counterpart in the linked BCR-IMA-MCD/MFD database were flagged and added to the research database.

Figure 3. Additional selection of breast cancer and testicular cancer patients using the MCD-MFD database as starting point.



3.3 EXPLORATION AND CHECK OF BCR DATA

Figure 4 gives an overview of the data selection, performed on the BCR dataset. The following steps were taken:

1. From the BCR dataset, selected as described above, the 845 records on non-melanoma skin tumours were omitted (due to an underregistration in the years 2001-2004).
2. Seventeen records were empty, because these patients, being foreigners, were omitted from the BCR database after the delivery of the data to the IMA. Furthermore, all records from patients who had any invasive tumour (including breast or testicular tumours) before 2001 were omitted, because previous invasive tumours may have significantly affected treatment of the breast or testicular cancer in the investigated period. In other words only patients with a first invasive breast or testicular carcinoma since 2001 were selected. In total, 2 803 records were deleted. Finally, 8 patients had a first invasive tumour between 2001 and 2006 that was not a breast or testicular tumour. These 8 were also omitted.
3. The resulting 57 092 records were split up into a file for testicular cancer and a file for breast cancer: 55 717 records concerned breast cancer patients, 1 375 records concerned testicular cancer patients. Furthermore, all records for men in the breast cancer database were deleted (471 records), resulting in a total of 55 246 records in the breast cancer database.
4. The next step was to obtain 1 record for each patient (Figure 5). The record that was chosen was the first reported invasive tumour within the topography investigated. If there was more than one tumour, the tumour with the highest pStage was chosen. If this selection did not result in one record per person, the tumour having a left laterality was chosen. The testis dataset with one record for each patient contained 1 337 patients, the breast dataset with one record for each patient contained 50 893 patients. In order to retain the information on multiple tumours, three variables were added to the dataset with one record per patient:
   - The number of multiple tumours
   - The number of multiple tumours within the same location as the primary tumour
   - Whether multiple tumours were metachronous or synchronous. The definition of The American Society of Clinical Oncology (www.asco.org) was followed, considering synchronous tumours as those tumours that fall within the first three months after the incidence date of the first tumour (for the same laterality).

Figure 4. Data selection scheme.

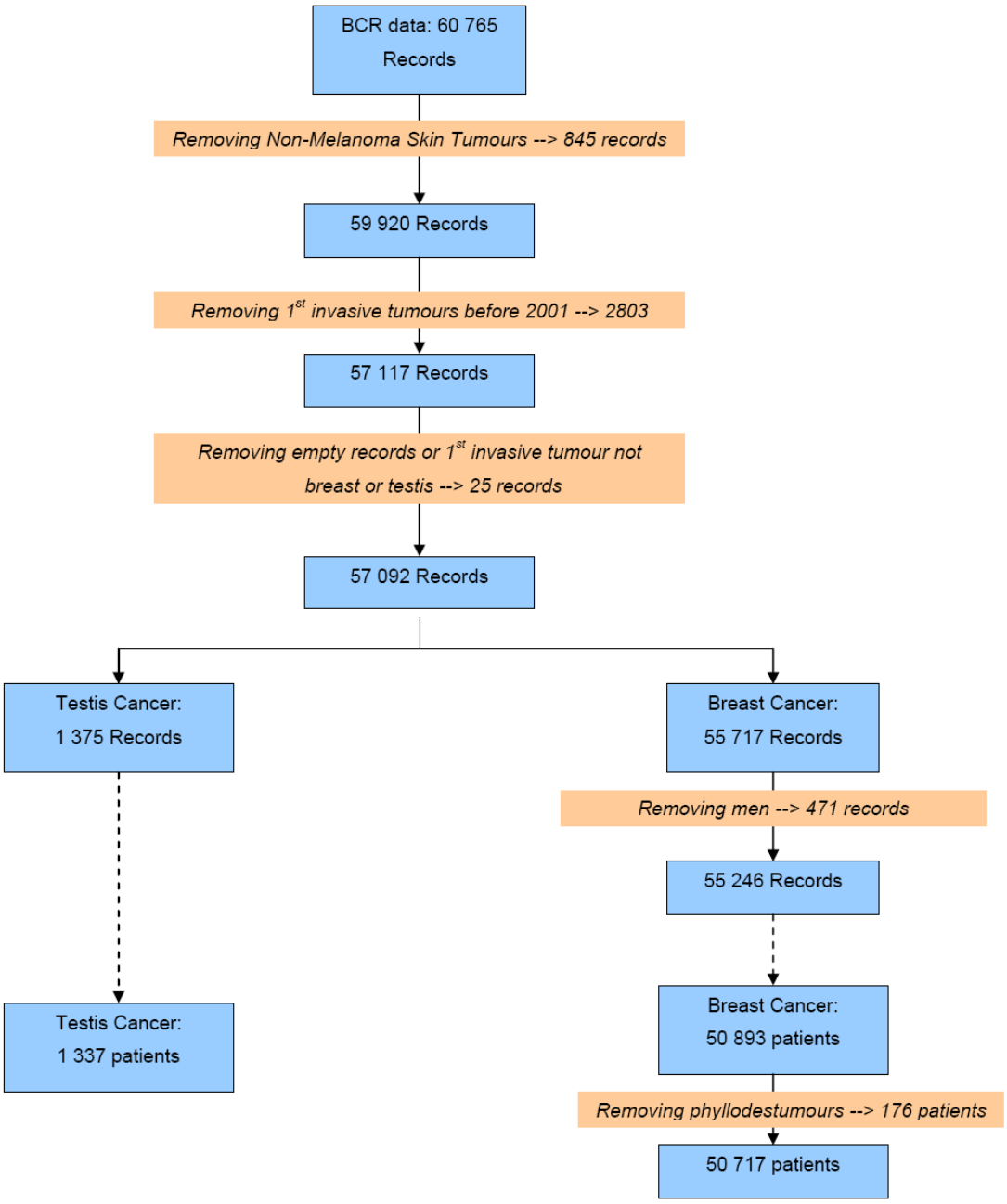
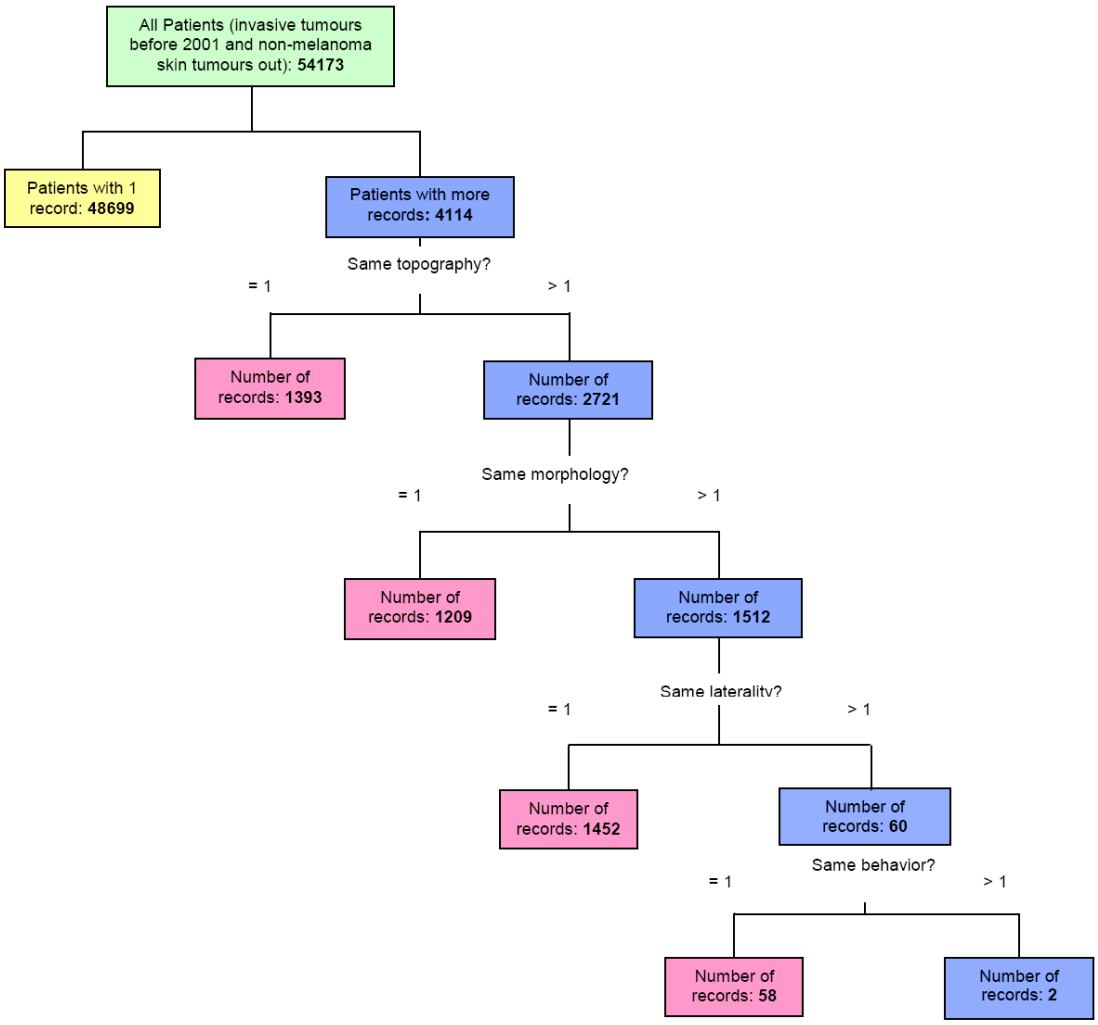


Figure 5. Steps for obtaining one record per patient.



The last step was to remove 176 patients with a phyllodes tumour as primary tumour from the breast cancer database. Phyllodes tumours call for a different treatment than other breast carcinomas. The common treatment for phyllodes is wide local excision. Other than surgery, there is no cure for phyllodes, as chemotherapy and radiation therapy are not effective[17,18].

The presence of double records was checked in the database (Figure 5). In the end, two records (of one patient) were still similar. Therefore, we consulted the original cancer registry database in order to check whether the records were indeed similar. Because this was the case, one of the records was omitted.

3.4 DATA LINKAGE

3.4.1 Linking BCR data to IMA data

The BCR data of the years 2001 to 2006 were linked to the IMA data from the same time interval (see Figure 6):

1. From the 52 024 selected BCR records, 51 376 could be found in the IMAHEALTH database.
2. 648 patients were present in the BCR data, but not in the IMAHEALTH data, including the empty records mentioned earlier.

Figure 6. Overview of match between IMA and BCR data.

This means that 98.8% of the BCR data could be linked to IMA data. The remaining records were probably of patients who had no medical insurance provided by the health insurance companies or of whom the National Number (INSS) was not valid.

3.4.2 Linking BCR data to MCD data

For the years 2002 to 2006, all MCD databases were delivered. First, the proportion of patients from the primary selection that were available in the MCD database was calculated for each year per tumour (Table 2). Because of some unexpected time delays in this project, the delivery of data had to be performed in two phases: first data from 2002 to 2004 were delivered to KCE, and the linkage of the three databases (MCD, BCR, IMA) could be performed. Then, in a second phase, MCD data were delivered for the years 2005 and 2006. Unfortunately, the linkage of those two years could not be performed on time to be included in this study. All analyses included MCD data are thus based only on years 2002 to 2004.

Table 2. Overview of match between BCR, IMA and MCD databases by year and tumour.

Tumour	Year	N BCR	N link with IMA (%)	N link with MCD (%)	N link with IMA and MCD (%)
Breast	2001	7 764	7 669 (98.8)	-	-
	2002	7 751	7 686 (99.2)	5 909 (76.2)	5 890 (76.0)
	2003	8 525	8 443 (99.0)	6 567 (77.0)	6 545 (76.8)
	2004	8 330	8 232 (98.8)	6 069 (72.9)	6 039 (72.5)
	2005	9 091	8 942 (98.4)	-	-
	2006	9 256	9 067 (98.0)	-	-
Testis	2001	212	209 (98.6)	-	-
	2002	177	175 (98.9)	126 (71.2)	125 (70.6)
	2003	215	214 (99.5)	154 (71.6)	154 (71.6
	2004	209	207 (99.0)	147 (70.3)	147 (70.3)
	2005	266	254 (95.5)	-	-
	2006	258	248 (96.1)	-	-

In general, 18 972 patients could be linked between the BCR and the MCD database for the years 2002-2004 (75.3%). The number of patients that could be retrieved in both the IMA, BCR and MCD databases was 18 900 (75%).

This means that the linkage between the MCD data and the BCR data is much lower than between the BCR and the IMA data. A number of possible causes can be formulated:

a. There was certainly a problem with the creation of the patient ID's in the MCD database

b. Patients received different ID's over consecutive years in the MCD database

c. Only hospitalized patients appear in the MCD data. If a patient is not hospitalized or hospitalization dates from before 01/01/2002 then this patient is not recorded in the MCD database

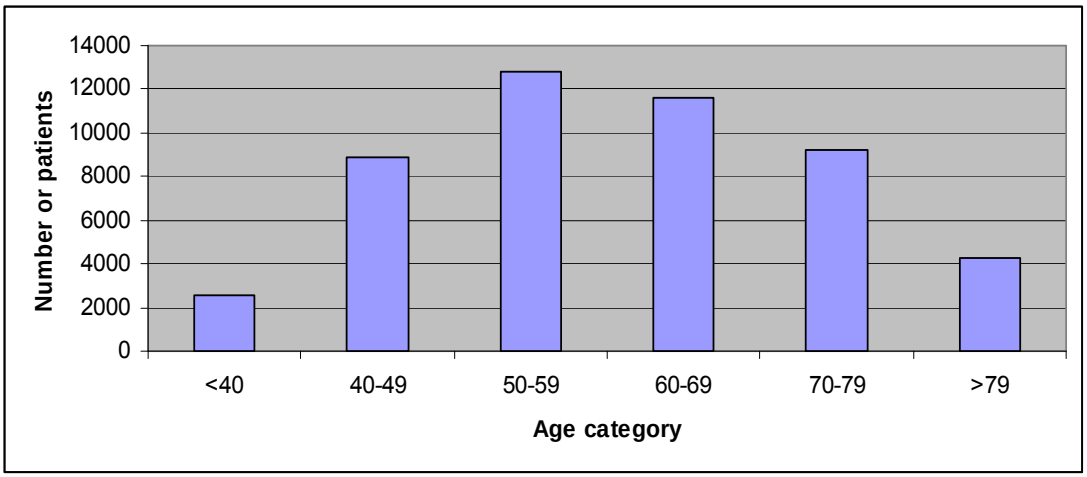
4 DESCRIPTIVE STATISTICS

In total, the number of breast cancer patients analyzed in the BCR dataset was 50 717. For the calculation of the descriptive statistics and the quality indicators, only the patients with a successful linkage between BCR and IMA data were considered (50 039; 98.4% of the BCR dataset).

4.1 DEMOGRAPHIC INFORMATION

Breast cancer is more frequent in the age category 50-69 years (Figure 7). The youngest woman in the dataset was 18 years, the oldest patient was 101. The mean age of the sample (n=50 039) was 60.8 years.

Figure 7. Age distribution among breast cancer women (2001 – 2006).



4.2 TUMOUR CHARACTERISTICS

4.2.1 Solitary vs. multiple tumours

Most patients had a solitary tumour (95.9%). Among the 3 955 multiple tumours, 1 725 were synchronous tumours (incidence last tumour within three months of incidence first tumour) and 2 230 were metachronous (incidence date of the second tumour more than three months after the incidence date of the first tumour). The multiple tumours were most frequently detected in colon-rectum (n = 306), corpus uteri (n = 230), cervix uteri (n = 176), bone marrow (n = 167), lung (n = 148), ovary (n = 146), skin-melanoma (n = 98) and kidney (n = 96).

Table 3 gives an overview of the number of breast tumours per patient.

Table 3. Distribution of number of breast tumours (BCR, 2001-2006; n=50 039).

Number of breast tumours	Number of patients	%
1	47 977	95.9
2	2 027	4.1
3	15	<1

Fifteen patients were diagnosed with three breast tumours. More precisely, these cases had one invasive tumour and two in situ tumours with a different laterality and/or different incidence date than the invasive tumour.

4.2.2 Morphology

As reported in Table 4, 70% of the breast cancers had a pure ductal morphology. Pure lobular breast cancer types were diagnosed in nearly 13% of all cases. Taking into account both pure and mixed ductal and/or lobular morphologies, 85% of the breast tumours could be classified within these categories. Mucinous, papillary, tubular, medullar and Paget's tumours were rare. Morphological information was lacking for 7 patients.

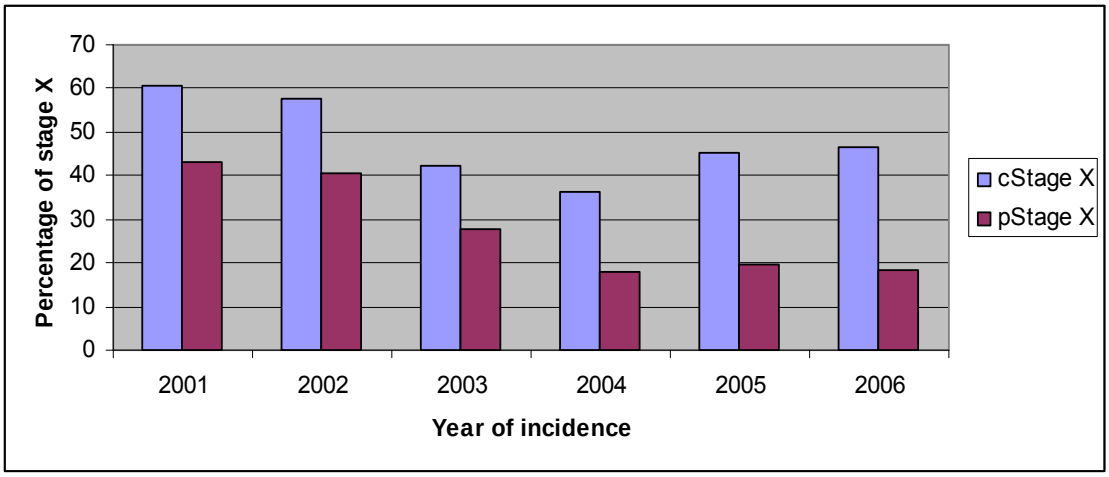
Table 4. Morphology of breast tumours (BCR, 2001 – 2006; n=50 039).

Breast Cancer Types	Number of patients	%
Ductal	35 028	70.0
Ductal mixed	559	1.1
Lobular	6 400	12.8
Lobular mixed	121	0.2
Mixed ductal and lobular	297	0.6
Medullar	2 451	4.9
Mucinous	499	1.0
Paget's	248	0.5
Papillary	389	0.8
Tubular	257	0.5
Other	3 783	7.6

4.2.3 TNM staging

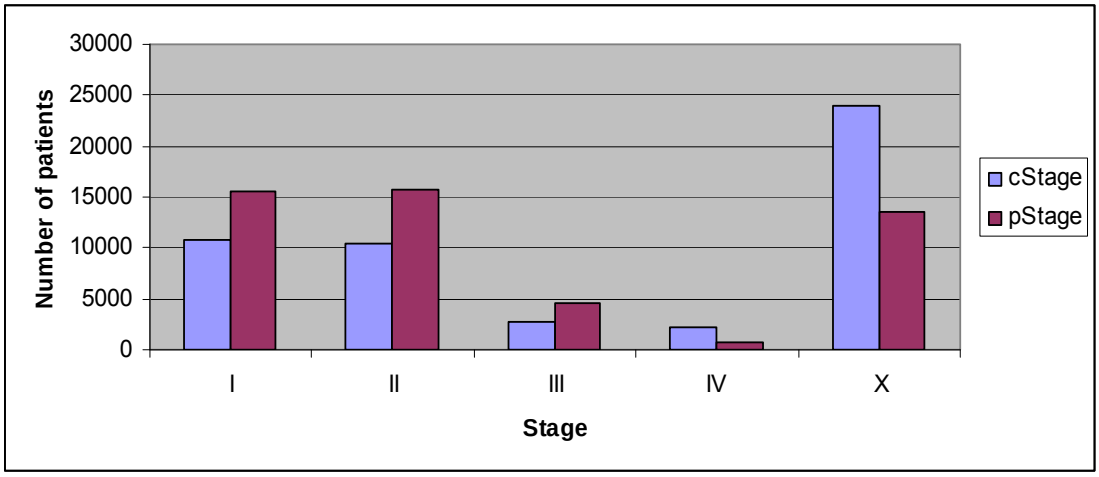
For some patients, TNM staging was lacking in the databases. cStage remained unreported for 23 942 patients (48%), while pStage was not recorded for 13 656 patients (27.1%). The evolution of unknown stage between 2001 and 2006 is presented in Figure 8. The percentage of unreported cStages and pStages remains high and stabilized around 20% for pStage between 2004 and 2006.

Figure 8. Evolution of cStage X and pStage X (2001 – 2006).



Most patients with a known cStage or pStage were in stage I (41.5% and 42.5% respectively) or II (39.7% and 43.1% respectively) (Figure 9). Patients with cStage 0 (91 patients) were not represented in Figure 9.

Figure 9. Distribution of cStages and pStages (2001 – 2006).



For all known cStages and pStages, a good correspondence was found (Table 5). In some cases, a higher pStage than cStage could indicate a wrong clinical staging. In other cases, as pStages were lower than the corresponding cStages, it is possible that neoadjuvant treatment succeeded in downstaging the initial tumour.

Table 5. Correspondence between cStage and pStage.

pStage	cStage				Total
	I	II	III	IV	
I	7 321	1 276	83	44	8 724
II	2 511	6 426	486	176	9 599
III	250	1 367	1 190	195	3 002
IV	10	36	33	370	449
Total	10 092	9 105	1 792	785	21 774

Next, the relation between age and TNM staging was analyzed. As expected, higher stages occurred more frequently in older age groups (Figure 10 and Figure 11). These age-related differences were significant for both pStage ($chi^2(df15)=949.2$; $p<0.001$) and cStage ($chi^2(df15)=1184.8$; $p<0.001$).

There was a clear relationship between clinical stage and patient age at diagnosis, but this relationship was not linear. Note that stage II was more common than stage I, except in the group between 50 and 69 years. This pattern can be partly explained by the role of screening programs, set up in 2001. Screening leads to an earlier detection of cancers and is responsible for a higher detection of stage I cancers.

cStage III and IV were more common after 70 years old. Proportions of pStage IV were lower in all age groups than cStage IV, possibly due to a successful neoadjuvant treatment before a surgical intervention, or a wrong diagnostic workup.

Figure 10. cStage distribution by age for breast cancer (2001 – 2006).

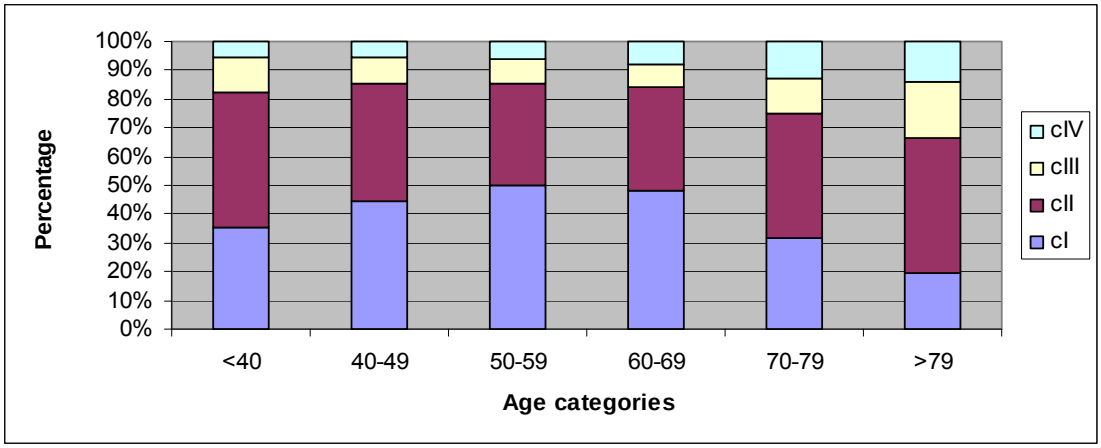
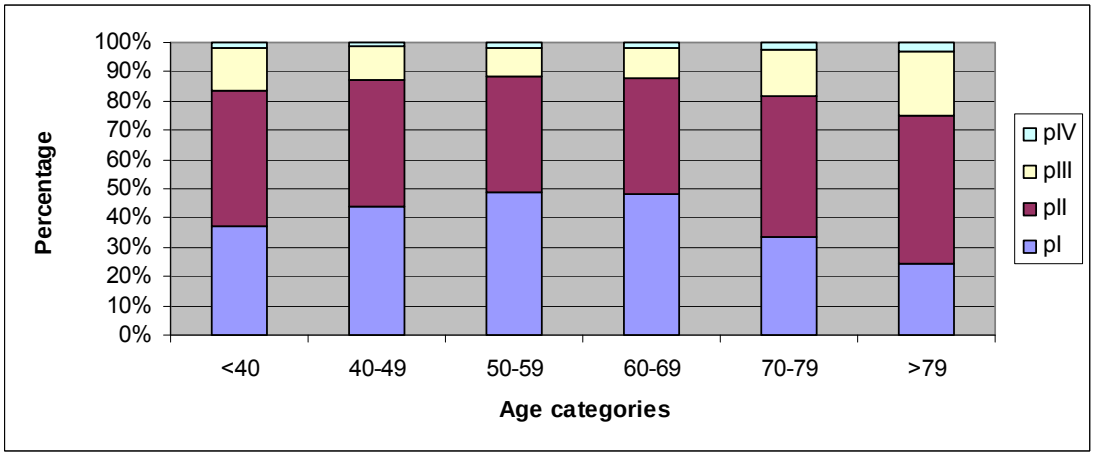


Figure 11. pStage distribution by age for breast cancer (2001 – 2006).



4.2.4 Incidence rates

Table 6 provides the European Standardized Rate (ESR) by province for all available years (2001 – 2006). This standardized incidence rate is a summary measure of a rate in which the population has a standard age structure (European population). Belgium has one of the highest incidence rates for breast cancer in Europe[19].

The age-standardized incidence evolved in the time period 2001-2006. However, as data for the Walloon provinces and Brussels were not complete for the years 2001-2003, it is difficult to interpret the positive evolution observed the last three years. In 2006, Brabant-Wallon had the highest ESR (170 new cases for 100 000 women) and Limburg the lowest (123 new cases for 100 000 women). The highest increases were observed in Brussels, Hainaut, Namur and Brabant wallon, but it is possible that such increases in a short period reflected an improvement in the overall recording of breast cancer cases.

Table 6. Age-standardized incidence (ESR) per year and per province for breast cancer (2001 – 2006).

Province	2001	2002	2003	2004	2005	2006
Antwerpen	141.25	137.91	147.05	137.61	142.53	144.46
Brussel-Bruxelles	-	-	-	144.56	139.07	160.28
Hainaut	-	-	-	130.76	142.99	141.90
Limburg	134.77	96.42	113.58	95.11	120.85	122.84
Liège	-	-	-	130.10	132.65	143.86
Luxembourg	-	-	-	116.84	135.08	131.12
Namur	-	-	-	95.45	161.85	146.85
Oost-Vlaanderen	144.74	141.73	159.85	140.63	146.71	148.60
Vlaams Brabant	139.86	136.08	145.95	147.23	143.25	149.59
Brabant Wallon	-	-	-	145.45	169.44	170.51
West-Vlaanderen	145.75	133.62	148.00	131.07	148.41	142.59

4.3 DIAGNOSIS AND STAGING

An overview of a selection of diagnostic techniques used in the workup of breast cancer (within 3 months of the incidence date) is given in Table 7. Most patients underwent a mammography during their diagnostic workup (90%). In most cases (87.1%), a diagnostic mammography was performed. Screening mammography preceeded the diagnosis of breast cancer in about 2.8% of the patients. About 86.2% of the patients underwent breast ultrasonography. The proportion of patients in whom a breast sonography was recorded evolved from 76.5% in 2001 to 91.3% in 2006. In total, 37 750 (75.4%) patients underwent a biopsy. A positive evolution was found for biopsy or breast puncture from 57% in 2001 to 87% in 2006. A MRI of the breast was performed in 21% of all patients (from 11.5% in 2001 to 30% in 2006) and a distant MRI was performed in 2.2% of patients. A CT was performed in 40% of the patients, but no specification of the CT location is available in the nomenclature data. Less than 3% of the patients underwent a PET scan, and most of these patients also underwent a CT and/or MRI.

Table 7. Overview of diagnostic procedures for breast cancer.

		Incidence year						All
		2001	2002	2003	2004	2005	2006	
N		**7669**	**7686**	**8443**	**8232**	**8942**	**9067**	**50039**
Mammography								
Diagnostic only	*N*	6088	6259	6790	6770	7359	7532	40798
	%	79.38	81.43	80.42	82.24	82.30	83.07	81.53
Screening only	*N*	80	215	300	240	263	312	1410
	%	1.04	2.80	3.55	2.92	2.94	3.44	2.82
Both	*N*	142	438	602	517	505	586	2790
	%	1.85	5.70	7.13	6.28	5.65	6.46	5.58
Biopsy or Breast puncture								
Biopsy (non specific code)	*N*	2261	3198	4226	4798	5630	6349	26462
	%	29.48	41.61	50.05	58.28	62.96	70.02	52.88
Breast puncture	*N*	3788	4627	5555	5780	6602	6949	33301
	%	49.39	60.20	65.79	70.21	73.83	76.64	66.55
Biopsy (non specific code) or Breast puncture	*N*	4370	5265	6328	6553	7376	7858	37750
	%	56.98	68.50	74.95	79.60	82.49	86.67	75.44
Breast ultrasonography (specific or non specific code)	*N*	5867	6382	7312	7295	8017	8277	43150
	%	76.50	83.03	86.60	88.62	89.66	91.29	86.23
CT	*N*	2835	2923	3376	3352	3660	4046	20192
	%	36.97	38.03	39.99	40.72	40.93	44.62	40.35
Distant MRI	*N*	138	177	210	191	196	212	1124
	%	1.80	2.30	2.49	2.32	2.19	2.34	2.25
Breast MRI	*N*	880	1187	1591	1769	2390	2698	10515
	%	11.47	15.44	18.84	21.49	26.73	29.76	21.01
PETscan (official code or double tomography code)	*N*	95	131	192	266	300	464	1448
	%	1.24	1.70	2.27	3.23	3.35	5.12	2.89
CT and/or distant MRI	*N*	2892	2992	3442	3424	3732	4116	20598
	%	37.71	38.93	40.77	41.59	41.74	45.40	41.16
(CT and/or distant MRI) and PETscan	*N*	75	4	141	202	234	317	1063
	%	0.98	1.22	1.67	2.45	2.62	3.50	2.12

4.4 TREATMENT

A general overview of treatments by cStage is provided in Table 8 (BCR-IMA data) and Table 10 (BCR-MCD-IMA data). Similar results were reported by pStage in Table 9 and Table 11.

Table 8. Treatment by cStage (BCR-IMA, 2001 – 2006).

	cStage						
Treatment	**c0**	**cI**	**cII**	**cIII**	**cIV**	**cX**	**Total**
Any breast surgery	89	10 499	9 871	2 291	797	21 175	44 722
Any hormonal treatment	47	5 877	3 322	620	606	10 838	21 310
Any chemotherapy	17	3 448	6 040	1 837	1 275	9 704	22 321
Radiotherapy	41	9 086	8 090	2 38	1 127	17 056	37 538
No/other treatment	2	123	137	59	158	773	1 252
Total number of patients	**91**	**10 827**	**10 363**	**2 676**	**2 140**	**23 942**	**50 039**

Table 9. Treatment by pStage (BCR-IMA, 2001 – 2006).

	pStage					
Treatment	**I**	**II**	**III**	**IV**	**X**	**Total**
Any breast surgery	15 071	15 278	4 387	363	9 623	44 722
Any hormonal treatment	9 663	5 156	961	160	5 370	21 310
Any chemotherapy	3 392	9 210	3281	448	5 990	22 321
Radiotherapy	12 427	12 537	3 923	351	8 300	37 538
No/other treatment	151	122	38	27	914	1 252
Total number of patients	**15 474**	**15 679**	**4 559**	**671**	**13 588**	**50 039**

Table 10. Treatment by cStage (BCR-MCD-IMA, 2002 – 2004).

	cStage						
Treatment	**c0**	**cI**	**cII**	**cIII**	**cIV**	**cX**	**Total**
Any breast surgery	37	4 292	3 930	874	370	7 414	16 917
Any hormonal treatment	28	3 264	2 811	628	553	5 793	13077
Any chemotherapy	7	1 420	2 369	661	495	3 287	8 239
Radiotherapy	0	3 635	3 176	800	454	5 864	13 943
No/other treatment	14	21	31	14	50	169	285
Total number of patients	**37**	**4 338**	**4 040**	**976**	**818**	**8 042**	**18 251**

Table 11. Treatment by pStage (BCR-MCD-IMA, 2002 – 2004).

	pStage					
Treatment	**I**	**II**	**III**	**IV**	**X**	**Total**
Any breast surgery	5 440	5 713	1 665	149	3 950	16 917
Any hormonal treatment	3 168	2 005	419	114	2 380	8 086
Any chemotherapy	1 227	3 444	1 240	169	2 159	8 239
Radiotherapy	4 541	4 730	1 484	144	3 115	14 014
No/other treatment	7	17	10	12	239	285
Total number of patients	**5 558**	**5 813**	**1 697**	**254**	**4 929**	**18 251**

When considering the coupled BCR and IMA databases (available for 50 039 patients during the period 2001-2006), 89.4% patients underwent a breast surgery, 75% received radiotherapy, 44.6% received chemotherapy and 42.6% received endocrine treatment. In most cases, a combination of these treatments was given. In general, 1 252 women (2.5%) received none of these treatments. It is however possible that these women received other treatments that were not recorded in these databases (e.g. women who participated in clinical trials or who received treatment according to the rule of the 'compassionate use'). When considering the coupled BCR-MCD-IMA database (2002-2004), 92.7% of breast cancer women underwent a surgical treatment, and 76.8% underwent an adjuvant radiotherapy. Using the MCD database had only a slight added value to reflect the number of surgical interventions and radiotherapy.

A more detailed analysis of the first surgical intervention (after the incidence date) is provided in Table 12. Among surgically treated breast cancer women, 58.3% underwent a breast conserving surgery (BCS) whereas 41.7% underwent a mastectomy. In general, an axillary dissection is performed during mastectomy, while this surgical technique does not systematically follow all breast conserving techniques. The proportion of BCS gradually decreased with breast cancer stage. While 72% of women with cStage I underwent a BCS, this proportion decreased to 48.9% in cSstage II group and to 23.3% in cStage III group. Of all women who were diagnosed as having a cStage IV and surgically treated (37.2% of cStage IV) between 2001 and 2006, 27.8% underwent a BCS. The Belgian data are similar with data reported in Nederland, where 90% of all breast cancer women underwent a surgical intervention; in 53% of operated women, a breast conserving surgery is realized[20].

Table 12. First surgical intervention by cStage, based on the IMA data 2001 – 2006 (n = 50 039).

	cStage						
Surgical intervention	**c0**	**cI**	**cII**	**cIII**	**cIV**	**cX**	**Total**
Mastectomy	55	2 931	5 035	1 757	575	8 826	19 179
Breast-conserving surgery	34	7 568	4 836	534	222	12 349	25 543
Total	**89**	**10 499**	**9 871**	**2 291**	**797**	**21 175**	**44 722**

In total, 22 321 patients (44.6%) received any type of chemotherapy. An overview of the administered chemotherapy products is given in Table 13. FEC, combining 5-fluorouracil, epirubicin and cyclophosphamide was administered the most frequently in this cohort.

Table 13. Overview of chemotherapy products used for breast cancer, 2001-2006 (n = 50 039).

Product	**Frequency**	**Percent**
Cyclophosphamide	19 758	39.5
Fluorouracil	18 279	36.5
Epirubicin	15 812	31.6
Docetaxel	5 711	11.4
Methotrexate	3 815	7.6
Doxorubicin	3 105	6.2
Paclitaxel	1 779	3.6
Capecitabine	1 583	3.2
Vinorelbine	1 365	2.7
Carboplatin	655	1.3
Cisplatin	470	0.9
Gemcitabine	462	0.9
Mitoxantrone	415	0.8
Any chemotherapy	**22 321**	**44.6**

Endocrine therapy was given to 21 310 patients (42.6%) (Table 14). Tamoxifen plays an important role in the adjuvant therapy of invasive breast cancer in (premenopausal or postmenopausal) patients with ER-positive tumours and was administered in 40.2% of breast cancer women. Of the aromatase inhibitors (anastrozole, exemestane and letrozole), anastrozole was the most frequently used agent and was administered to 16.5% of breast cancer women. The use of luteinising hormone releasing hormone agonist (LHRHa), leading to the ovarian suppression in pre-menopausal women, was less frequent (see goserelin, buserelin, triptorelin, leuprorelin). The differences observed in use of these products can be explained by the target group (premenopausal vs. postmenopausal women) for each product but also by the sequential administration of these treatments, some of them being administered when the previous ones failed to obtain a clinical result. Moreover, if an endocrine treatment is not reimbursed, all women who received it were not registered.

Table 14. Overview of endocrine therapy products used for breast cancer (BCR-IMA 2001-2006).

Endocrine therapy	Frequency	Percent
Tamoxifen	20 140	40.2
Anastrozole	8 242	16.5
Exemestane	4 488	9.0
Letrozole	3 876	7.7
Goserelin	2 140	4.3
Toremifene	41	0.1
Buserelin	12	<1
Triptorelin	11	<1
Leuprorelin	6	<1
Any endocrine therapy	**21 310**	42.6

4.5 HOSPITALIZATION

Most patients were hospitalized in the surgical APR-DRGs 362 and 363 (50% of the total sample) (Table 15). However, more than 40% of the patients were hospitalized in APR-DRGs not specific to breast cancer.

Table 15. Overview of hospitalizations for breast cancer by APR-DRG, 2002 – 2004 (n =18 251).

APR-DRG	Labels	2002	2003	2004
APR-DRG 362	Mastectomy	1 336	1 556	1 499
APR-DRG 363	Breast surgery, excluding mastectomy	1 455	1 635	1 565
APR-DRG 382	Malignant breast disease	248	249	226
APR-DRG 385	Other skin or breast disease	37	42	30
APR-DRG 692	Radiotherapy	17	12	11
APR-DRG 693	Chemotherapy	257	246	195
Other		2 466	2 731	2 438

5 INDICATOR RESULTS

5.1 OVERALL MEASURABILITY OF THE SELECTED QUALITY INDICATORS

Of the 32 selected indicators, 13 were found to be measurable with data recorded between 2001 and 2006 and 1 indicator was measurable using a proxy indicator (Table 16). In the absence of national data on reasons for mortality, disease-specific survival is not measurable as such. Therefore, relative survival was used as a proxy indicator.

The most important reasons for being not measurable was the absence of administrative codes (N=12) or the absence of the procedure's results in the administrative databases (N=3). Moreover, as the focus of this study specifically concerned women having an invasive breast cancer, women who had suspicious screening results or who were diagnosed with a DCIS were not included in this study. For both reasons, indicators focusing on these sub-populations could not be measured (N=3).

Table 16. Measurability of breast cancer quality indicators.

					In	
Code	**P/O**	**Description**	**Measurable**	**Reason**	**A.**	**B.**
General quality indicators						
BC1	O	Overall 5-year survival rate by stage	Yes			x
BC2	O	Disease specific 5-year survival by stage	Yes			x
BC3	O	Disease-free 5-year survival rate by stage	No	No administrative code for recurrence disease; could be measured with prospective registration		
BC4	O	5-year local recurrence rate after curative surgery, by stage	No	No administrative code for recurrence disease; could be measured with prospective registration		
BC5	P	Proportion of breast cancer women discussed at the multidisciplinary team meeting	Yes		x	x
BC6	P	Proportion of women with breast cancer who participate in clinical trials	No	No administrative code for clinical trials; could be measured with prospective registration		

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

Diagnosis and staging						
BC7	P	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	No	Only breast cancer patients were included		
BC8	P	Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy	No	Only breast cancer patients were included		
BC9	P	Proportion of newly diagnosed cstage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery	Yes		x	x
BC10	P	Proportion of patients who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment	No	No code for FNAC of axillary lymph nodes		
BC11	P	Proportion of patients in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment	No	Codes for HER2 assessment were only introduced in 2007; could be measured in the future		
BC12	P	Proportion of patients in whom a ER and PgR status assessment were performed before any systemic treatment	Yes		x	x
BC13	P	Proportion of breast cancer women with cytological and/or histological assessment before surgery	Yes		x	x
BC14	P	Proportion of sentinel lymph nodes biopsy in cN0 patients without contraindications	No	There is no specific code to identify contraindications		

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

Neoadjuvant treatment						
BC15	P	Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	Yes		x	x
Surgery						
BC16	P	Proportion of breast cancer women who underwent an ALND after positive SNLB > 2 mm	No	No administrative code for SNLB nor for its result		
BC17	O	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)	No	DCIS patients were not selected in the cancer registry database and status of the resection margins is not reported; could be measured with prospective registration		
BC18	P	Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy	Yes		x	x
BC19	P	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy	No	No administrative code for recurrence; could be measured with prospective registration		

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

Adjuvant treatment						
BC20	P	Proportion of women with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen	No	No code allowed to check the documentation of the planned chemotherapy regimen		
BC21	P	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer	Yes		x	x
BC22	P	Proportion of women with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI)	No	The status of ER/PgR receptors is not available in the administrative databases; could be measured after individual revision of all pathology protocols available at the Cancer Registry and/or prospective registration		
BC23	P	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of ≥ 50-55% who received chemotherapy and Trastuzumab	No	The reporting of HER2 status, lymph node status and LVEF could only be obtained in patient' medical file or for the first three variables after individual revision of all pathology protocols available at the Cancer Registry, and not in administrative databases		

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

BC24	P	Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months	Yes		x	x
BC25	P	Proportion of women who received radiotherapy after breast conserving surgery	Yes		x	x
BC26	P	Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND	No	No code for the number of positive lymph nodes unless individual revision of the pathology protocols. It is impossible to distinguish between chest wall radiotherapy and radiotherapy on axilla		
Treatment of metastatic breast cancer						
BC27	P	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment	No	The status of HER2 receptors is not available in the administrative databases; could be measured with individual revision of all pathology protocols available at the cancer registry or with prospective registration		
BC28	P	Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment	Yes		x	x
BC29	P	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	Yes		x	x

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

Follow-up						
BC30	P	Proportion of women who benefit from an annual mammography after a history of breast cancer	Yes		x	x
Histopathologic examination						
BC31	P	Proportion of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the lymphovascular invasion (LVI) and the histologic grade.	No	No code exists to evaluate the content of the pathology reports unless individual revision is carried out of all pathology protocols available at the cancer registry		
BC32	P	Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed	No	No code for the number of positive lymph nodes unless revision of pathology protocols.		

P/O = Process or Outcome QI
Measureable using A (administrative database (IMA and/or MCD)) or B (BCR database)

5.2 INDICATOR RESULTS

5.2.1 Survival

Three measures of survival were considered: overall 5-year survival, 5-year relative survival (as a proxy for disease-specific survival) and disease-free survival.

5.2.1.1 Overall 5-year survival rate by stage

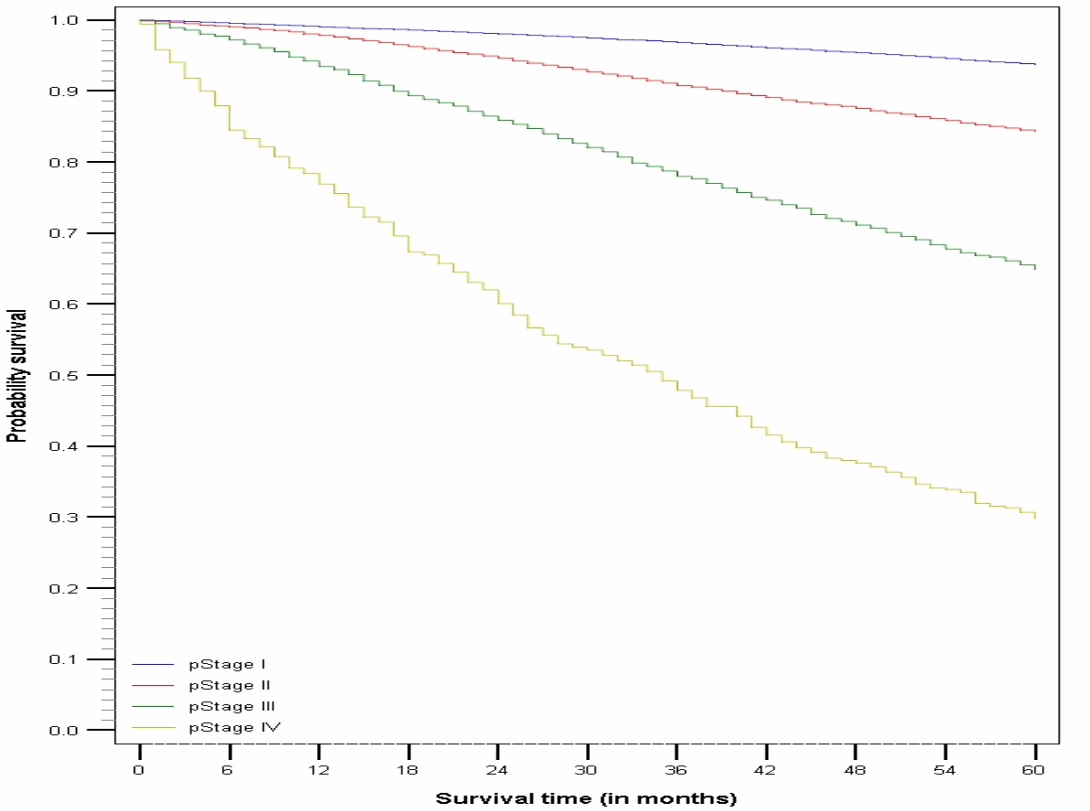
Observed survival rates were calculated for all patients with recorded pStage and vital status (36 278 patients or 72.5% of the entire cohort).

Taken all incidence years together, the 5-year observed survival probability was 0.93 for pStage I and decreased to 0.28 for pStage IV (Table 17 and Figure 12). For pStage X, survival was 0.93 after one year, 0.85 after three years and 0.79 after five years.

Table 17. Observed survival probability by pStage.

		N	# deaths	Survival time				
				1 year	2 years	3 years	4 years	5 years
pStage	I	15 437	1 165	0.99	0.97	0.96	0.95	0.93
	II	15 617	2 877	0.96	0.93	0.89	0.86	0.83
	III	4 553	1 697	0.89	0.82	0.75	0.69	0.64
	IV	671	494	0.68	0.54	0.42	0.35	0.28

Figure 12. 5-year observed survival probability by pStage.



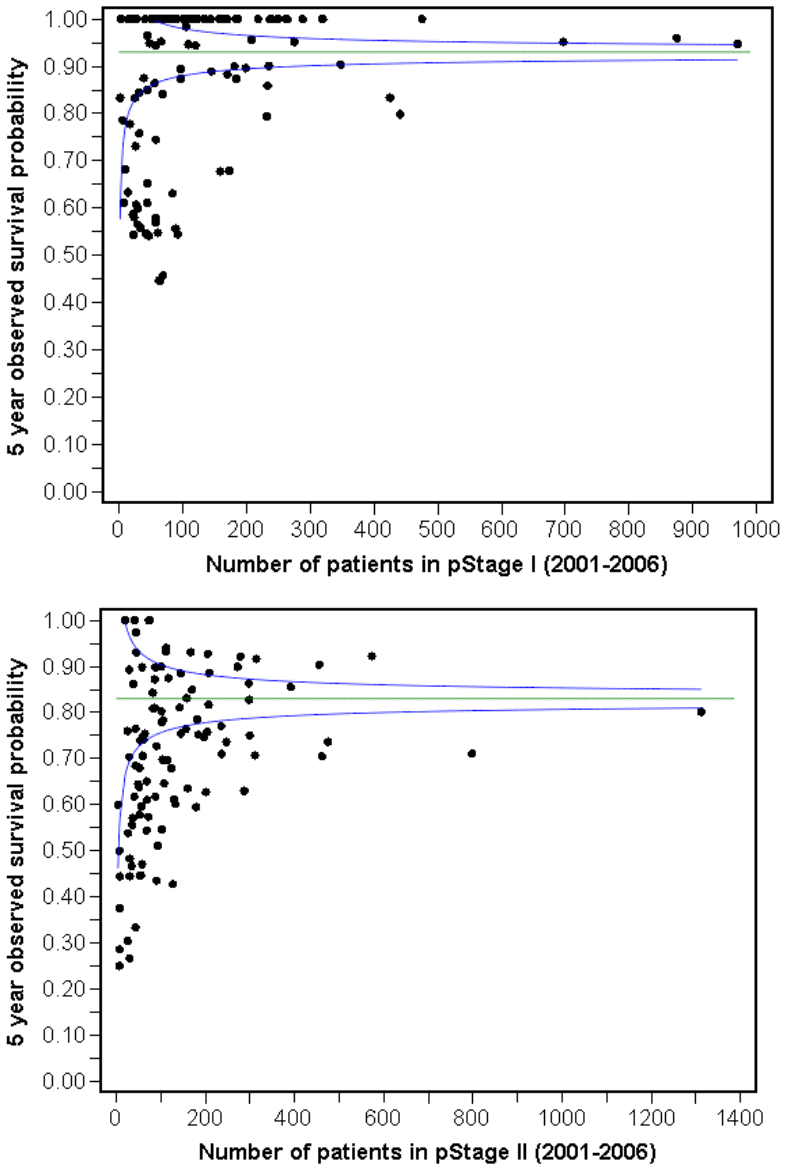
As demonstrated in Table 18, the evolution of 5-year survival probability remained relatively stable according to incidence year, with a slight increase for pStages II and III.

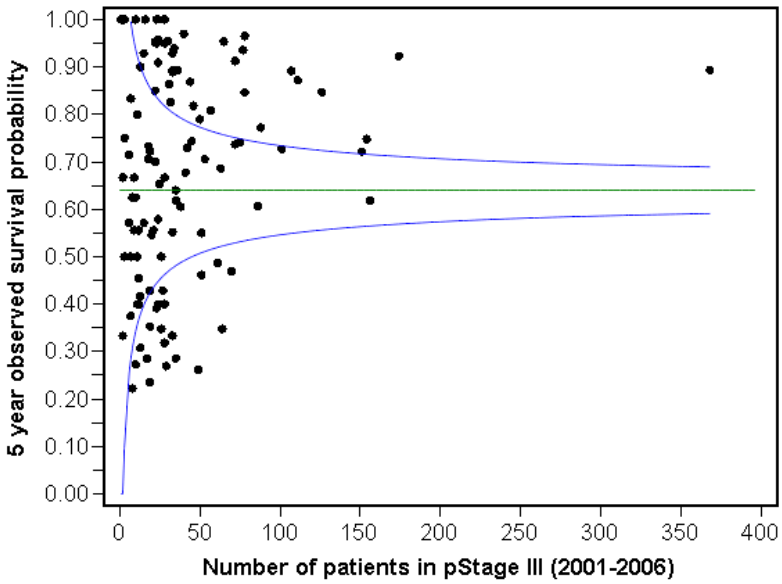
Table 18. Evolution of 5-year observed survival probability by pStage according to incidence year.

		Incidence year			
		2001	2002	2003	2004
pStage	I	0.93	0.93	0.92	0.93
	II	0.81	0.82	0.83	0.84
	III	0.59	0.57	0.63	0.64
	IV	0.30	0.24	0.30	0.27

Variability between centres was large for pStage I-III (Figure 13). Because of the low volume of women with metastatic breast cancer treated by centre (maximal volume of 18 women in the highest volume centre between 2001 and 2006), a funnel plot was considered less useful to illustrate variability.

Figure 13. 5-year observed survival probability per pStage, analyzed per centre.





5.2.1.2 *Relative 5-year survival by stage*

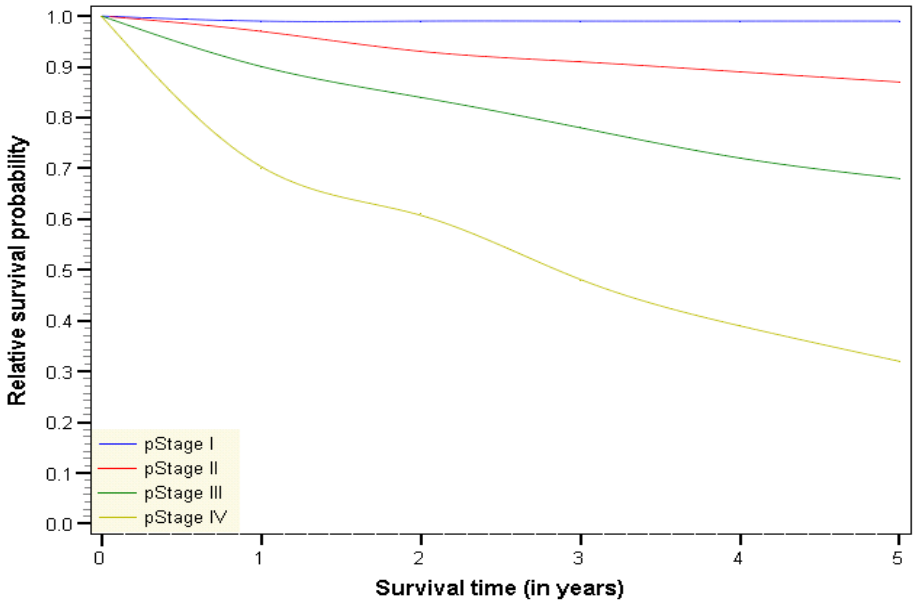
Since no national data are available on the cause of death, disease-specific survival as such is not measurable at this moment. However, relative survival is a frequently used parameter in cancer epidemiology and can be used as a proxy of the disease-specific survival[21].

Relative survival rates were calculated for all patients with recorded pStage and vital status (36 278 patients or 72.5% of the entire cohort). The current analyses showed a 5-year relative survival between 0.32 for pStage IV disease and 0.98 for pStage I (Table 19 and Figure 14). Relative survival for pStage X was 0.96 after one year, 0.90 after 3 years and 0.86 after five years.

Table 19. Relative survival probability by pStage.

		N	# deaths	Survival time				
				1 year	2 years	3 years	4 years	5 years
pStage	I	15 437	1 165	1	1	0.99	0.99	0.98
	II	15 617	2 877	0.97	0.93	0.91	0.89	0.87
	III	4 553	1 697	0.90	0.84	0.78	0.72	0.68
	IV	671	494	0.70	0.61	0.48	0.39	0.32

Figure 14. Relative survival probability by pStage.



5.2.1.3 Disease-free 5-year survival rate by stage

Disease-free survival could not be determined since recurrence is not registered on a population level at the BCR. An indirect measurement of the disease-free 5-year survival by investigating the number of retreatments also seemed invalid for this cancer type. Indeed, a retreatment can only be determined if there is a clear interval between the first-line and the second-line treatment. Endocrine therapy may be a long-term treatment which makes a treatment-free interval difficult to determine.

5.2.2 Diagnosis and staging

Only women who finally received a diagnostic confirmation of breast cancer are recorded in the BCR. Women having an abnormal mammogram that was finally not cancer-related were not included in the dataset. So, only newly diagnosed breast cancer patients who underwent further diagnostic assessments were considered in this section.

5.2.2.1 Mammography and ultrasonography

Mammography remains one of the primary tools used to evaluate a palpable breast mass or other signs of breast disease. Ultrasound has emerged as an important tool to assess a palpable mass in women with dense breast tissue and/or to complement mammography[16]. Two-view mammography should be performed as part of triple assessment (clinical assessment, imaging and tissue sampling) in a unit specialized in breast imaging[6].

Of all cStage I, II or III breast cancer patients treated by a surgical intervention without neoadjuvant treatment, 93.8% had a two-view mammography or breast sonography before surgery. In 86% of the cases (17 838 patients), these examinations were performed within 3 months prior to surgery (Table 20).

Table 20. Proportion of newly diagnosed cStage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	2 042	2 405	84.9
2002	2 339	2 667	87.7
2003	3 486	3 969	87.8
2004	3 543	4 144	85.5
2005	3 296	3 879	85.0
2006	3 132	3 686	85.0
Total	**17 838**	**20 750**	**86.0**

Numerator: All women diagnosed with breast cancer (cStage I-III) in a given year undergoing two-view mammography or breast sonography within 3 months before surgery
Denominator: All women diagnosed with breast cancer (cStage I-III) in a given year who were surgically treated (breast conserving surgery or mastectomy)

5.2.2.2 *Assessment of hormonal receptor assessment*

HER2 receptors

HER2 protein expression, and if positive confirmed with gene amplification, should be evaluated in every primary invasive breast cancer at the time of diagnosis and at the time of recurrence whenever possible[6].

Before 2007, FISH HER2 was not reimbursed, and no nomenclature code existed. The first codes for HER2 assessment were introduced on August 1st 2007 and July 1st 2009. Consequently, using IMA data from 2001-2006, it is impossible to evaluate the use of HER2 receptor assessment in clinical practice. Since January 1st 2011, a prospective registration will be conducted including all hormonal receptor assessments, but also the result of these assessments (e.g. status of HER2 receptors).

ER and PgR receptors

ER and PgR status are predictive of a benefit from endocrine treatment (tamoxifen, chemical ovarian ablation, aromatase inhibitors and fulvestrant) in both the adjuvant and metastatic settings[22]. Estrogen and progesterone receptors (ER/PgR) should be measured on all ductal carcinomas in situ (DCIS) and primary invasive breast cancers (1B evidence)[6]. Between 2001 and 2006, the proportion of breast cancer patients who received chemotherapy or endocrine treatment was 87.2%. Of these 43 631 patients receiving systemic treatment, 41 910 (96.1%) had an immunohistological examination within three months prior to treatment start (Table 21). The number of patients with an immunohistological examination may be slightly overestimated, since a combination of the general nomenclature codes (588070 – 588081) and the specific codes for ER and PgR (435831 – 435842) was used. However, when focusing on the specific codes for ER and PgR (435831 – 435842), only 145 patients (0.3%) were withdrawn.

The proportion of patients with an immunohistological examination three months prior to systemic treatment increased over the years. In 2001, 90.5% was assessed by immunohistology, while this was true for 98% in 2006. In 2006, almost all centres performed an immunohistological examination in all their patients.

Table 21. Proportion of patients with assessment of ER and PgR status before any systemic treatment (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	5 935	6 555	90.5
2002	6 367	6 684	95.3
2003	7 130	7 360	96.9
2004	7 042	7 230	97.4
2005	7 629	7 839	97.3
2006	7 807	7 963	98.0
Total	**41 910**	**43 631**	**96.1**

Numerator: All women diagnosed with breast cancer in a given year undergoing ER and PgR status assessment before any systemic treatment.
Denominator: All women diagnosed with breast cancer receiving systemic treatment in a given year.

5.2.2.3 *Cytological and/or histological assessment*

A lesion considered to be malignant following clinical examination, imaging or cytology alone should, where possible, have histopathological confirmation of malignancy before any surgical procedure takes place[6]. Of all patients who underwent breast surgery (44 722 or 89.4%), 28 876 (64.6%) had a histological and/or cytological examination within 2 months before surgery. There is a clear increase over the years: while in 2001 about 50% of patients had a histological examination, the proportion raised to more than 60% in 2003 and more than 70% in 2006 (Table 22). In 2001, there was a large variability between centres, which decreased in 2006 (Figure 15 and Figure 16). Moreover, in 2006 fewer centres were below the lower limit.

Table 22. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	3 324	6 596	50.4
2002	4 156	6 976	59.6
2003	4 939	7 629	64.7
2004	5 053	7 400	68.3
2005	5 612	8 021	70.0
2006	5 792	8 100	71.5
Total	**28 876**	**44 722**	**64.6**

Numerator: All women diagnosed with breast cancer in a given year undergoing cytological and/or histological assessment within 2 months before surgery.
Denominator: All women diagnosed with breast cancer and treated with surgery in a given year.

Figure 15. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery, analyzed per centre (2001).

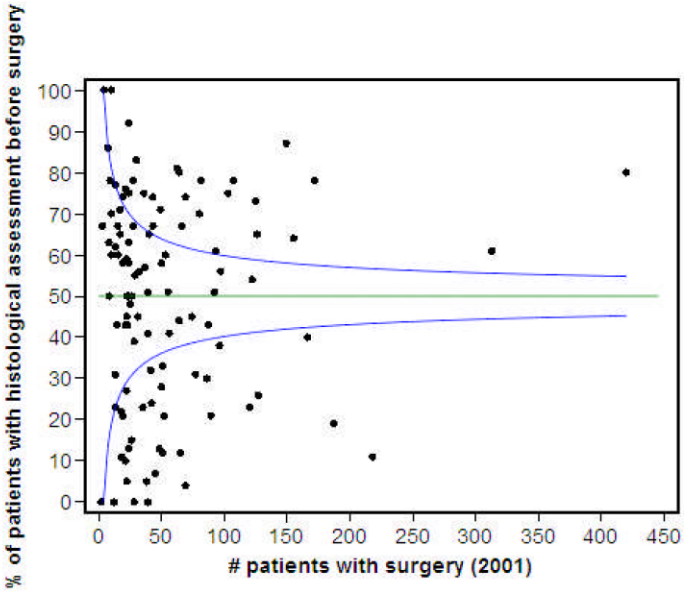
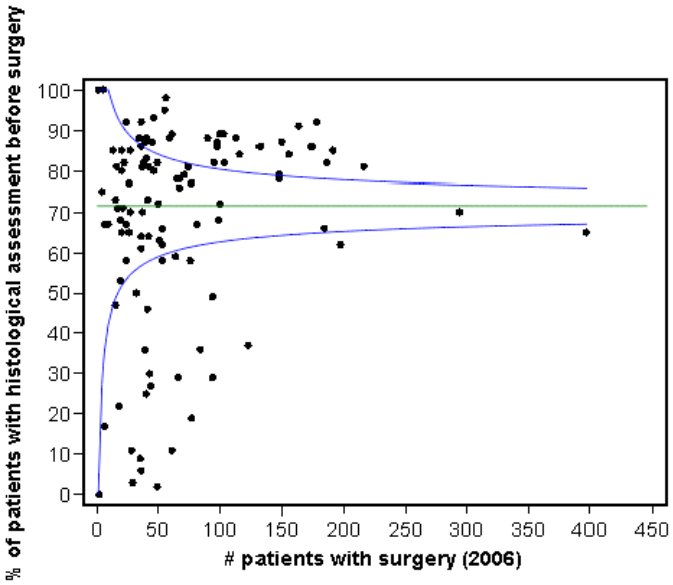


Figure 16. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery, analyzed per centre (2006).



5.2.2.4 *Proportion of breast cancer women discussed at the multidisciplinary team meeting*

Since breast cancer is a complex cancer and asks for a specialized approach, a discussion of the therapeutic approach in a multidisciplinary setting, and based on the diagnostic and staging results, is necessary. Of the 34 012 patients with breast cancer diagnosed after February 1st 2003, 79.2% were discussed at a MDT meeting. In 74% of the cases, the discussion was held within 1 month before and 6 months after the incidence date. The proportion of patients, discussed at a MDT, increased over time. In the first year the MDT nomenclature codes were introduced, only 61.4% of the patients were discussed. This percentage rose to more than 80% in 2006, indicating that a multidisciplinary approach is gaining interest in breast cancer treatment (Table 23).

Table 23. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per year (2003-2006).

	Numerator	Denominator	Proportion (%)
2003	4 770	7 771	61.4
2004	6 285	8 232	76.3
2005	6 831	8 942	76.4
2006	7 280	9 067	80.3
Total	**25 166**	**34 012**	**74.0**

Numerator: All women diagnosed with breast cancer in a given year (after February 1st 2003) discussed at the MDT meeting within one month before and 6 months after incidence date
Denominator: All women diagnosed with breast cancer in a given year (after February 1st 2003)

The analysis per centre indicated that in 2004, 7 centres (6.4%) recorded no nomenclature code for MDT meeting, while 8 centres (7.2%) discussed all patients in a multidisciplinary setting (Figure 17). Comparable numbers were found for 2006, with 7 centres (6.3%) organising no multidisciplinary consult and 10 centres (9.0%) discussing all patients multidisciplinary (Figure 18). Importantly, the absence of a nomenclature code for a MDT meeting for a particular patient does not necessarily mean that no MDT was held. Some centres might not bill MDT meetings, and in turn, they do not appear in the IMA database. Moreover, these data do not allow an evaluation of the quality of this multidisciplinary discussion.

Figure 17. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per centre (2004).

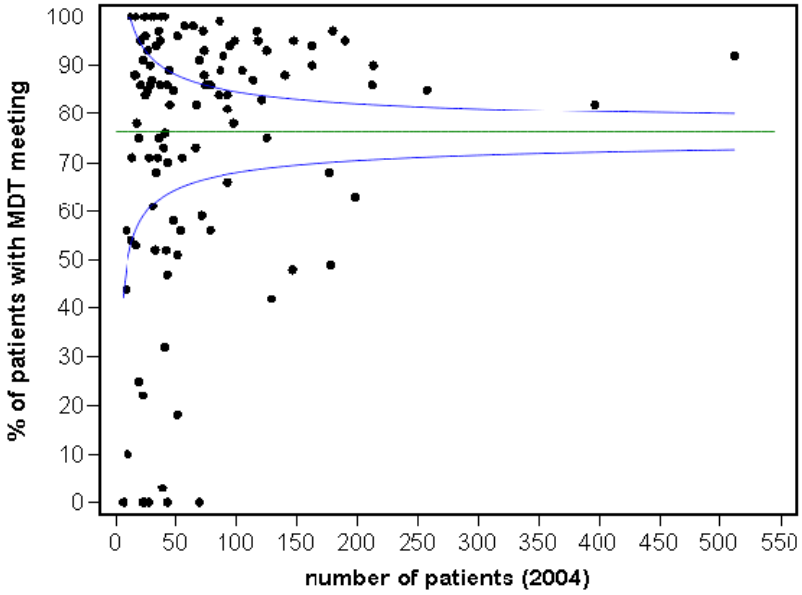
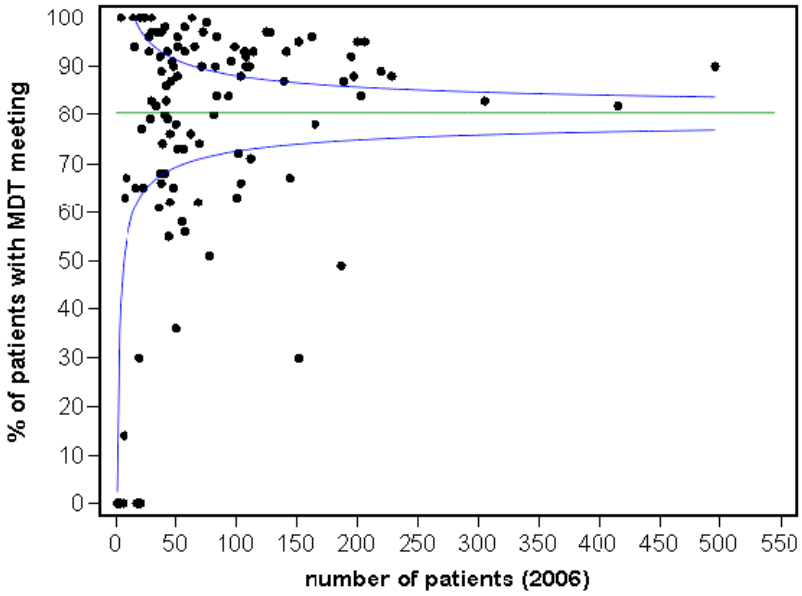


Figure 18. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per centre (2006).



5.2.3 Neoadjuvant treatment

Preoperative treatment increases the possibility for breast conserving surgery because of shrinkage of the tumour before surgical intervention, yet at the associated cost of increased locoregional recurrence rates[23]. In women with unifocal operable tumours too large for breast conserving surgery, downstaging with neoadjuvant systemic therapy should be considered[6].

The number of patients considered to be operable (cStage I-III) was 23 866 (91.5% of all patients with known cStage). Of these patients, 10 311 (43.2%) had a tumour size larger than 2 cm without direct extension to the chest wall or skin (cT2 or cT3).

From the operable cT2 and cT3 tumours, 9 423 (93.9%) were surgically treated and from this group, 61.3% received chemotherapy. A total of 1 147 patients (11.8%) received systemic treatment in a neoadjuvant setting (Table 24).

The analyses per year showed a clear increase in the proportion of patients treated with neoadjuvant chemotherapy, but also a sharp increase in the number of cT2-cT3 women who benefited from surgery. Whereas in 2001 only 5.5% of the patients received neoadjuvant treatment (chemotherapy), this percentage increased above 13% in 2004 and above 18% in 2006.

Table 24. Proportion of operable cT2-cT3 patients who received neoadjuvant systemic therapy (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	59	1 065	5.5
2002	85	1 145	7.4
2003	155	1 758	8.8
2004	242	1 809	13.4
2005	265	1 846	14.4
2006	341	1 800	18.9
Total	**1 147**	**9 423**	**12.2**

Numerator: patients with operable cT2-cT3 disease receiving chemotherapy between incidence and surgery date
Denominator: patients with operable cT2-cT3 disease who were surgically treated

5.2.4 Surgery

Breast-conserving surgery followed by radiotherapy offers the same benefits regarding local tumour control, recurrence free survival and overall survival as modified radical mastectomy in women with stage I or II breast cancer who are candidates for breast-conserving surgery[6]. The choice of surgery must be tailored to the individual patient with stage I or II breast cancer, who should be fully informed of the options.

For all patients in cStage I or II (21 190 or 42.3%), the number of patients with mastectomy and breast conserving surgery was investigated. In total, 12 404 patients (58.5%) were treated with breast conserving surgery and 7 966 patients (37.6%) with mastectomy. The observed ratio breast conserving surgery/mastectomy remained relatively stable over time (Table 25). Between centres, this ratio varied between 0 and 8 in 2001 and between 0 and 7 in 2006. For both extreme years, outliers in the surgical ratio were preferentially observed in smaller centres.

Subsequent analyses reported that the proportion of women who underwent a surgical re-intervention (mastectomy or other breast surgery) within 6 months or 1 year after a first breast conserving surgery fell from 12% in 2001 to 10% in 2006. Reasons for this re-intervention (e.g. recurrence, positive resection margins, …) were not evaluated in the absence of data.

Table 25. Proportion of cStage I and II patients who undergo breast conserving surgery/mastectomy (IMA data, 2001-2006).

Year	Number of surgically treated women	% of surgically treated women	Number of women with BCS	% of women with BCS	Number of women with mastectomy	% of women with mastectomy	Ratio BCS/ mastectomy
2001	2 276	93.0	1 352	55.3	924	37.8	1.463
2002	2 574	97.0	1 595	60.1	979	36.9	1.629
2003	3 824	96.8	2 362	59.8	1 462	37.0	1.616
2004	4 116	96.8	2 538	59.7	1 578	37.1	1.608
2005	3 842	96.4	2 280	57.2	1 562	39.2	1.460
2006	3 738	95.8	2 277	58.4	1 461	37.4	1.559
Total	**20 370**	**96.1**	**12 404**	**58.5**	**7 966**	**37.6**	**1.556**

5.2.5 Adjuvant treatment

5.2.5.1 Chemotherapy and/or endocrine therapy

The choice of adjuvant systemic treatment for invasive breast cancer should be driven by the hormonal sensitivity, risk profile of the tumour, age, menopausal status and comorbidities of the patient[6]. The treatment should ideally start within 120 days of diagnosis. This time frame allows for completion of surgery and appropriate consultation regarding adjuvant treatment options[10]. As hormonal therapy is generally prescribed after the completion of the chemotherapy, the panel of experts proposed an interval of 9 months between the surgical intervention and the start of the endocrine therapy.

From the 44 722 operated patients (89.4% of all patients), 18 941 (42.4%) had additional chemotherapy (with or without endocrine therapy) and 19 143 (42.8%) had additional endocrine treatment (without chemotherapy), administered in the period 2001-2006. As a consequence, 38 084 operated women received an adjuvant systemic treatment (85.1%).

The chemotherapy was administered within four months after surgery for 16 752 women (37.5%) and the hormonal therapy was administered within 9 months for 18 134 patients (40.5%) (Table 26).

It is also important to note that some patients, diagnosed and surgically treated in 2006 received their adjuvant systemic treatment in the beginning of 2007. These patients were not counted as being treated with adjuvant systemic treatment (possible underestimation for 2006). Moreover, a certain proportion of breast cancer women were entered in clinical trials or received chemotherapy in 'compassionate use'. The exact number of these women is currently unknown. In conclusion, it is possible that the number of patients who received adjuvant systemic therapy is underestimated.

Variability between centres remains important for both types of adjuvant systemic treatment.

Table 26. Proportion of women receiving adjuvant endocrine therapy within 9 months or chemotherapy within 4 monhts after breast surgery for invasive breast cancer (IMA data, 2001-2006).

	# surgery	# adjuvant chemo	# adjuvant hormonal	% adjuvant chemo	% adjuvant hormonal
2001	6 596	2 553	2 438	38.7	37.0
2002	6 976	2 657	2 688	38.1	38.5
2003	7 629	2 862	2 982	37.5	39.1
2004	7 400	2 779	3 001	37.6	40.6
2005	8 021	2 914	3 479	36.3	43.4
2006	8 100	2 987	3 546	36.9	43.8
Total	**44 722**	**16 752**	**18 134**	**37.5**	**40.5**

5.2.5.2 *Trastuzumab*

As trastuzumab was not reimbursed before July 1st 2006, it was impossible to trace trastuzumab treatment before this date. Consequently, it was impossible to determine when patients with incidence date before July 1st 2006, started their trastuzumab treatment. After July 1st 2006, 2 104 patients received at least one trastuzumab-based treatment.

An increased risk of grade III-IV congestive heart failure and an asymptomatic drop of left ventricular ejection fraction was reported with trastuzumab[24]. In view of the safety profile of trastuzumab, cardiac function should be monitored during treatment with trastuzumab[6, 25]. Cardiac function was monitored in only 169 patients (8%). No patient received a cardiac function assessment 4 times a year. However, the follow-up period is too short to draw conclusions based on the available data.

5.2.5.3 *Radiotherapy*

In women with early breast cancer, adjuvant irradiation is indicated after breast conserving surgery[6].

Of the 50 039 patients, 23 875 (47.7%) had breast conserving surgery without further mastectomy. From these patients 20 596 (86.6%) were irradiated postoperatively. Over the years, an increase in the number of patients with radiotherapy after breast conserving surgery was reported. In 2001, this proportion was about 82%, while in 2006 it had increased to 89.8% (Table 27). The use of MCD data had no added-value to measure and to interpret this indicator. The variability between centres was similar for 2001 and 2006 (Figure 19 and Figure 20).

Table 27. Proportion of patients who received RT after breast conserving surgery (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	2 716	3 302	82.3
2002	3 003	3 608	83.2
2003	3 525	4 131	85.3
2004	3 550	4 039	87.9
2005	3 780	4 318	87.5
2006	4 022	4 477	89.8
Total	**20 596**	**23 875**	**86.3**

Figure 19. Proportion of patients who received RT after breast conserving surgery: analysis per centre (2001).

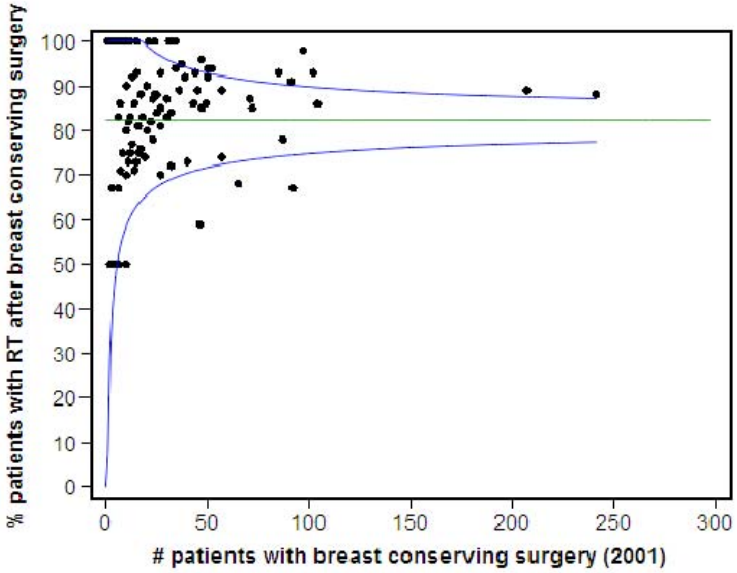
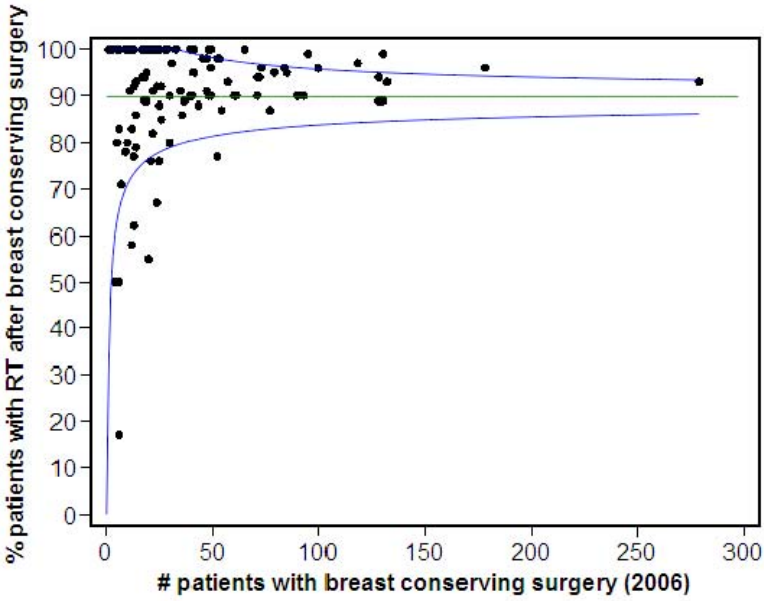


Figure 20. Proportion of patients who received RT after breast conserving surgery: analysis per centre (2006).



5.2.6 Treatment of metastatic cancer

5.2.6.1 Systemic therapy

Chemotherapy is indicated for women with hormone refractory or HR-negative metastatic breast cancer, rapidly progressive disease or symptomatic disease, or with life-threatening disease (e.g. diffuse lung or liver metastases, massive bone marrow metastases with pancytopenia)[6].

The number of patients with metastatic breast cancer was 2 140 (4.3%). Of these patients, 1 881 (87.9%) received chemotherapy or endocrine treatment in first or second line. The proportion of cStage/pStage IV patients with systemic therapy slightly increased over time, reaching a maximum of 91.2% in 2005 (Table 28). The observed decrease in 2006 can be explained by the fact that treatments administered in 2007 were not identifiable in the available database (2001-2006).

Table 28. Proportion of metastatic breast cancer women who receive systemic therapy (IMA data, 2001-2006).

	Numerator	Denominator	Proportion (%)
2001	246	283	86.9
2002	260	296	87.8
2003	335	379	88.4
2004	400	453	88.3
2005	333	365	91.2
2006	307	364	84.3
Total	**1 881**	**2 140**	**87.9**

Numerator: All women diagnosed with cStage IV breast cancer in a given year who received systemic therapy as first-line treatment and/or 2nd line treatment
Denominator: All women diagnosed with cStage IV breast cancer in a given year

5.2.6.2 Biphosphonates for bone metastases

To measure the proportion of metastatic breast cancer women who received biphosphonates, we used coupled IMA-MCD data recorded between 2002 and 2004. The ICD-9 code for bone and bone marrow metastasis (198.5) could be used as proxy to determine patients with lytic bone metastases.

From all patients recorded between 2002 and 2004, 818 were in cStage IV; 186 (22.7%) of them had bone or bone marrow metastasis. Most of these patients (n=174 or 93.5%) were treated with biphosphonates, with a relatively stable proportion over time (Table 29).

Table 29. Proportion of women with metastatic breast cancer and lytic bone metastases who received bisphosphonates (BCR-MCD- IMA, 2002-2004).

	Numerator	Denominator	Proportion (%)
2002	44	50	88.0
2003	64	65	98.5
2004	66	71	93.0
Total	**174**	**186**	**93.5**

Numerator: All women diagnosed with cStage IV breast cancer and bone mestastases in a given year who received biphosphonates
Denominator: All women diagnosed with cStage IV breast cancer and bone mestastases in a given year

5.2.7 Follow-up

5.2.7.1 Mammography

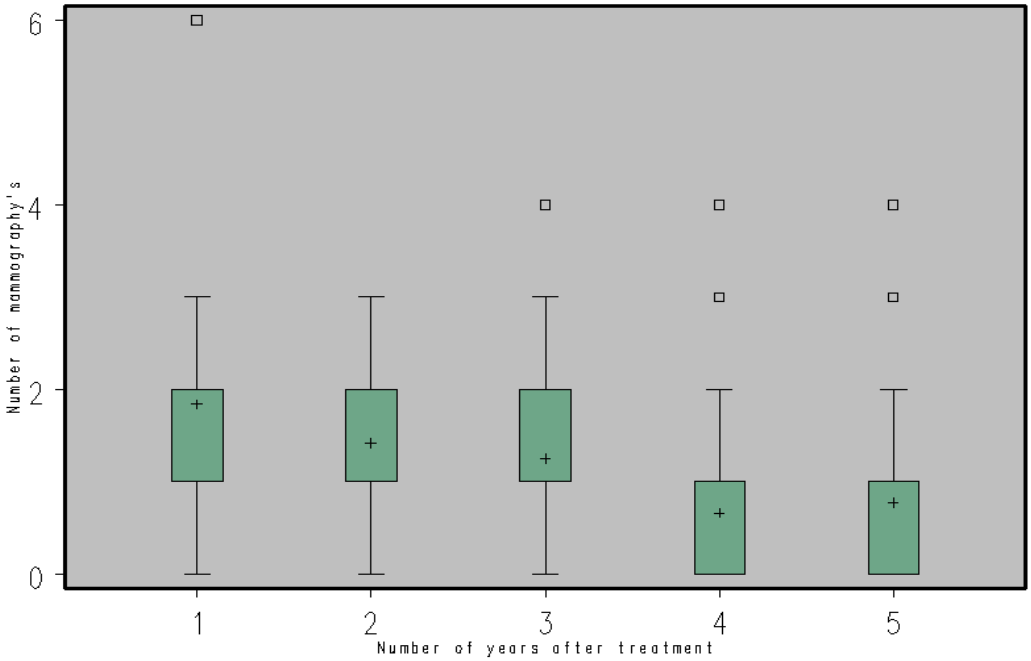
Yearly mammography with or without ultrasound should be used during the first 10 years to detect recurrence or second primaries in patients who have undergone previous treatment for breast cancer (1C evidence)[6]. In current practice, mammography is offered once yearly after treatment for breast cancer to detect ipsilateral or contralateral breast cancer[26].

Of the patients in pStage I-III (n=35 712 or 71.4%), 34 881 had a known treatment (97.7%). In 27 934 (80.1%) of these patients, at least one mammography after treatment was performed. The analysis of the number of mammograms performed per patient according to the year of treatment and the follow-up period shows that patients who were more recently treated underwent more mammograms during follow-up. Furthermore, the annual number of mammograms decreased slightly with increasing follow-up time after treatment, as expected (Table 30 and Figure 21).

Table 30. Mean and median number of mammograms per patient after last treatment: analysis per year of treatment and per year of follow-up (IMA, 2001-2006).

Variable	Mean	SD	Median	25th pct	75th pct
Year of treatment=2001 (n=2 047)					
mammo after 1 year of treatment	1.35	1.21	1	0	2
mammo after 2 years of treatment	1.25	1.00	1	0	2
mammo after 3 years of treatment	1.20	0.98	1	0	2
mammo after 4 years of treatment	1.19	0.98	1	0	2
mammo after 5 years of treatment	1.18	1.00	1	0	2
Year of treatment=2002 (n=3 565)					
mammo after 1 year of treatment	1.90	1.76	2	1	2
mammo after 2 years of treatment	1.85	1.72	2	1	2
mammo after 3 years of treatment	1.82	1.75	2	0	2
mammo after 4 years of treatment	1.73	1.65	2	0	2
Year of treatment=2003 (n=4 571)					
mammo after 1 year of treatment	2.20	2.19	2	0	4
mammo after 2 years of treatment	2.18	2.02	2	1	4
mammo after 3 years of treatment	2.09	2.04	2	0	4
Year of treatment=2004 (n=5 895)					
mammo after 1 year of treatment	2.17	2.08	2	1	4
mammo after 2 years of treatment	2.18	2.08	2	1	4
Year of treatment=2005 (n=6 695)					
mammo after 1 year of treatment	1.73	1.69	2	0	2

Figure 21. Number of mammograms after last treatment.



5.2.8 Histopathologic examination

The information contained in pathology reports of breast cancer specimens provides the tumour size and stage information that are of critical importance to orientate physicians in their selection of local regional treatment, adjuvant therapy, evaluation of therapy, estimation of prognosis, and analysis of outcomes[12]. Incomplete cancer resection pathology reports may result in misclassification of women, rework and delays, and suboptimal management. However, available data did not allow to assess the completeness and availability of the required information in the pathology reports. Only manual revision of every pathology report could give such information. Reabstraction and recoding of pathology reports was not feasible due to the large number of breast cancer patients in this study (N = 50 039).

5.3 RELATIONSHIP BETWEEN HOSPITAL VOLUME, PROCESSES AND OUTCOMES

Figure 22 presents the survival function by the annual volume of centres (computed on the number of patients treated in 2004, 2005 and 2006). Hospitals with less than 100 patients per year were labelled "small-volume" (83 hospitals, 10 591 patients treated in total), hospitals that treated between 100 and 149 patients were labelled "medium volume" (14 hospitals, 5 008 patients treated in total), and hospitals with at least 150 patients treated were labelled "high volume"(14 hospitals, 9 579 patients treated in total, Table 31). The mean annual volume was 76 patients, and half of the hospitals treated less than 48 patients per year.

Table 31. Annual volume of centres (2004-2006).

	N hospitals	N patients	Mean	Median	Std Dev
1-<100/year	83	10 591	42.5	39.0	23.3
100-<150/year	14	5 008	119.2	115.3	14.1
≥ 150/year	14	9 579	228.1	190.2	101.8
All hospitals	**111**	**25 178**	**75.6**	**48.3**	**75.4**

The 5-year survival was 77% for small-volume centres, 80% for medium-volume centres and 84% for high-volume centres (Figure 22).

Figure 22. Survival curves (KM) for breast cancer patients, by volume of centres (incidence years 2004, 2005, 2006)

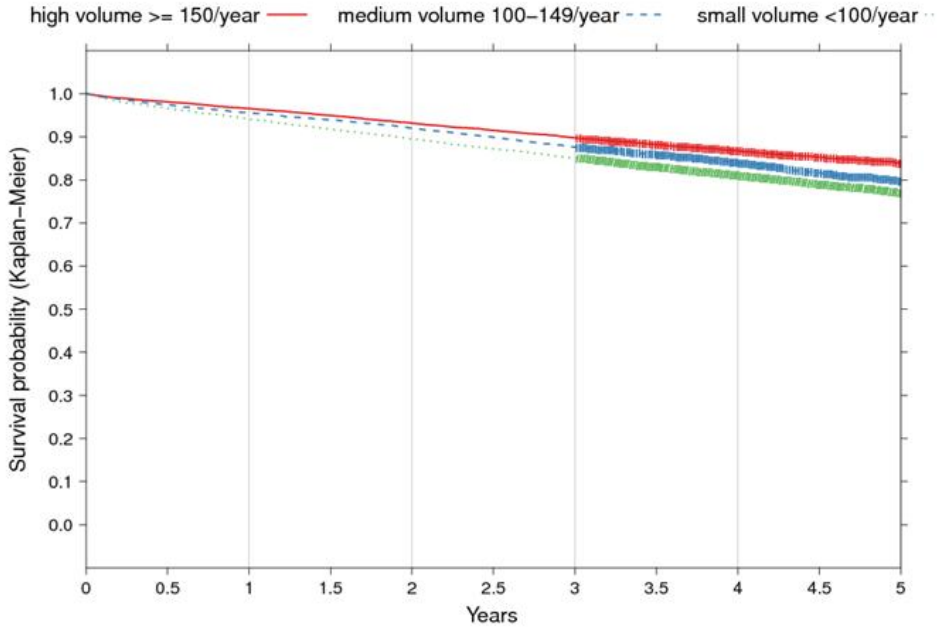


Table 32 presents the results of the Cox Proportional Hazard (PH) model. In the first model, the effect of the hospital volume is presented alone. In the second model, the case mix is taken into account (patient age, breast cancer stage, grade of the tumour). These results show that, after adjustment for the case mix, patients treated in small-volume hospitals had a 20% higher probability of death within 5 years after diagnosis than patients treated in high-volume centres.

For patients treated in medium-volume centres, the impact on the hazard of death was lower (increase of 10%) and not statistically significant. The comparison of the estimates from Model 1 and Model 2 also showed that differences in case mix between small and high-volume centres accounted for approximately 60% of the differences observed in 5-year survival. These differences are described in Table 33.

Table 32. Results of Cox PH model: Determinants of survival after breast cancer (follow-up maximum 5 years)

Model	Variable	Hazard Ratio (HR)	95% CI	
1, no case mix adjustment	Small (<100) versus high volume (≥ 150)	1.49	1.27	1.75
	Medium (100-149) versus high volume (≥ 150)	1.26	1.04	1.53
2, with case mix adjustment	Small (<100) versus high volume (≥ 150)	1.20	1.07	1.34
	Medium (100-149) versus high volume (≥ 150)	1.10	0.98	1.24
	Increase of 1 year in age	1.05	1.05	1.06
	Stage IV versus Stage I	14.46	12.77	16.38
	Stage III versus Stage I	4.58	4.16	5.04
	Stage II versus Stage I	2.05	1.88	2.22
	Stage missing (X) versus Stage I	5.03	4.43	5.72
	Grade 4 versus Grade I	2.20	1.57	3.08
	Grade 3 versus Grade I	1.88	1.69	2.10
	Grade 2 versus Grade I	1.23	1.10	1.38
	Grade Missing versus Grade I	1.60	1.41	1.81

Table 33 presents differences in case mix between small, medium and high-volume centres. Patients treated in small-volume hospitals are on average 3 years older than patients treated in high-volume centres. Also, the percentage of missing values is much higher in small-volume centres (13.7% missing stage) than in high-volume centres (5.8%).

Table 33. Differences in case mix between small, medium and high volume centres.

		Annual volume of centres (2004-2006)			
		Small 1-<100 /year	**Medium, 100-<149 /year**	**High, ≥ 150/year**	**All patients**
N patients		10 591	5 008	9 579	25 178
N hospitals		83	14	14	111
Age	Mean	62.2	60.9	59.3	60.8
	Median	62.0	60.0	59.0	60.0
	Std	14.0	13.7	13.4	13.8
% of missing Stage	%	13.7	9.1	5.8	9.8
% of missing Grade	%	16.4	14.3	9.1	13.2
Stage					
I	%	41.3	42.0	40.5	41.1
II	%	38.4	38.5	40.3	39.2
III	%	14.3	14.0	14.1	14.1
IV	%	6.0	5.6	5.2	5.6
Grade					
1	%	18.2	17.3	14.4	16.5
2	%	42.9	44.9	42.8	43.2
3	%	38.3	37.4	41.9	39.6
4	%	0.5	0.5	0.9	0.7

Table 34 presents differences in process indicators in small, medium and high volume centres. The following process indicators were analyzed:

- For the entire sample of patients: the proportion of MDT meeting was 76.7% in small-volume hospitals and 82.1% in high-volume hospitals.
- For patients with stage I, II or III and having undergone a surgery:
  - the proportion of breast conserving surgery was 62.3% in small-volume hospitals versus 65.8% in high-volume hospitals
  - the proportion of patients who got any radiotherapy overall was 75.7% in small-volume hospitals versus 82.8% in high-volume hospitals, and by type of surgery was 54.5% of patients with radiotherapy after a mastectomy in small-volume hospitals versus 65.7% in high-volume hospitals
  - the proportion of patients who received chemotherapy was 41.1% in small-volume hospitals versus 43.2% in high-volume hospitals.

Table 34. Differences in process indicators between small, medium and high-volume centres (patients in Stage I, II, III and with surgery)

		Annual volume of centres (2004-2006)			
		Small 1-<100 /year	**Medium 100-149/year**	**High ≥150/year**	**All patients**
N patients (all)		10591	5008	9 579	25 178
MDT meeting	%	76.7	84.7	82.1	80.4
Subgroup of patients (Stage I, II, III undergoing a surgical intervention) N		8161	4011	8 104	20 276
Stage					
I	%	45.0	46.3	44.1	44.9
II	%	40.9	40.6	42.4	41.5
III	%	14.1	13.0	13.5	13.7
Surgery					
Mastectomy	%	37.7	35.9	34.2	35.9
Breast Conserving surgery*	%	62.3	64.1	65.8	64.1
Any Radiotherapy ***	%	75.7	79.5	82.8	79.3
Any Radiotherapy after BCS*, ***		88.5	92.0	91.5	90.4
Any Radiotherapy after a mastectomy, ***		54.5	57.2	65.7	59.4
Any chemotherapy **	%	41.1	38.4	43.2	41.4

* patients with both interventions are counted in the mastectomy category
** given within 180 days before incidence date to 365 days after incidence date
*** given within 180 days before incidence date to 180 days after incidence date

6 DISCUSSION

6.1 INDICATOR RESULTS

6.1.1 National level

The quality of breast cancer management is improving

The descriptive statistics and selected quality indicators showed a systematic improvement of most assessable processes for women with breast cancer in Belgium for the period 2001-2006 (Table 35). Positive evolutions were found for the diagnosis and staging procedures, the surgical procedures (proportion of surgically treated women and proportion of women who underwent breast conserving surgery), the adjuvant treatments (systemic treatment and radiotherapy) for invasive breast cancer and follow-up procedures.

Table 35. Evolution of measurable quality indicators between 2001 and 2006.

Indicator	Result 2001	Result 2006
Proportion of newly diagnosed cstage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery	84.9%	86%
Proportion of patients in whom a ER and PgR status assessment were performed before any systemic treatment	90.5%	98.0%
Proportion of breast cancer women with cytological and/or histological assessment before surgery	50.4%	71.5%
Proportion of breast cancer women discussed at the multidisciplinary team meeting	61.4% *(2003 results)*	80.3%
Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	5.5%	18.9%
Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy • Proportion of operated women • Ratio BCS/mastectomy	 93.0% 1.46	 95.8% 1.56
Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer • Chemotherapy within 4 months after surgery • Endocrine therapy within 9 months after surgery	 38.7% 37.0%	 36.9% 43.8%
Proportion of women who received radiotherapy after breast conserving surgery	82.0%	89.8%
Proportion of metastatic breast cancer women who received systemic therapy as 1st and/or 2nd line treatment	86.9%	84.3%
Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	88.0% *(2002 results)*	93.0% *(2004 results)*
Proportion of women who benefit from an annual mammography after a history of breast cancer • Mean number of mammograms per patient 1 year after last treatment	1.35	1.73
Observed 5-year survival by stage • pStage I • pStage II • pStage III • ptage IV	 93% 81% 59% 30%	 93% 84% 64% 27% *(2004 results)*

Survival is slightly increasing and comparable to neighbouring countries

From 2001 to 2004, a slight improvement was observed in the 5-year observed survival for pStage II (from 81% to 84%) and pStage III (from 59% to 64%). These probabilities remained stable for pStage I (93%) and pStage IV (27%).

Five-year relative survival was reported by pStage, and the difference between pStage I (98%) and pStage IV (32%) was found to be large. These results are comparable to those reported for France[27]. French data were collected between 1994 and 1999 from incident cases who were hospitalised (27 080 patients) (Table 36). They covered only one region, Ile-de-France representing 20% of the French population. Comparison has to be made cautiously since periods covered by French and Belgian data are different. Results are similar for Stage I and III, and are better for stages II and IV in Belgium. The proportion of unknown stages is clearly higher in Belgium, and an improvement in reporting these essential data is required.

Table 36. Five-year relative survival rate by stage in Belgium (n=50 039; 2001-2004) and Ile-de-France (n=27 080; 1994-1999).

	Belgium		Ile-de-France	
Stage	**5-Year survival (%)**	**Repartition of cases (%)**	**5-Year survival (%)**	**Repartition of cases (%)**
Stage I	98	30.8	98	37.8
Stage II	87	31.2	80	36.9
Stage III	68	9.1	70	13.0
Stage IV	32	1.3	20	6.1
Unknown	86	27.5	unknown	6.2

Older results from 6 European countries (Estonia, France, Italy, Netherlands, Spain and UK) participating in EUROCARE (17 population-based cancer registries; 1990-1992) were reported according to TNM classification[28]. For women who underwent surgery, pathologic T and N were used (pStage), whereas clinical information on T, N, and M was used for the fraction of women not treated surgically (cStage). Women were grouped into five stage categories for survival analyses. Early stage tumours (T1N0M0) had a mean 5-year relative survival of 97.5%, large lymph node-negative tumours (T2–3N0M0) 87%, lymph node-positive tumours (T1–3N+M0) 76.5%, locally advanced tumours (T4M0) 54.6%, and metastatic tumours (M1) 18.4%.

In all countries, a higher proportion of breast cancers diagnosed at earlier stages had better overall survival and survival decreased with advancing stage. Importantly, the number of metastatic patients is low (less than 10 patients in some cases), rendering interpretation of survival rates for this stage group difficult. The differences between survival rates are more impressive for advanced stage categories, from 1% in Italy to 46.5% in Spain. Five-year survival was always higher than 90% when tumours remained confined to the breast, whereas for women with node-positive tumours, survival fell below 80% and even below 30% in Estonia[28].

Large differences between countries are not easy to interpret. Longer survival may be explained by the availability of better treatment, similar treatments being more effective because diagnosis is made at an earlier stage of disease, or simply early diagnosis without any advantage to the patient (lead-time bias)[29]. Adjustment of all results for age, surgery, stage, and the number of lymph nodes evaluated can potentially reduce the differences between countries[29].

Diagnosis and staging could be improved

Between 2001 and 2006, 86% of all cStage I-III women underwent a breast mammography or sonography within 3 months prior to surgery. This is low compared to a prospective sample of 1 378 breast cancer patients treated from 1995 to 2001 in Taiwan. Cheng[8] reported a 91.2% adherence rate for the same process indicator in the same target group. All patients' clinical information was retrieved from medical records. In a more restrictive target group including 727 stage I-II invasive BC women treated in 1993-1994 in the USA, Shank et al.[16] obtained a similar adherence rate (91.5%). They selected a random sample of women from their medical records and surveys and specified that mammography took place no more than 3 months prior to the excision of a mass. In Belgium, even when considering a longer timeframe between diagnostic procedure and surgery (i.e. 6 months), such an adherence rate was not reached (88.7%). Comparing a random sample of hospitalized women with population data is not ideal. However, no population data were found in the literature for diagnostic mammography. Screening mammography is commonly evaluated at a population level, but can not be compared with diagnostic mammography.

The routine use of MRI of the breast is not recommended in the preoperative assessment of patients with biopsy-proven invasive breast cancer or DCIS (1C evidence)[6]. In Belgium, a MRI of the breast was performed in 21% of all patients (11.5% in 2001, 30% in 2006) and a distant MRI was performed in 2.2% of patients.

For M-staging (visceral or bone metastases), MRI/CT can be considered[6]. A CT was performed in 40% of the patients, but no specification of the CT location is available in the nomenclature data. Less than 3% of the patients underwent a PET scan, and most of these patients also underwent a CT and/or MRI.

While a positive evolution was found for biopsy or breast puncture, increasing from 57% in 2001 to 87% in 2006, this rate still needs to improve since core biopsy and/or fine needle aspiration cytology are recommended when mammography and/or ultrasonography have identified a localized abnormality[6].

In Belgium, 98% of women underwent a ER and PgR assessment before any systemic treatment. This adherence rate is comparable to that reported in the Taiwanese sample of 1 378 breast cancer patients (96.6%)[8]. Ideally, the rate should reach 100%, as recommended in the Belgian guidelines[6]. However, increasing the rate of these assessments also supposes an adequate ER/PgR testing performance to avoid an increasing rate of false positive and false negative results.

Despite the improvement in breast cancer staging, cytological and/or histological assessment was significantly underused before surgery. A sharp increase was observed from 50% in 2001 to more than 70% in 2006. This result remains disappointing since 30% of all breast cancer women did not benefit from a core biopsy 2 months before their surgical intervention. A similar indicator referring to the appropriate use of fine-needle aspiration cytology or needle histology was evaluated in the scientific literature. The standard was set by different authors at ≥70% or ≥90%[16]. This indicator was also qualitatively defined by Cheung[30] who considered that the quality of fine-needle aspiration samples from lesions, which subsequently proved to be breast cancer, should be adequate as deemed by the breast pathologist. In this study involving 100 women with operable primary BC < 5 cm, the overall adherence rate was 99%, exceeding the target standard of ≥90%[30].

Clinicians are in favour of multidisciplinary consultation

In 2002, the health authorities created the multidisciplinary oncology consultation (MDT), as it was recognized that there was a need to organize and to reimburse the existing multidisciplinary approach[31]. The purpose of the MDT is to discuss the overall care of an individual within a planned meeting and to develop a strategic plan of diagnosis, treatment and follow-up. Specific nomenclature codes for a multidisciplinary oncologic consultation are available since February 1st 2003. The proportion of breast cancer patients, discussed at a MDT within 1 month before and 6 months after the incidence date, increased over time from 61.4% in 2003 to more than 80% in 2006. In comparison to other tumour types, the proportion is high. For testicular cancer for example, the proportion of patients discussed at a MDT only reached 67.3% (Vlayen et al. 2010, in progress) while in the year the nomenclature code was implemented (2003), the proportion was 65% for rectal cancer (cT3-4, cN+ and/or cStage IV)[2]. Note that this indicator measures the recording and the organisation of MDT consultations and not their content nor the specialists who were involved. In particular, the increase in MDT meetings does not lead to an increase in cancer stage reporting, since 45% of cStages and about 20% of pStages remained unreported in 2006. The definition of MDT can vary between institutions from organised and well-prepared group discussions, to informal opinion exchanges regarding the patient's diagnosis, treatment and/or referral. These discussions can be conducted concurrently when care is provided and/or prospectively with an adequate planning[26].

One barrier to organize MDT is the high cost, which is about six times higher than originally foreseen. However, this is balanced by a more standardized management of breast cancer women and a higher quality of care. Indeed, every new event (relapse, progression of disease, unexpected side-effects, etc.) experienced by the individual is (or should be) discussed in multidisciplinary meetings[31].

Rates of neoadjuvant treatment seem to be adequate

In 2006, about one in five women with operable cT2-3 breast cancer received neoadjuvant systemic treatment against only one in twenty women in 2001. Meanwhile, the number of cT2-3 patients who underwent breast conserving surgery has almost doubled within 5 years. This rate is well in accordance with what the experts expected. In Belgium, neoadjuvant systemic treatment is specifically administered to a restricted group of women who are preferentially orientated to breast conserving surgery instead of mastectomy. In these situations, neoadjuvant treatment has an added value[23].

More breast conserving surgery could be performed

In selecting the BCS/mastectomy ratio as a quality measure, breast conserving surgery was considered to be feasible for most cStage I and II patients, to be the less invasive and less life-altering procedure, and to have a long-term survival equivalent to that of mastectomy. However, mastectomy was considered the more appropriate or the preferred surgical therapy for other patients. European guidelines have suggested that breast conservation surgery should be achievable in 70% to 80% of all cases[32]. However, patients who can be treated with BCS, but wish to undergo a mastectomy, should be treated according to their wish. After adequate information, up to 20% of patients may choose for mastectomy[32]. Modified radical mastectomy is also advised in patients who have insufficient remission of the primary tumour after neoadjuvant chemotherapy[32]. Belgian ratios are lower than the European targets, since less than 60% of all surgically treated women underwent BCS. Variations in BCS/mastectomy rates can be explained by different factors such as patients' age, patients' preferences, patients' socioeconomic status, tumour size, acceptability of further treatment, but also reflect surgical judgement experience, technique, performance and practical guidelines adopted in the hospital[32].

Adjuvant systemic treatment can be improved but is probably underestimated

Results revealed an increase for adjuvant treatment in non-metastatic invasive breast cancer whereas a decrease was reported for metastatic breast cancer women. However, according to clinicians, more and more patients having metastatic disease are recruited in clinical trials, benefitting from strict procedure protocols. Between 2006 and 2008 for example, an increase in the number of clinical trial applications (+17.0%) was observed[33]. The share of industry-sponsored trials has been increasing and varies between 81.7% and 89.0%[33]. In the context of an industry-sponsored trial, treatments administered to patients recruited in the investigational arm are not traceable leading to an underestimation of systemic treatment in adjuvant settings.

Systemic adjuvant treatment has to be chosen according to hormonal sensitivity, risk profile of the tumour, age and menopausal status and patients comorbidities. Most of these criteria cannot be assessed using retrospective administrative databases. The time frame of 4 months for the definition of adjuvant treatment was based on the Belgian guideline[6] that recommended to start adjuvant chemotherapy within 120 days of diagnosis. This time frame allows for completion of surgery and appropriate consultation regarding adjuvant treatment options. For hormonal treatment, it was decided to take a longer time interval (9 months) since such treatment habitually follows chemotherapy. In Belgium, registered data revealed that 42.4% of surgically treated women received adjuvant chemotherapy (with or without endocrine therapy) within 4 months after surgery and 42.8% received endocrine treatment (without chemotherapy) in the period 2001-2006. So, at least 85.1% of all operated women received an adjuvant systemic treatment. Adjuvant treatment was administered in the recommended time frame in 91.6% of all patients who received such treatment. It is also important to note that some patients, diagnosed and surgically treated in 2006 could receive adjuvant systemic treatment in the beginning of 2007. These patients are not identifiable in the dataset considered.

A similar measure evaluated in the NICCQ report was the initiation of chemotherapy within 8 weeks of surgery among women younger than age 50 with stage II and III cancer and any hormone receptor status. Adherence varied widely, from 60% to 91%, across sites[10].

Adjuvant radiotherapy rates after breast conserving surgery are increasing

Adjuvant irradiation is indicated after breast conserving surgery. A time frame of 9 months for the start of adjuvant radiation was selected because surgical complications and/or prolonged chemotherapy treatment may result in substantial, but clinically appropriate delays in the initiation of radiotherapy. In the USA, a time frame of 1 year was considered[10], whereas in Taiwan, radiation therapy has to be started within 6 weeks after BCS or 6 weeks after completion of chemotherapy if BCS is followed by chemotherapy and then radiotherapy[8].

Of all women who underwent breast conserving surgery (not followed by a mastectomy) in the period 2001-2006, 86.3% were irradiated postoperatively. While this proportion was about 82% in 2001, it increased to 89.8% in 2006. These results did not take into account women's age, in contrast to other studies limiting this indicator to women younger than age 70[10]. In the NICCQ report, adherence to a similar measure was reported to be 96% to 99%. Recent data from NCCN institutions (1997-2002) show an overall rate of radiation for invasive cancers after BCS of 94%[34]. With shorter time intervals between BCS and radiotherapy, Cheng reported adherence rate of 87.5% in a prospective cohort (1995-2001).

Better follow-up is required

Yearly mammography with or without ultrasound is essential to detect recurrence or second primaries in patients who have undergone previous treatment for breast cancer. In Belgium, only 80% of pStage I-III patients diagnosed between 2001 and 2006 underwent at least one mammography after primary treatment. It is possible that the remaining 20% underwent physical examination or other imaging procedures, such as X-rays, CT or MRI, although these tests should not be performed in asymptomatic women[35-37]. Another author reported better results (84.6%) in a random sample of 99 women living in 12 US metropolitan areas in the USA[38] while Cornfeld (2001)[39] reported that 100% of invasive breast cancer women treated in a private practice benefited from a physical examination and 98% received a mammography as follow-up.

The frequency of follow-up consultations is not extensively studied, and therefore mainly based on expert opinion. Follow-up consultations can be provided every 3 to 4 months in the first two years after diagnosis, every 6 months until 5 years after diagnosis, and every year after 5 years[6]. The mean number of yearly mammograms naturally decreased with a longer follow-up after treatment. After 5 years, more than 50% of all treated women underwent a mammogram. Patients who were treated more recently underwent twice as much mammograms during follow-up. Data recorded until 2011 could allow the measurement of the proportion of women undergoing yearly mammogram 10 years after their treatment.

No information on number of patients included in clinical trials

No exact data are available on the number of patients with breast cancer that are included in a clinical trial. According to the clinicians, mainly the larger academic centres and specialized centres include patients in clinical trials. Metastatic patients are frequently entered in such trials in order to test new molecules, new treatment regimens or sequences.

Recently, Deloitte analysed the number of clinical trials in Belgium that are registered at the Federal Agency for Medicines and Health Products[33]. About 24% of the newly started clinical trials between 2006 and the first semester of 2009 (n = 1 943) were in the domain of antineoplastic and immunomodulating agents.

6.1.2 Variability of practices between centres

Although results at a national level show that almost all indicators follow a positive trend, yet there remains considerable variability of care between centres.

For instance, while a histopathological confirmation of malignancy is needed before undergoing surgery, only 70% of all women benefited from a cytological and/or histological assessment. In a lot of hospitals, this proportion was below 50%. Another example is the multidisciplinary team consultation. Despite the creation and financing of a MDT, 7 centres (6.3%) held no multidisciplinary consults in 2006, and only 10 centres (9.0%) discussed all patients multidisciplinary. In fact, it is still possible to exclude patients from this system as it remains a voluntary act to present a patient's case to the MDT[31].

This was illustrated graphically with funnel plots, which picture the results of each centre, taking into account the expected variability due to the sample size. For all indicators, funnel plots easily identify centres with results outside the expected limits of variability, and whose results should be further scrutinized. The fact that a centre is an outlier does not automatically implies suboptimal quality of care: possible data errors, differences in billing habits, differences in case mix should be investigated first.

6.1.3 Volume outcome relationship

A considerable variability in processes and outcomes between high-volume centres and small-volume centres was observed in our analyses. High-volume hospitals were defined as those treating at least 150 patients per year (on basis on their annual volume computed on the years 2004, 2005, 2006). Medium-volume hospitals were defined as those treating 100 to 150 patients per year. Small-volume hospitals treated less than 100 patients per year.

In 2004, 2005 and 2006, the annual volume of many hospitals was too low to guarantee quality of care: half of the hospitals treated less than 50 patients per year. New regulations were introduced by a Royal Decree on July 20th 2007 to be recognized as a Breast clinic. Each clinic has to treat surgically 100 new patients per year in 2008 and 2009 and 150 new patients since 2010. Each surgeon will also have to reach a volume of 50 patients per year, surgically treated for a breast pathology.

Survival of patients depends of the centre volume. The 5 year-survival was 84% for high-volume centres whereas it was only 77% for small-volume centres. When results were adjusted for case mix (age, stage, tumour grade), patients treated in small-volume hospitals had a 20% higher probability of dying within 5 years after diagnosis than patients treated in high-volume centres. Differences in case mix between small and high-volume centres accounted for approximately 60% of the difference observed in 5-year survival. This indicates that 40% of the difference could be explained by other factors, such as variability in diagnostic and therapeutic practices between hospitals.

Such differences in process indicators were investigated further.

In Belgium, the probability of organizing a MDT consultation is higher in high-volume centres than in small-volume centres. In fact, between 2004 and 2006, 82% of Stage I-III operated women were discussed during such a consultation. This was only true for 77% of women in small-volume centres. Guller et al.[40] hypothesize that high-volume hospitals have a better pre-, peri- and postoperative management of patients. They mentioned the possibility that the collaboration between physicians, nurses, anaesthesiologists, physical therapists and other practitioners is better in high-volume centres.

Other indicators were compared on the pStage I-III patients who had a surgery. In high-volume centres, the proportion of women who underwent a mastectomy was lower compared to small-volume centres (34.2% vs. 37.7%). Guller et al.[40] mentioned similar statistically significant differences in undergoing BCS between small and high-volume hospitals. Variability in mastectomy rates can be explained by different factors such as patients' age, patients' preferences, socioeconomic status, tumour size, acceptability of further treatment, but also reflect surgical judgement experience, technique, performance and practical guidelines adopted in the hospital[32].

In the same way, a high variability between centres was observed for administration of radiotherapy after BCS. In high-volume centres, 83% of stage I-III patients received radiotherapy after breast cancer surgery whereas only 76% of similar patients received such treatment in small-volume centres. After a mastectomy, 54.5% of patients received radiotherapy in small-volume hospitals while 65.7% of women underwent radiotherapy in high-volume hospitals. Buccholz et al. also reported variability in practice patterns across NCCN institutions. Radiation was most frequently omitted in patients with favourable disease characteristics, patients with comorbidities, and patients who did also not receive guideline-recommended systemic treatment[34].

The administration of (neo)adjuvant chemotherapy showed less variability between small-volume (41.1%) and high-volume centres (43.2%).

6.2 INDICATORS MEASURABILITY AND INTERPRETABILITY

Of the 32 selected indicators, 13 were found to be measurable and 1 indicator was measurable using a proxy indicator (Table 17). One reason of this low proportion of measurable indicators is that the current nomenclature was not conceived for quality measurement but for activity tarification and reimbursement purposes. Moreover, when codes exist in the nomenclature, they are not always specific to a pathology or an organ. This is the case for biopsy, medical imaging (CT and MRI) and histology assessment. This prevents researchers to evaluate many diagnostic, staging and follow-up procedures.

Although the nomenclature is not always adapted to the current state-of-the-art medicine, it evolved to include more recent diagnostic procedures. Consequently, it will be possible in the near future to trace women in whom HER2 receptor was assessed prior to systemic treatment, since a specific nomenclature code was introduced in 2007.

Quality indicators that measured clinical results of specific techniques (e.g. resection margins after surgery, status of HER2 receptor, status of ER/PgR receptors, number of positive lymph nodes) are currently impossible to measure. Nevertheless, as prospective registrations will be conducted in hospitals treating breast cancer women, the status of this HER2 receptor (positive or negative) will be known and reported.

The formulation of other quality indicators such as 'the proportion of cN0 women who underwent a sentinel lymph node biopsy in the absence of contraindications' results in the inability to measure this quality indicator. Parameters such as contraindications of a diagnostic procedure are never reported in administrative databases and can only be found in the medical file. At a national level, it is of course impossible to consult all medical records to obtain such information. In the same way, analysing the content of all medical files to assess the chemotherapy regimen (drug[s] prescribed, dose, and duration) is impossible due to the large number of patients considered (n=50 039). However, a random sample of medical files could be selected (for example 30 in each centre) to be analysed in depth at regular intervals. Similar surveys are conducted in France by the National Federation of French Cancer Centres (FNCLCC), a federation of 20 cancer centres. In a project evaluating the use of radiotherapy, 13 indicators on radiotherapy were compared across the 20 cancer centres using medical charts from 2007[41, 42]. Based on this evaluation, action points were identified and corrective actions were initiated. A second measurement will take place by the end of 2010.

In the present report, only women recorded with ICD-10 code C50 (invasive breast tumours) were included in the analyses. Women having an ICD-10 code D05 (DCIS) were not selected in our study sample. Quality indicators focusing on women with high-grade and/or palpable and/or large DCIS of the breast were therefore not measurable in the present study.

Local or distant recurrence as well as disease-free survival are essential outcomes to evaluate treatment effectiveness and are regularly included in quality indicators dataset. Two quality indicators related to disease-free survival and local recurrence were selected and defined in this report. However, they were found to be not measurable, because information about local recurrences is currently not registered at the BCR at a population level and no nomenclature code exists to record a relapse or a new treatment administered due to a recurrence. An indirect measurement of this indicator by investigating the number of retreatments also seemed invalid for this cancer type. Indeed, a retreatment can only be determined if there is a clear interval between the first-line and the second-line treatment. Endocrine therapy may be a long-term treatment which makes a treatment-free interval difficult to determine. Therefore, adding "recurrence" to the current list of variables with obligatory registration at the cancer registry should be considered, at least for a selected group of cancer types (including the most frequent cancer types and some less frequent cancer types with high impact). In a first phase, this could be done in the context of a well-defined (prospective) registration protocol, as was done for PROCARE[2].

The absence of national data on causes of mortality hampered the calculation of the disease-specific survival. Relative survival, a frequently used parameter in cancer epidemiology, was used as a proxy of the disease-specific survival[21]. However, in the near future, national data should again (and mandatory) be available and also be made linkable to the cancer registration data. The upcoming European regulation in this domain should enhance the capacity to have data on causes of mortality with a delay of less than a 2-year period.

Since an increasing proportion of women is recruited in clinical trials, it would be particularly interesting to prospectively register these patients, as they receive specific therapeutic products (chemotherapy, endocrine therapy, biological therapy) and are submitted to specific surveillance procedures. In the investigational arm, both treatments and surveillance procedures are not recorded in general databases leading to an underestimation of administered treatments, particularly in specialized hospitals or in large academic centres that conduct a lot of clinical trials.

One of the outcomes of this feasibility report was to evaluate the added value of MCD data to increase the measurability of the included indicators. However, many technical problems led to an incomplete linkage of MCD data to linked BCR-IMA data. Eventually, linked BCR-IMA-MCD data were only available for the years 2002-2004 and for a limited number of cases. MCD data only had an impact when evaluation of lytic bone metastases was required. The impact on other results was much less clear or absent. Because of the above mentioned technical problems, the exhaustivity of the BCR data could not be checked with the MCD data.

Based on the above discussion, actions are suggested to increase the measurability of some quality indicators (Table 37). Some suggested actions have an impact on several indicators, and are not always repeated.

Table 37. Suggested actions to increase measurability of breast cancer quality indicators.

Quality indicator		Action
General indicators: outcomes		
BC1	Overall 5-year survival rate by stage	-
BC2	Disease-specific 5-year survival by stage	Collect national data on causes of mortality
BC3	Disease-free 5-year survival rate by stage	Oblige registration of recurrence?
BC4	5-year local recurrence rate after curative surgery, by stage	Oblige registration of recurrence?
General indicators: process		
BC5	Proportion of breast cancer women discussed at the multidisciplinary team meeting	-
BC6	Proportion of women with breast cancer who participate in clinical trials	Include information in MDT form
Diagnosis and staging		
BC7	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	Regular surveys on a random sample of patients medical files to know the result of the mammogram
BC8	Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy	Regular surveys on a random sample of patients medical files to know the result of the mammogram
BC9	Proportion of newly diagnosed cstage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery	-
BC10	Proportion of patients who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment	Create specific nomenclature codes for axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes reflecting the current state-of-the-art (with

		unambiguous specification of the anatomic location : axilla)
BC11	Proportion of patients in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment	-
BC12	Proportion of patients in whom a ER and PgR status assessment were performed before any systemic treatment	-
BC13	Proportion of breast cancer women with cytological and/or histological assessment before surgery	-
BC14	Proportion of sentinel lymph nodes biopsy in cN0 patients without contraindications	Include information in MDT form / Regular surveys on a random sample of patients medical files
Neo-adjuvant treatment		
BC15	Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy	-
Surgery		
BC16	Proportion of breast cancer women who underwent an ALND after positive SNLB > 2 mm	Include information in MDT form / Regular surveys on a random sample of patients medical files
BC17	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)	Include DCIS in data selection and record resection margins in the pathology report
BC18	Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy	-
BC19	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy	Oblige registration of recurrence?
Adjuvant treatment		
BC20	Proportion of women with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen	Regular surveys on a random sample of patients medical files
BC21	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer	-
BC22	Proportion of women with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI)	Include information in MDT form / Enlarge the data selection to include DCIS
BC23	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of > or= 50-55% who received chemotherapy and Trastuzumab	Regular surveys on a random sample of patients medical files
BC24	Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months	-
BC25	Proportion of women who received radiotherapy after breast conserving surgery	-
BC26	Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND	Include information in MDT form / Regular surveys on a random sample of patients medical files andpathology reports
BC27	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment	Include information on HER2 status in MDT form
BC28	Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment	-
BC29	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	-

Follow-up		
BC30	Proportion of women who benefit from an annual mammography after a history of breast cancer	-
Histopathology		
BC31	Proportion of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade.	Oblige to record all these informations, use of a standard pathology report form Regular surveys on a random sample of pathology reports
BC32	Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed	Oblige to record all these informations Regular surveys on a random sample of pathology reports

6.3 USE OF INDICATORS FOR QUALITY IMPROVEMENT

Quality indicators were considered in this study as tools for quality improvement. From all quality indicators identified from the literature review, only those that answered to criteria of reliability, relevance, interpretability and actionability were retained. In other words, a quality indicator was considered acceptable if the topic area and aspect of health that the indicator addresses are of significant clinical importance. An indicator that does not concern many patients is unable to measure the quality of care and to identify potential problems. This indicator also should produce a similar result when repeatedly applied to the same population/organisation/practitioners. The potential for improvement has to be recognized by clinicians and the numeric values of the indicator should be comprehensible for the user. The results of the measurement have to result in actions that are under control of the user, leading to real improvements. Finally, only indicators that assist in decision-making were selected by the panel of clinicians involved in the selection procedure. Once results for the indicators have been calculated, a reflexion about how to present and interpret them took place. Beside the summarizing tables reporting the comparison between two extreme years, a graphical tool that allows to easily identify outlying centres has been proposed.

Measuring quality indicators defines a baseline, the first step in quality improvement. To go beyond evaluation, each center can adopt a cycle of improvement, such as Plan, Do, Check, Act (PDCA) circle, first defining the problem or area requiring a quality improvement effort.

For all identified problems, targets had to be set. A target is a clear statement of planned results (including outputs and outcomes) to be achieved within a specified timeframe, against which reported results can be compared[43]. In this report, some standards coming from the literature were reported (e.g. >90% of women who underwent a pre-operative mammography and/or breast sonography; 100% of women have to benefit from a cytological/histological assessment). The analysis per centre could also allow to benchmark results from one centre against those of other centres. In this report, all centres were anonymised; however, the Belgian Cancer Registry could identify all centres helping them to situate themselves against others. Such transparency would allow each centre to identify and explore significant variances between its data and data reported by other centres. While variances do not necessarily indicate a problem, they do represent areas for further assessment and evaluation. Possible data errors, differences in billing habits, differences in case-mix should be investigated first to explain discrepancies between reality and statistics and between centres. Second, as results reflect different processes of care on same patients groups, centres that desire engaging in a quality improvement approach can identify those centres that scored higher on the incriminated indicators and understanding the processes and practices before potentially adopting them. However, it will be more effective to focus on all aspects of an organization's operations rather than just one element because the results for a best-in-class organization may result from numerous determinants[43].

Timeliness of information is an important issue in this approach, since a lot of procedures can evolve overtime. For this feasibility study, data from 2001-2006 were used and results reflect an outdated situation. The delay between the incidence year and the availability of these data for publication and research must be kept as short as possible, and a delay of maximum 2 years should be pursued. The BCR which masters the know-how in calculating indicators and communicating results could reproduce the analyses on 2008 data.

Finally, besides recurrent evaluations on the whole set of measurable indicators, in-depth evaluations could be conducted on specific indicators choosen for their potential for improvement, the priority for stakeholders, or national objectives pursued in the field of oncology. For a quality system to be effective, the focus can change from time to time, for example concentrating on pathology in year 1, on medical oncology in year 2, on diagnostics in year 3. Sampling strategies will be more informative than standard analysis of major databases. Such initiative is currently taken in France by the National Federation of French Cancer Centres (FNCLCC) that currently evaluates procedures for radiotherapy.

6.4 CONCLUSIONS

The following conclusions can be drawn from the present report:

- The present study showed that it is feasible to implement a quality indicator set for breast cancer, covering the whole range of diagnostic and therapeutic options. Based on current nomenclature and cancer registry data, the set contains 14 measurable indicators.
- This analysis, based on 2001-2006 data, shows a positive and improving overall picture of the quality of care for breast cancer women in Belgium. Survival is high for early-advanced stages and progressively decreases for more advanced stages. However, there are indications of underuse of recommended interventions having an impact on survival, recurrence or aesthetics (e.g. breast conserving surgery, radiotherapy after surgery).
- A high rate of unknown cStages and pStages was found. An improvement in the reporting of these data is essential to refine some analyses.
- The added value of the hospital administrative discharge data (MCD) is rather limited for this quality indicator set as it improved the measurability of only one indicator (the identification of lytic bone metastases).
- This analysis also showed a wide variability in diagnostic and therapeutic approaches between centres. A graphical tool allowing an easy identification of outlying centres has been proposed. However, the fact that a centre is an outlier in a funnel plot does not automatically imply suboptimal quality of care. Possible data errors, differences in billing habits, differences in case-mix should be investigated first.
- The annual volume of women per centre is on average low, as half of the centres treated less than 50 women (volume based on period 2004-2006). Lower volume has been shown to be associated with lower survival rates. However, this is not systematically observed in all low-volume centres, a finding which asks for an in-depth evaluation of their organisational and functional characteristics. New regulations, introduced by Royal Decree on July 20th 2007, stipulate that, in order to be recognized as a Breast clinic, a centre should have treated surgically at least 100 new women per year in 2008 and 2009 and 150 new women from 2010 on. In addition, any surgeon treating breast pathology should also reach a volume of 50 surgically treated women per year.

7 APPENDIX

7.1 SEARCH STRATEGY OVID MEDLINE

Search date: November 30th 2009

1.	"Quality of Health Care"/
2.	Patient Care Management/
3.	"Organization and administration"/
4.	Quality Assurance, Health Care/
5.	Quality Indicators, Health Care/
6.	1 or 2 or 3 or 4 or 5
7.	(breast adj5 neoplasm$).tw.
8.	(breast adj5 cancer$).tw.
9.	(breast adj5 carcinoma$).tw.
10.	(breast adj5 metasta$).tw.
11.	(breast adj5 tumo$).tw.
12.	(breast adj5 malig$).tw.
13.	or/7-12
14.	6 and 13

Search date: December 10th 2009

1.	exp Physician's Practice Patterns/
2.	exp Guideline Adherence/
3.	exp "Diffusion of Innovation"/
4.	exp Registries/
5.	exp Health Care Surveys/
6.	or/1-5
7.	(breast adj5 neoplasm$).tw.
8.	(breast adj5 cancer$).tw.
9.	(breast adj5 carcinoma$).tw.
10.	(breast adj5 metasta$).tw.
11.	(breast adj5 tumo$).tw.
12.	(breast adj5 malig$).tw.
13.	or/7-12
14.	6 and 13

7.2 OVERVIEW OF ALL IDENTIFIED QUALITY INDICATORS

Quality indicator	Discipline	Subdiscipline(s)	Source	Ex/inclusion	Final formulation
<10% of all new cases of women with breast cancer should attend the clinic/hospital on > 2 occasions for diagnostic purposes	Diagnosis	General category	AHRQ	Exclusion	
>90% of women with breast cancer detected by screening should attend an assessment centre within 3 weeks of mammography	Diagnosis	General category	AHRQ; Perry (2008)	Exclusion	
Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	Diagnosis	General category	KCE / experts	Inclusion	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography
≥90% of women requiring an operation for diagnostic purposes should be admitted within 14 days of the surgical decision	Diagnosis	General category	AHRQ	Exclusion	
≥90% of women with breast cancer or with an abnormality requiring diagnostic operation need to be told of this within 5 working days of investigations leading to this diagnosis	Diagnosis	General category	AHRQ	Exclusion	
Appropriate use of an evaluation in compliance with guidelines	Diagnosis	General category	AHRQ	Exclusion	
Appropriate use of initial examination	Diagnosis	General category	AHRQ	Exclusion	
Appropriate use of referrals to surgeon by general practitioner according to breast referral guidelines	Diagnosis	General category	AHRQ	Exclusion	
Diagnosis of breast disease: percentage of class 4 or class 5 abnormal mammograms that are followed by a biopsy within 7 to 10 days	Diagnosis	General category	NQMC (ICSI)	Exclusion	
Management of cases coming to surgery from the screening program carried out by surgeons who have acquired the	Diagnosis	General category	AHRQ	Exclusion	

necessary specialist knowledge					
Women attending for diagnostic purposes seen on at least 1 occasion by a breast specialist surgeon	Diagnosis	General category	AHRQ	Exclusion	
Radiology: percentage of women undergoing diagnostic mammograms that are classified as "suspicious" or "highly suggestive of malignancy" with documentation of direct communication of findings from the diagnostic mammogram to the patient within 5 business days of exam interpretation	Diagnosis	General category	NQMC (ACR)	Exclusion	
Radiology: percentage of women undergoing diagnostic mammograms that are classified as "suspicious" or "highly suggestive of malignancy" with documentation of direct communication of findings from the diagnostic mammogram to the practice that manages the patient's on-going care within 3 business days of exam interpretation.	Diagnosis	General category	NQMC (ACR)	Exclusion	
Urgent referrals of women with breast cancer to be seen within 5 working days	Diagnosis	General category	AHRQ	Exclusion	
Women with breast cancer to be seen by specialist in timely fashion post referral for diagnostic purposes	Diagnosis	General category	AHRQ	Exclusion	
Appropriate use of imaging &/or cytology or needle biopsy, if required, to be performed at the initial visit	Diagnosis	Preoperative diagnosis	AHRQ	Exclusion	
Appropriate use of preoperative diagnosis by fine-needle aspiration cytology, needle histology or biopsy	Diagnosis	Preoperative diagnosis	AHRQ	Exclusion	
Appropriate use of preoperative mammographic evaluation	Diagnosis	Preoperative diagnosis	AHRQ; Owen (2009)	Exclusion	
Appropriate use: A biopsy or fine-needle aspiration should be performed	Diagnosis	Preoperative diagnosis	AHRQ	Exclusion	

within 6 weeks either when the mammography suggests malignancy or the persistent palpable mass is not cystic on ultrasound					
Appropriate use: If a breast mass has been detected on two separate occasions, then either a biopsy, fine-needle aspiration or ultrasound should be performed within 3 months of the second visit	Diagnosis	Preoperative diagnosis	AHRQ	Exclusion	
Appropriate use: If a palpable breast mass has been detected, at least one of the following procedures should be completed within 3 months: fine-needle aspiration, mammography, ultrasound, biopsy and/or a followup visit	Diagnosis	Preoperative diagnosis	AHRQ	Inclusion	Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 month after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy
Mammography or breast sonography should be performed within 3 mos prior to surgery for newly diagnosed breast cancer women with pathologic stage I-III disease	Diagnosis	Preoperative diagnosis	Cheng (2009)	Inclusion	Proportion of newly diagnosed cstage I-III breast cancer women who underwent two-view mammography or breast sonography within 3 months prior to surgery
Proportion of operations for benign lesions (evaluated with triple diagnosis)	Diagnosis	Preoperative diagnosis	KCE / experts	Exclusion	
Proportion of breast cancer women who have diagnosis in cytology and histology before surgery	Diagnosis	Preoperative diagnosis	Chung (2007)	Inclusion	Proportion of breast cancer women with cytological and/or histological assessment before surgery
Proportion of women aged over 50 who received bilateral mammography 3 months before surgery	Diagnosis	Preoperative diagnosis	Chung (2007)	Exclusion	
Proportion of women who received a preoperative 99mTc-MIBI scintimammography	Diagnosis	Preoperative diagnosis	KCE / experts	Exclusion	
Proportion of women who received a preoperative MRI	Diagnosis	Preoperative diagnosis	KCE / experts	Exclusion	
Quality of fine-needle aspiration samples from lesions, which subsequently prove	Diagnosis	Preoperative diagnosis	AHRQ	Exclusion	

to be breast cancer, should be adequate as deemed by the breast pathologist					
Proportion of women subsequently proven to have clinically occult breast cancer with a preoperative FNAC or core biopsy that is diagnostic for cancer	Diagnosis	Pre-operative diagnosis	Perry (2008)	Exclusion	
Determination of human epidermal growth factor receptor 2 status	Diagnosis	Pretreatment diagnosis	Owen (2009)	Inclusion	Proportion of women in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment
Proportion of women in whom a ER and PgR were performed before any treatment	Diagnosis	Pretreatment diagnosis	Cheng (2009); Owen (2009)	Inclusion	Proportion of women in whom a ER and PgR status assessment were performed before any systemic treatment
Appropriate use of first localization biopsy operation to correctly identify impalpable lesions	Diagnosis	Surgical procedures	AHRQ	Exclusion	
Appropriate use: A biopsy should be performed within 6 weeks if fine-needle aspiration cannot rule out malignancy	Diagnosis	Surgical procedures	AHRQ	Exclusion	
Quality of breast biopsy: primary operable breast cancer receives a frozen section	Diagnosis	Surgical procedures	AHRQ	Exclusion	
There is no evidence for pretreatment routine bone scanning, liver ultrasonography and chest radiography, or tumour markers for asymptomatic women with negative clinical findings, unless there is at least clinical stage II disease and/or neoadjuvant treatment is considered, or a mastectomy is planned	Diagnosis	Staging	KCE / experts	Exclusion	
The use of PET in staging axillary lymph nodes for breast cancer is not recommended. PET sensitivity is inferior to axillary node dissection and sentinel node biopsy	Diagnosis	Staging	KCE / experts	Exclusion	
Quality of hormone receptor assay	Diagnosis	Surgical procedures	AHRQ	Exclusion	
Axillary ultrasonography with fine	Diagnosis	Surgical procedures	KCE / experts	Inclusion	Proportion of women who received

needle aspiration cytology of axillary lymph nodes suspicious for malignancy is recommended before preoperative systemic treatment					axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment
Quality of sampling nodes for invasive breast cancer, to include ≥ 4 nodes	Diagnosis	Surgical procedures	AHRQ	Exclusion	
Quality of technique to determine histological node status for all invasive tumours, either by sampling or clearance	Diagnosis	Surgical procedures	AHRQ	Exclusion	
Ten or more axillary lymph nodes should be examined in women with pathologic stage I-III disease	Diagnosis	Surgical procedures	Cheng (2009)	Inclusion	Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed
Change in QOL after diagnosis of breast cancer	General	QOL and patient satisfaction	AHRQ	Exclusion	
Women reporting an overall satisfaction with the quality of breast care	General	QOL and patient satisfaction	AHRQ	Exclusion	
Access to care	General	End-of-life	Grunfeld (2008)	Exclusion	
Access to palliative care	General	End-of-life	Grunfeld (2008)	Exclusion	
Advance care directives	General	End-of-life	Grunfeld (2008)	Exclusion	
Adverse events	General	End-of-life	Grunfeld (2008)	Exclusion	
Assessment of financial and caregiving resources	General	End-of-life	Grunfeld (2008)	Exclusion	
Community-centred services	General	End-of-life	Grunfeld (2008)	Exclusion	
Continuity of care	General	End-of-life	Grunfeld (2008)	Exclusion	
Enrollment in palliative care within 6 months of death / Enrollment in palliative care within 3 days of death	General	End-of-life	Grunfeld (2008)	Exclusion	
Frequency of emergency room visits	General	End-of-life	Grunfeld (2008)	Exclusion	
Hospital/ICU stay near the end of life	General	End-of-life	Grunfeld (2008)	Exclusion	
Interval between last chemotherapy and death	General	End-of-life	Grunfeld (2008)	Exclusion	
Interval between new chemotherapy and death	General	End-of-life	Grunfeld (2008)	Exclusion	
Multidisciplinary care	General	End-of-life	Grunfeld (2008)	Exclusion	
Physician reimbursement for home visits	General	End-of-life	Grunfeld (2008)	Exclusion	
Regular palliative care assessments	General	End-of-life	Grunfeld (2008)	Exclusion	

Site of death	General	End-of-life	Grunfeld (2008)	Exclusion	
Time and location of care in last 2 weeks of life / Time and location of care at monthly visits	General	End-of-life	Grunfeld (2008)	Exclusion	
5-year overall survival rate by stage	Outcomes	General category	Cheng (2009); Chung (2007)	Inclusion	overall 5-year survival rate by stage
5-year disease-specific survival by stage	Outcomes	General category	KCE / experts	Inclusion	disease-specific 5-year survival by stage
5-year progression-free survival rate by stage	Outcomes	General category	Cheng (2009); Chung (2007)	Inclusion	disease-free 5-year survival rate by stage
Arm oedema rate for breast conservation surgery patient after radiation therapy	Outcomes	General category	Chung (2007)	Exclusion	
Five-year local recurrence rate after surgery	Outcomes	General category	Chung (2007)	Inclusion	5-year local recurrence rate after curative surgery, by stage
Local recurrence rate for breast conservation surgery patient after radiation therapy	Outcomes	General category	Chung (2007)	Exclusion	
Oncology: percentage of women, regardless of age, with a diagnosis of breast, colon, or rectal cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation of the new treatment regimen.	Reporting / documentation	Chemotherapy	NQMC (ASTRO/ASCO)	Inclusion	Proportion of women with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen
Presence of body surface area calculations on chemotherapy flow sheets	Reporting / documentation	Chemotherapy	AHRQ	Exclusion	
Presence of chemotherapy flow sheets in active treatment charts	Reporting / documentation	Chemotherapy	AHRQ	Exclusion	
Size of mammographic abnormality	Reporting / documentation	Imaging	AHRQ	Exclusion	
Palliative care: percentage of adult women with a progressive, debilitating disease who have a palliative care plan documented in the medical record.	Reporting / documentation	Palliative care	NQMC (ICSI)	Exclusion	

Oncology: percentage of women, regardless of age, with a diagnosis of breast cancer who are seen in the ambulatory setting who have a baseline cancer stage or documentation that the cancer is metastatic in the medical record at least once during the 12 month reporting period	Reporting / documentation	Pathology	NQMC (ASTRO / ASCO)	Exclusion	
Pathology reports on chart	Reporting / documentation	Pathology	AHRQ	Exclusion	
Pathology: percentage of breast cancer resection pathology reports that include the pT category (primary tumour), the pN category (regional lymph nodes) and the histologic grade.	Reporting / documentation	Pathology	NQMC (CAP); Imperato (2003)	Inclusion	Proportion of breast cancer resection pathology reports that include the tumour size (macro- and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade.
Proportion of breast cancer patient with pathology report of tumour-size in the medical record after surgery	Reporting / documentation	Pathology	Chung (2007)	Exclusion	
Proportion of invasive breast cancer after surgery with 10 or more lymph nodes removed on pathology report	Reporting / documentation	Pathology	Chung (2007)	Exclusion	
Proportion of invasive breast cancer women with oestrogen receptor analysis results in the medical record	Reporting / documentation	Pathology	Chung (2007)	Exclusion	
Proportion of zero-stage breast cancer women with 10 or more lymph nodes on pathology report	Reporting / documentation	Pathology	Chung (2007)	Exclusion	
Reporting assessment of microscopic margins	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting Bloom Scarf Richardson scale (tumour grade) (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting carcinoma confirmed microscopically	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting cytometry ploidy	Reporting /	Pathology	AHRQ	Exclusion	

(microscopic)	documentation				
Reporting description of background breast (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting description of cut surface of the tumour (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting description of nipple (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting description of skin (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting distance of tumour from nipple (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting distance to the closest margin (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting ductal carcinoma in situ (DCIS) present/absent (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting estrogen receptor status (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting extent of tubule formation (microscopic)	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting gross observation of lesion	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting having performed flow cytometry (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting histological grade (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting histological type (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting identification of affected quadrant (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting involvement of apical lymph nodes (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting laterality of surgical specimen (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting lymph node presence/absence (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting lymph-vascular invasion (microscopic)	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	

Reporting measurement of macroscopic margins of carcinoma	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting mitotic rate (microscopic)	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting nature of specimen (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting nuclear grade (microscopic)	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting number of lymph nodes present (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting number of positive lymph nodes (microscopic)	Reporting / documentation	Pathology	AHRQ; Imperato (2003)	Exclusion	
Reporting pathological extent of primary tumour (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting presence or absence of fascia or skeletal muscle (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting progesterone receptor status (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting size of concurrent ductal carcinoma in situ (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting size of invasive carcinoma (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting size of overlying skin (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting size of specimen (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting specimen inked (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting the orientation of the pathology specimen (gross examination)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting TNM staging (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting tumour size (macroscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting tumour size (microscopic)	Reporting / documentation	Pathology	AHRQ	Exclusion	
Reporting verification tumour size	Reporting /	Pathology	AHRQ; Cheng	Exclusion	

(microscopic)	documentation		(2009); Imperato (2003)		
In women with unifocal operable tumours too large for breast conserving surgery, downstaging with neoadjuvant systemic therapy should be considered	Treatment	Neo-adjuvant treatment	KCE / experts	Inclusion	Proportion of operaple cT2-T3 women who received neo-adjuvant systemic therapy
Adjuvant hormonal therapy is recommended for women with ER positive DCIS	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
If adjuvant chemotherapy and radiotherapy are indicated, the chemotherapy should be given first	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
Adjuvant chemotherapy or radiotherapy should be started maximum within 8 weeks of completion of surgery	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
Any patient regardless of age who started adjuvant chemotherapy should be given for at least four cycles	Treatment	Adjuvant systemic therapy	Cheng (2009)	Exclusion	
Appropriate decision not to provide adjuvant systemic therapy for women > 65 years of age with high risk, estrogen receptor (-), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate decision not to provide adjuvant systemic therapy for women node (-), low risk, breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of adjuvant systemic therapy after breast-conserving surgery	Treatment	Adjuvant systemic therapy	AHRQ	Inclusion	Proportion of women receiving adjuvant systemic therapy after breast-conserving surgery for invasive breast cancer
Appropriate use of any adjuvant systemic therapy	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of any adjuvant systemic therapy in women with node (-) breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of any adjuvant systemic therapy in women with node (+) breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy	Treatment	Adjuvant systemic	AHRQ	Exclusion	

		therapy			
Appropriate use of chemotherapy &/or ovarian ablation in premenopausal women with node (+), estrogen receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy and hormone therapy (tamoxifen)	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy and hormone therapy (tamoxifen) in premenopausal women, node (+), hormone receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in postmenopausal women cancer with node (+), estrogen receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in postmenopausal women with node (+), estrogen receptor (-), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in premenopausal women with node (-), high risk, estrogen receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in premenopausal women with node (+), estrogen receptor (-), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in women <50 years of age with node (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ; Cheng (2009)	Exclusion	
Appropriate use of chemotherapy in women with node (-), estrogen receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of chemotherapy in women with node (-), high risk, estrogen receptor (-), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of tamoxifen	Treatment	Adjuvant systemic therapy	AHRQ	Inclusion	Proportion of women with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine

					treatment (Tamoxifen/AI)
Appropriate use of tamoxifen in postmenopausal women with node (-), high risk, estrogen receptor (+), breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of tamoxifen in postmenopausal women with node (-), intermediate risk, breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of tamoxifen in postmenopausal women with node (+)	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use of tamoxifen in premenopausal women with node (-), intermediate risk, breast cancer	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Appropriate use: Women with invasive breast cancer that is node-positive, or node-negative and primary tumour > 1 cm, should be treated with adjuvant systemic therapy to include combination chemotherapy (and/or tamoxifen, 20mg/d)	Treatment	Adjuvant systemic therapy	AHRQ		
Availability of office procedure manual used for chemotherapy administration	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
Breast cancer: percentage of women for whom combination chemotherapy is considered or administered within 4 months (120 days) of diagnosis for women under 70 with T1c, or stage II or III hormone receptor negative breast cancer.	Treatment	Adjuvant systemic therapy	NQMC (ASCO / NCCN)	Exclusion	
Breast cancer: percentage of women for whom tamoxifen or third generation aromatase inhibitor is considered or administered within 1 year (365 days) of diagnosis for women with T1c or stage II or III hormone receptor positive breast cancer.	Treatment	Adjuvant systemic therapy	NQMC (ASCO / NCCN)		
ER-positive women with pathologic	Treatment	Adjuvant systemic	Cheng (2009)	Exclusion	

stage I-III should have adjuvant hormonal therapy		therapy			
Oncology: percentage of female women aged 18 years and older with Stage IC through IIIC, estrogen receptor (ER) or progesterone receptor (PR) positive breast cancer who were prescribed tamoxifen or aromatase inhibitor (AI) during the 12 month reporting period	Treatment	Adjuvant systemic therapy	NQMC (ASTRO / ASCO)	Exclusion	
One year treatment with adjuvant trastuzumab is indicated for women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of > or= 50-55% and without important cardiovascular risk factors who received chemotherapy	Treatment	Adjuvant systemic therapy	KCE / experts	Inclusion	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of > or= 50-55% who received chemotherapy and trastuzumab
During treatment with trastuzumab, cardiac function should be monitored every 3 months	Treatment	Adjuvant systemic therapy	KCE / experts	Inclusion	Proportion of women treated by trastuzumab in whom cardiac function is monitored every 3 months
Patient older than 18 years, with stage I to stage III breast cancer (> 1 cm) received tamoxifen or AI within 1 year of diagnosis	Treatment	Adjuvant systemic therapy	Desch (2008; ASCO/NCCN)	Exclusion	
Patient older than 18 years (< 70 years) having a ER negative and PR negative Stage II-III breast cancer received adjuvant chemotherapy within 120 days of diagnosis	Treatment	Adjuvant systemic therapy	Desch (2008; ASCO/NCCN)	Exclusion	
Proportion of post-menopausal breast cancer women with positive lymph node receiving adjuvant hormone therapy or chemotherapy	Treatment	Adjuvant systemic therapy	Chung (2007)		
Proportion of pre-menopausal breast cancer women with positive lymph node receiving adjuvant chemotherapy	Treatment	Adjuvant systemic therapy	Chung (2007)		

Quality of chemotherapy: proper doses administered (≥ 85% dose intensity [DI] & relative dose intensity [RDI]) of CMF	Treatment	Adjuvant systemic therapy	AHRQ	Exclusion	
In premenopausal women with hormone receptor positive or hormone receptor unknown metastatic breast cancer, suppression of ovarian function (e.g. with LHRH analogs, bilateral oophorectomy, irradiation of the ovaries) in combination with tamoxifen is the first-line hormonal therapy	Treatment	Adjuvant systemic therapy	KCE / experts		
In postmenopausal women with hormone receptor positive or hormone receptor unknown metastatic breast cancer, first-line treatment consists of third generation aromatase inhibitors (anastrozole, letrozole, exemestane) or Tamoxifen. The choice of the agent should take into consideration the adjuvant endocrine therapy received. As second-line treatment, the use of a third generation aromatase inhibitor or Fulvestrant is recommended	Treatment	Adjuvant systemic therapy	KCE / experts		
In postmenopausal women with hormone receptor positive or hormone receptor unknown metastatic breast cancer, first-line treatment consists of third generation aromatase inhibitors (anastrozole, letrozole, exemestane) or Tamoxifen. The choice of the agent should take into consideration the adjuvant endocrine therapy received. As second-line treatment, the use of a third generation aromatase inhibitor or Fulvestrant is recommended	Treatment	Adjuvant systemic therapy	KCE / experts		
Potent antiemetic treatment for highly emetogenic chemotherapy	Treatment	End-of-life	Grunfeld (2008)	Exclusion	

RTx for uncontrolled bone pain for women with painful bony metastases	Treatment	palliative care	Grunfeld (2008)	Exclusion	
Women with a single or small number of potentially resectable brain metastases can be treated with radiosurgery or with surgery followed by whole brain radiotherapy. Offer whole brain radiotherapy only to women for whom surgery or radiosurgery is not appropriate	Treatment	palliative care	KCE / experts	Exclusion	
Annual mammography rate for breast cancer women after treatment	Treatment	Follow-up	Chung (2007)	Inclusion	Proportion of women who benefit from an annual mammography after a history of breast cancer
Appropriate use of guidelines for followup surveillance of breast cancer	Treatment	Follow-up	AHRQ	Exclusion	
Appropriate use of prophylactic radiotherapy in women with high risk of flap recurrence	Treatment	Follow-up	AHRQ	Exclusion	
Appropriate use: Women with a history of breast cancer should have a yearly mammography	Treatment	Follow-up	AHRQ	Exclusion	
Women with breast cancer developing local recurrence within 5 years after breast-conserving surgery	Treatment	Follow-up	AHRQ	Exclusion	
Women with breast cancer developing local recurrence within 5 years after mastectomy	Treatment	Follow-up	AHRQ	Exclusion	
Intensive surveillance monitoring (CBC testing, chest x-ray, bone scans, liver ultrasound and computed tomography) is not recommended for routine breast cancer surveillance	Treatment	Follow-up	KCE / experts	Exclusion	
Do not offer MRI for routine post-treatment surveillance in women who have been treated for early invasive breast cancer or DCIS	Treatment	Follow-up	KCE / experts	Exclusion	
Follow-up consultations could be	Treatment	Follow-up	KCE / experts	Exclusion	

provided every 3 months in the two years after diagnosis, every 6 months until 5 years after diagnosis, and every year after 5 years					
In view of the rapidly changing evidence in the field of breast cancer, clinicians should encourage women with breast cancer to participate in clinical trials	Treatment	General category	KCE / experts	Inclusion	Proportion of women with breast cancer who participate in clinical trials
≥90% of women admitted for an operation within 21 days of the surgical decision to operate for therapeutic purposes	Treatment	General category	AHRQ	Exclusion	
Appropriate use of alternative definitive therapy (radiotherapy after breast-conserving surgery + axillary lymph node dissection or adjuvant treatment)	Treatment	General category	AHRQ	Exclusion	
Appropriate use of definitive locoregional therapy (total mastectomy + axillary lymph node dissection, or, breast-conserving surgery + axillary lymph node dissection + radiotherapy)	Treatment	General category	AHRQ	Exclusion	
Appropriate use of treatment sequences according to guidelines (including surgery; radiotherapy; chemotherapy; hormone therapy; initial examination; and followup)	Treatment	General category	AHRQ	Exclusion	
Appropriate use: Women with metastatic breast cancer should be offered hormonal therapy, chemotherapy, and/or enrollment in a clinical trial with documentation of informed consent within 6 weeks of the identification of metastases	Treatment	General category	AHRQ	Exclusion	
Anthracycline- and/or taxane based regimens are to be preferred as first-line treatment depending on adjuvant chemotherapy received and disease-free	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	

interval					
In women with anthracycline-resistance or failure and taxane-naive, considered for further chemotherapy, taxane-based treatment (monotherapy or combination of a taxane with gemcitabine or capecitabine) should be used, taking into account quality of life, toxicity, characteristics of the disease and the ease of administration	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
For women pretreated with anthracyclines and taxanes, capecitabine monotherapy is the preferred treatment	Treatment	Adjuvant systemic therapy	KCE / experts	Inclusion	Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment
Trastuzumab with/without non-anthracycline-based chemotherapy or endocrine therapy is the treatment of choice for first-line therapy of all HER2 positive MBC except in the presence of cardiac contra-indications for the use of Trastuzumab	Treatment	Adjuvant systemic therapy	KCE / experts	Inclusion	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment
In women progressing on taxane plus Trastuzumab given in the metastatic setting, anti-HER2 therapy (Trastuzumab or lapatinib) should be continued in combination with capecitabine	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
For women with HER-2 negative metastatic breast cancer bevacizumab associated with a taxane can be offered as first line therapy	Treatment	Adjuvant systemic therapy	KCE / experts	Exclusion	
Biphosphonates should be routinely used in combination with other systemic therapy in women with metastatic breast cancer with multiple or symptomatic lytic bone metastases	Treatment	General category	KCE / experts	Inclusion	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates
Board certified medical doctors in medical oncology	Treatment	General category	AHRQ	Exclusion	

Cases not receiving recommended treatment (radiotherapy after breast-conserving surgery or systemic therapy) due to system failure	Treatment	General category	AHRQ	Exclusion	
Documentation of Continuing Medical Education credits for the 2 years preceding audit	Treatment	General category	AHRQ	Exclusion	
Evidence of discussion about surgical options	Treatment	General category	AHRQ	Exclusion	
Proportion of breast cancer women who had been discussed by multi-disciplinary team	Treatment	General category	Chung (2007)	Inclusion	Proportion of breast cancer women discussed at the multidisciplinary team meeting
Referral to oncologist for treatment	Treatment	General category	AHRQ	Exclusion	
Women with breast cancer given the opportunity to see a breast cancer specialist nurse	Treatment	General category	AHRQ	Exclusion	
For monitoring women with metastatic disease during active therapy, CA 27.29, CA 15-3 or CEA can be used in conjunction with diagnostic imaging, history, and physical exam	Treatment	Monitoring	KCE / experts	Exclusion	
Change in QOL by time and treatment arm in postmenopausal, node (-) breast cancer women who underwent adjuvant therapy	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Change in QOL in women with metastatic breast cancer	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Change in QOL over time	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Overall changes in QOL over time, before & after radiotherapy	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Participation of women with breast cancer in decision-making as much as they wanted	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	

Received enough information about surgery and radiotherapy	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Satisfaction of women with breast cancer with the treatment choice	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Women with a significant improvement in QOL in clinical phases of breast cancer	Treatment	QOL and patient satisfaction relating to treatment	AHRQ	Exclusion	
Appropriate use of palliative radiotherapy for women with progression or recurrence	Treatment	Radiotherapy	AHRQ	Exclusion	
Appropriate use of parasternal radiotherapy for tumours located in the medial part of breast	Treatment	Radiotherapy	AHRQ	Exclusion	
Appropriate use of radiotherapy	Treatment	Radiotherapy	AHRQ	Exclusion	
Appropriate use of radiotherapy after breast-conserving surgery	Treatment	Radiotherapy	AHRQ	Inclusion	Proportion of women who received radiotherapy after breast conserving surgery
Appropriate use of radiotherapy after mastectomy	Treatment	Radiotherapy	AHRQ	Exclusion	
Appropriate use of radiotherapy on axilla following axillary lymph node dissection, to deal with increased risk of local recurrence (i.e. extracapsular extension; ≥ 4 positive nodes)	Treatment	Radiotherapy	AHRQ	Inclusion	Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND
Appropriate use: Women treated with breast-conserving surgery should begin radiation therapy within 6 weeks of completing either of the following: the last surgical procedure on the breast (including reconstructive surgery that occurs within 6 weeks of primary resection) or chemotherapy, if patient receives adjuvant chemotherapy, unless wound complications prevent the initiation of treatment	Treatment	Radiotherapy	AHRQ	Exclusion	

BC with > or = 4 positive axillary nodes: radiotherapy to internal mammary nodes (optional)	Treatment	Radiotherapy	Owen (2009)	Exclusion	
BC with > or = 4 positive axillary nodes: radiotherapy to whole breast with boost to tumour bed and supraclavicular area	Treatment	Radiotherapy	Owen (2009)	Exclusion	
BC with 1-3 positive axillary nodes: Radiotherapy to supraclavicular area or to internal mammary nodes (optional)	Treatment	Radiotherapy	Owen (2009)	Exclusion	
BC with 1-3 positive axillary nodes: Radiotherapy to whole breast with boost to tumour bed	Treatment	Radiotherapy	Owen (2009)	Exclusion	
BC with negative axillary nodes: Radiotherapy to whole breast with boost to tumour bed	Treatment	Radiotherapy	Owen (2009)	Exclusion	
Breast cancer: percentage of women for whom radiation therapy is administered within 1 year (365 days) of diagnosis for women under age 70 receiving breast conserving surgery for breast cancer.	Treatment	Radiotherapy	NQMC (ASCO / NCCN)	Exclusion	
For stage I-III women with BCS and radiation therapy, radiation therapy should be completed within a 7-wk interval from the start of XRT	Treatment	Radiotherapy	Cheng (2009)	Exclusion	
Patient older than 18 years (< 70 years), with a Stage I to Stage III breast cancer, started breast radiation therapy within 1 year of diagnosis	Treatment	Radiotherapy	Desch (2008; ASCO/NCCN)	Exclusion	
Women having mastectomy and radiation therapy should have XRT completed within a 6-wk interval from start of XRT	Treatment	Radiotherapy	Cheng (2009)	Exclusion	
Women with pathologic stage I-III disease and BCS should have radiation therapy (XRT) started within: 1. Six weeks of BCS if BCS is followed by	Treatment	Radiotherapy	Cheng (2009)	Exclusion	

XRT. 2. Six weeks after completion of chemotherapy if BCS is followed by chemotherapy then XRT. 3. Credit it					
Proportion of women with invasive cancer who receive radiation treatment after BCS	Treatment	Radiotherapy	Chung (2007)	Exclusion	
Quality of radiotherapy after breast-conserving surgery (following guidelines)	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy via planning on a dedicated simulator	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: both tangent fields treated daily	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: done 5 days/week	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: electron beam breast radiation used	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: homogenous dose distribution of radiotherapy	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: receiving 4,500-5,000 cGy total breast dose given in 180-200 cGy fractions	Treatment	Radiotherapy	AHRQ	Exclusion	
Quality of radiotherapy: use of wedges on tangent breast fields	Treatment	Radiotherapy	AHRQ	Exclusion	
Radiation oncology: percentage of women who had radiotherapy for breast conservation (pT1-3, any nodal staging, M0), during the 6 month time period, who had complete follow-up.	Treatment	Radiotherapy	NQMC (ACHS)	Exclusion	
Regional recurrence needing further surgery or radiotherapy	Treatment	Radiotherapy	AHRQ	Exclusion	
Osteoporosis: percentage of women aged 18 years and older receiving aromatase therapy for breast cancer who had a central dual-energy X-ray absorptiometry (DXA) ordered or performed or pharmacologic therapy prescribed within 12 months.	Treatment	Supportive care	NQMC (AAFP / AAOS / AACE / ACR / ES)	Exclusion	

Management of early precursor lesions is preferably discussed in a multidisciplinary setting	Treatment	General category	KCE / experts	Exclusion	
The treatment of the metastatic breast cancer should be discussed within a multidisciplinary team and patient preferences should always be taken into account	Treatment	General category	KCE / experts	Exclusion	
When pleomorphic lobular carcinoma in situ or lobular carcinoma in situ with comedonecrosis is found in a core biopsy, complete excision with negative margins is recommended, and anti-hormonal treatment as well as radiotherapy is an option	Treatment	Surgery	KCE / experts	Exclusion	
Women with high-grade and/or palpable and/or large DCIS of the breast who are candidates for breast conserving surgery should be offered the choice of local wide excision or mastectomy after the patient is correctly informed. In case of multicentricity local wide excision is not recommended	Treatment	Surgery	KCE / experts	Inclusion	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)
Discuss immediate breast reconstruction with all women who are being advised to have a mastectomy, and offer it except where significant comorbidities may preclude this option	Treatment	Surgery	KCE / experts	Exclusion	
Sentinel lymph node biopsy is not recommended in women with a preoperative diagnosis of DCIS who are having breast conserving surgery, unless they are considered to be at a high risk of invasive disease. Women at high risk include those with a palpable mass or extensive micro-calcifications	Treatment	Surgery	KCE / experts	Exclusion	
Absolute sensitivity of core biopsy	Treatment		Perry (2008)	Exclusion	

Absolute sensitivity of FNAC	Treatment	Surgery	Perry (2008)	Exclusion	
Appropriate number of therapeutic operations (≤ 2) for women having breast-conserving surgery	Treatment	Surgery	AHRQ	Exclusion	
Appropriate use of all surgery	Treatment	Surgery	AHRQ	Exclusion	
Appropriate use of axillary lymph node dissection	Treatment	Surgery	AHRQ	Inclusion	Proportion of breast cancer women who underwent an ALND after positive SLNB > 2 mm
Sentinel lymph node biopsy is not recommended in the presence of suspicious palpable axillary lymph nodes	Treatment	Surgery	KCE / experts	Exclusion	
In women with primary breast cancer less than 3 cm and with clinically and ultrasonographically negative nodes, a sentinel lymph node biopsy should be performed	Treatment	Surgery	KCE / experts	Inclusion	Proportion of sentinel lymph nodes biopsy in cN0 women without contraindications
Appropriate use of breast-conserving surgery	Treatment	Surgery	AHRQ	Exclusion	
Appropriate use of mastectomy	Treatment	Surgery	AHRQ; Mc Cahill (2009)	Exclusion	
Appropriate use: Women with stage I or stage II breast cancer should be offered a choice of modified radical mastectomy or breast-conserving surgery, unless contraindications to breast-conserving surgery are present	Treatment	Surgery	AHRQ	Exclusion	
Benign to malignant open surgical biopsy ratio in women at initial and subsequent examinations	Treatment	Surgery	Perry (2008)	Exclusion	
Complete sensitivity of core biopsy	Treatment	Surgery	Perry (2008)	Exclusion	
Complete sensitivity of FNAC	Treatment	Surgery	Perry (2008)	Exclusion	
Initial breast cancer surgery within 30 days	Treatment	Surgery	Mc Cahill (2009); Perry (2008)	Exclusion	
No breast-conserving surgery or mastectomy in metastatic disease	Treatment	Surgery	AHRQ	Exclusion	
Nodes examined following axillary dissection	Treatment	Surgery	Perry (2008)	Exclusion	

Number of SLNs identified	Treatment	Surgery	Mc Cahill (2009)	Exclusion	
Proportion of benign diagnostic biopsies on impalpable lesions weighing less than 30 grams	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of image-guided core/vacuum procedures with an insufficient result	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of image-guided FNAC procedures from lesions subsequently proven to be malignant, with an insufficient result	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of image-guided FNAC procedures with insufficient result	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of localised impalpable lesions successfully excised at the first operation	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of women where a repeat operation is needed after incomplete excision	Treatment	Surgery	Perry (2008)	Exclusion	
Proportion of stage I and II women who undergo breast-conserving surgery / mastectomy	Treatment	Surgery	Chung (2007)	Inclusion	Proportion of cstage I and II women who undergo breast-conserving surgery / mastectomy
Immediate breast reconstruction after mastectomy offers the same survival benefits as mastectomy without reconstruction	Treatment	Surgery	KCE / experts	Exclusion	
Proportion of wires placed within 1 cm of an impalpable lesion before excision	Treatment	Surgery	Perry (2008)	Exclusion	
Reexcision rate	Treatment	Surgery	Mc Cahill (2009)	Exclusion	
Specificity of core biopsy	Treatment	Surgery	Perry (2008)	Exclusion	
Specificity of FNAC	Treatment	Surgery	Perry (2008)	Exclusion	
Positive and close margin rate following initial partial mastectomy	Treatment	Surgery	Mc Cahill (2009)	Exclusion	
A local recurrence in the thoracic wall should be treated preferentially with surgery and adjuvant radiotherapy whenever possible	Treatment	Surgery / radiotherapy	KCE / experts	Exclusion	

A recurrence after breast-conserving treatment should be treated by a salvage mastectomy	Treatment	Surgery	KCE / experts	Inclusion	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy
Systemic treatment for a locoregional recurrence should be discussed in the multidisciplinary team	Treatment	General category	KCE / experts	Exclusion	
Supportive treatment with erythropoesis stimulating proteins can be considered in women with symptomatic anemia. For acute symptoms or failure of the erythropoesis stimulating proteins, erythrocyte transfusions can be administered	Treatment	Supportive treatment	KCE / experts	Exclusion	
Physiotherapy for mobility after axillary clearance should be recommended	Treatment	Supportive treatment	KCE / experts	Exclusion	
Physical training including specific exercises for cancer-related fatigue can be recommended after treatment for breast cancer	Treatment	Supportive treatment	KCE / experts	Exclusion	
Menopausal hormonal replacement therapy is contraindicated in women with breast cancer	Treatment	Supportive treatment	KCE / experts	Exclusion	
Psychological support should be available to all women diagnosed with breast cancer	Treatment	Supportive treatment	KCE / experts	Exclusion	

7.3 EVALUATION SCORES OF THE LONG LIST OF QUALITY INDICATORS

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Diagnosis	Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography	3,5	2	5	0,50	4	2	5	0,63	4	1	5	0,63	3	2	5	0,38
Diagnosis	Proportion of women requiring an operation for diagnostic purposes (SNB/FNAC) who were admitted within 14 days of the surgical decision	3,5	1	5	0,50	3,5	1	5	0,50	4	1	5	0,63	3	2	5	0,38
Diagnosis	Proportion of women with breast cancer or with an abnormality requiring diagnostic operation (SNB/FNAC) having obtained an adequate information within 5 working days of investigations leading to this diagnosis	2,5	1	5	0,25	2	1	5	0,38	2,5	1	5	0,25	2	2	5	0,25
Diagnosis	Proportion of class 4 or class 5 abnormal mammograms that are followed by a cytology or histology	3,5	3	5	0,50	4	3	5	0,63	4	2	5	0,63	3,5	2	5	0,50
Diagnosis	Proportion of women attending for diagnostic purposes who were seen on at least 1 occasion by a breast specialist surgeon/gynaecologist	4	1	5	0,63	4	1	5	0,63	3,5	2	5	0,50	4,5	1	5	0,75
Diagnosis	Proportion of patients undergoing diagnostic mammograms that are classified as "suspicious" or "highly suggestive of malignancy" with documentation of direct communication of findings from the diagnostic mammogram to the patient within 5 working days of exam interpretation	2,5	1	5	0,38	2	1	5	0,38	2,5	1	5	0,38	2,5	1	5	0,25
Diagnosis	Proportion of patients undergoing diagnostic mammograms that are classified as "suspicious" or "highly suggestive of malignancy" with documentation of direct communication of findings from the diagnostic mammogram to the practice that manages the patient's on-going care within 5 working days of exam interpretation.	4	1	5	0,63	3	1	5	0,38	3,5	1	5	0,50	2,5	1	5	0,38
Diagnosis	Proportion of patients with a clinical breast abnormality who have at least one of the following procedures within 1 month: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy.	4	1	5	0,63	4	1	5	0,63	3	1	5	0,38	3,5	1	5	0,50
Diagnosis	Proportion of newly diagnosed stage I-III breast cancer patients who undergo two-view mammography or breast sonography within 3 months prior to surgery	4	1	5	0,86	4	1	5	0,71	4	1	4	0,57	4	1	4	0,71

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Diagnosis	Proportion of operations for benign lesions (evaluated with triple diagnosis)	4	2	5	0,88	4	2	5	0,75	3,5	2	5	0,50	4	2	5	0,63
Diagnosis	Proportion of breast cancer patients who have diagnosis in cytology and histology before surgery	4	2	5	0,88	4,5	2	5	0,88	4	2	5	0,88	4	2	5	0,75
Diagnosis	Proportion of women who received a preoperative 99mTc-MIBI scintimammography	2	1	4	0,13	1	1	4	0,13	1,5	1	4	0,13	1,5	1	4	0,13
Diagnosis	Proportion of women who received a preoperative MRI	4	1	5	0,75	4,5	1	5	0,63	3	1	5	0,50	3	1	5	0,38
Diagnosis	Proportion of patients in whom human epidermal growth factor receptor 2 status was assessed before any treatment	5	4	5	1,00	5	4	5	1,00	4,5	4	5	1,00	5	3	5	0,83
Diagnosis	Proportion of patients in whom a ER and PgR were performed before any treatment	5	4	5	1,00	5	4	5	1,00	5	4	5	1,00	5	3	5	0,86
Diagnosis	Proportion of patients who received a biopsy within 6 weeks if fine-needle aspiration cannot rule out malignancy	4	2	5	0,63	3	2	5	0,50	4	2	5	0,63	3,5	2	5	0,50
Diagnosis	Proportion of asymptomatic patients with negative clinical findings who received routine bone scanning, liver ultrasonography, chest radiography or tumour markers before any treatment; whatever the stadium and the type of the tumour	3	2	5	0,14	3	2	5	0,29	3	1	5	0,14	2	1	5	0,14
Diagnosis	Proportion of patients who received PET in staging axillary lymph nodes for breast cancer before any treatment.	3	1	5	0,43	2	1	4	0,29	2	1	4	0,29	2	1	4	0,43
Diagnosis	Proportion of patients who received axillary ultrasonography with fine needle aspiration cytology of axillary lymph nodes before any treatment	4	3	5	0,75	4	3	5	0,75	3,5	3	5	0,50	4	3	5	0,63
Diagnosis	Proportion of patients for which sampling nodes (FNAC) include ≥ 4 nodes	3	1	5	0,33	4	1	5	0,83	3	1	5	0,33	2,5	1	5	0,33
Diagnosis	Proportion of invasive breast cancer undergoing ALND having 10 or more lymph nodes removed	4	3	5	0,67	4	3	5	0,83	3,5	3	5	0,50	3	2	5	0,33
Diagnosis	Proportion of patients subsequently proven to have clinically occult breast cancer with a preoperative FNAC or core biopsy that is diagnostic for cancer	3	1	5	0,14	3	1	5	0,29	4	1	5	0,57	2	1	5	0,29
General	Proportion of women with breast cancer who participate in clinical trials	4	2	5	0,60	5	4	5	1,00	4	3	5	0,80	4	4	5	1,00

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
General	Proportion of breast cancer patients who had been discussed by multi-disciplinary team	4	4	5	1,00	5	4	5	1,00	4	3	5	0,86	5	4	5	1,00
General	Proportion of breast cancer patients who were referred to an oncologist for treatment	5	3	5	0,83	5	3	5	0,83	4	2	5	0,50	5	2	5	0,83
General	Proportion of women having met a specialised nurse in oncology	3	2	5	0,33	4,5	3	5	0,83	3,5	2	5	0,50	4,5	2	5	0,83
General	Proportion of patients who participated in decision-making throughout the disease management process	2	1	5	0,33	3,5	2	5	0,50	2	1	5	0,33	2	2	5	0,33
General	Proportion of patients who received enough information about surgery and radiotherapy	2,5	1	5	0,33	4	2	5	0,50	2,5	1	5	0,33	2,5	2	5	0,33
General	Number of MOC meetings for recurrent breast cancer patients	4	2	5	0,67	4	2	5	0,67	3,5	2	5	0,50	5	2	5	0,60
Monitoring	Proportion of patients with metastatic disease who underwent CA 27.29, CA 15-3 or CEA assessment during active therapy	4,5	2	5	0,67	3,5	2	5	0,50	3	2	5	0,33	4	2	5	0,67
Outcome	Proportion of women reporting an overall satisfaction with the quality of breast care	3	2	5	0,29	4	2	5	0,57	2	2	5	0,29	2	2	5	0,29
Outcome	5-year overall survival rate by stage	5	3	5	0,86	5	4	5	1,00	5	3	5	0,86	5	3	5	0,86
Outcome	5-year progression-free survival rate by stage	5	3	5	0,86	5	4	5	1,00	5	3	5	0,86	5	3	5	0,71
Outcome	Arm oedema rate for breast conservation surgery patient after surgery/radiation therapy	4	3	5	0,57	4	3	5	0,86	4	3	5	0,57	4	2	5	0,57
Outcome	5-year local recurrence rate after surgery	5	4	5	1,00	5	4	5	1,00	5	3	5	0,86	5	3	5	0,86
Outcome	5 year disease specific survival by stage	5	4	5	1,00	5	4	5	1,00	5	3	5	0,86	5	3	5	0,86
Outcome	Proportion of patients in whom QoL changed over time	3	1	5	0,29	5	3	5	0,71	2	1	5	0,29	3	2	5	0,29
Outcome	Proportion of patients satisfied with the treatment choice	3	1	5	0,29	4	2	5	0,57	2	1	5	0,29	2	2	5	0,29
Reporting	Proportion of patients with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen.	4,5	1	5	0,67	5	4	5	1,00	4,5	1	5	0,67	5	4	5	1,00
Reporting	Proportion of patients, regardless of age, with a diagnosis of breast cancer who are seen in the ambulatory setting who have a baseline cancer stage or documentation that the cancer is metastatic in the medical record at least once during the 12 month reporting period	3,5	1	5	0,50	5	4	5	1,00	3,5	1	5	0,50	4	3	5	0,83
Reporting/pathology	Proportion of breast cancer resection pathology reports that include the tumour size (macro_and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumor), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade.	4,5	3	5	0,83	5	4	5	1,00	4,5	4	5	1,00	4,5	4	5	1,00

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Reporting/pathology	Proportion of zero-stage breast cancer patients with 10 or more lymph nodes on pathology report (excluding sentinel node procedure)	3	1	5	0,33	3	1	5	0,33	3,5	1	5	0,50	3,5	1	5	0,50
Reporting/pathology	Reporting assessment of microscopic margins including closest margin	4,5	3	5	0,83	5	4	5	1,00	4,5	3	5	0,67	4	4	5	1,00
Reporting/pathology	Reporting carcinoma confirmed microscopically	4,5	3	5	0,67	5	4	5	1,00	4,5	3	5	0,83	4	4	5	1,00
Reporting/pathology	Reporting distance of tumor from nipple (gross examination)	3	2	5	0,33	2	1	5	0,33	3	2	5	0,33	4	2	5	0,67
Reporting/pathology	Reporting distance to the closest margin (microscopic)	4,5	3	5	0,83	5	4	5	1,00	4,5	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting ductal carcinoma in situ (DCIS) present/absent (microscopic)	4	3	5	0,50	4	1	5	0,50	4	3	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting gross observation of lesion	3	3	5	0,33	3	1	5	0,33	3	3	5	0,33	4	3	5	0,83
Reporting/pathology	Reporting histological grade (microscopic)	5	3	5	0,80	5	5	5	1,00	5	3	5	0,80	5	4	5	1,00
Reporting/pathology	Reporting histological type (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4,5	3	5	0,83	4,5	4	5	1,00
Reporting/pathology	Reporting identification of affected quadrant (gross examination)	4	3	5	0,67	4	1	5	0,67	4,5	3	5	0,67	4	3	5	0,83
Reporting/pathology	Reporting involvement of apical lymph nodes (microscopic)	3,5	2	5	0,50	5	2	5	0,83	3,5	2	5	0,50	4	2	5	0,80
Reporting/pathology	Reporting laterality of surgical specimen (gross examination)	4	3	5	0,50	3,5	1	5	0,50	4	2	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting lymph-vascular invasion (microscopic)	4	3	5	0,50	5	4	5	1,00	4	3	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting measurement of macroscopic margins of carcinoma	3	3	5	0,33	5	3	5	0,83	3,5	3	5	0,50	4	3	5	0,83
Reporting/pathology	Reporting nature of specimen (gross examination)	4,5	3	5	0,67	3	1	5	0,50	4	3	5	0,67	4	4	5	1,00
Reporting/pathology	Reporting number of lymph nodes present (gross examination)	4	3	5	0,50	5	3	5	0,83	4	3	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting number of positive lymph nodes (microscopic) and size of metastasis < 2 mm (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4,5	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting pathological extent of primary tumor (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4	3	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting HER2 status (microscopic)	4,5	3	5	0,67	4,5	3	5	0,67	4,5	3	5	0,67	4,5	4	5	1,00

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Reporting/pathology	Reporting size of concurrent ductal carcinoma in situ (microscopic)	4	3	5	0,50	3	1	5	0,50	4	3	5	0,50	4,5	3	5	0,83
Reporting/pathology	Reporting size of invasive carcinoma (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4,5	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting size of specimen (gross examination)	4,5	3	5	0,67	5	3	5	0,83	4	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting the orientation of the pathology specimen (gross examination)	4	3	5	0,50	4	1	5	0,50	4	3	5	0,50	4,5	2	5	0,83
Reporting/pathology	Reporting TNM staging (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4,5	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting tumor size (macroscopic)	4	3	5	0,67	5	3	5	0,83	4	3	5	0,67	4	3	5	0,83
Reporting/pathology	Reporting tumor size (microscopic)	4,5	3	5	0,83	5	4	5	1,00	4,5	3	5	0,67	4,5	4	5	1,00
Reporting/pathology	Reporting verification invasive tumor size (microscopic)	4,5	3	5	0,67	5	4	5	1,00	4	3	5	0,50	4,5	4	5	1,00
Reporting/pathology	Reporting proliferation index (microscopic)	3,5	3	5	0,50	5	1	5	0,67	3,5	3	5	0,50	4,5	3	5	0,83
Support	Proportion of patients with symptomatic anemia who received erythropoesis stimulating proteins / erythrocyte transfusions	4	2	5	0,50	4	1	5	0,50	4	2	5	0,50	4	3	5	0,50
Support	Proportion of women who benefit from physiotherapy to facilitate mobility	3,5	1	5	0,50	4	1	5	0,50	3	1	5	0,50	4	3	5	0,50
Support	Proportion of women who benefit from physical training for cancer-related fatigue	2,5	1	5	0,33	3,5	1	5	0,50	2,5	1	5	0,33	3	1	5	0,33
Support	Proportion of women who received menopausal hormonal replacement therapy	4	3	5	0,67	4	1	5	0,50	4	3	5	0,67	4	4	5	1,00
Support	Proportion of patients who benefit from psychological support	4	2	5	0,50	4	3	5	0,50	4	2	5	0,50	4,5	3	5	0,67
Treatment	Proportion of operable T2-T3 patients who received neo-adjuvant systemic therapy	5	4	5	1,00	5	3	5	0,83	5	4	5	1,00	5	4	5	1,00
Treatment	Proportion of patients with ER positive DCIS who received hormonal therapy	5	4	5	1,00	5	3	5	0,83	5	4	5	1,00	5	4	5	1,00
Treatment	Proportion of patients who received chemotherapy *before* radiotherapy	3,5	2	5	0,50	3	2	5	0,17	3,5	2	5	0,50	4	2	5	0,83
Treatment	Proportion of patients treated with surgery having their adjuvant therapy within 8 weeks	4	3	5	0,50	4,5	3	5	0,83	4	3	5	0,50	4,5	2	5	0,83
Treatment	Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer	4,5	3	5	0,67	5	3	5	0,83	5	4	5	1,00	5	4	5	1,00
Treatment	Proportion of patients with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI)	4,5	3	5	0,83	5	3	5	0,83	5	4	5	1,00	5	4	5	1,00

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Treatment	Proportion of pre-menopausal patients for whom combination chemotherapy is considered or administered within 4 months (120 days) of diagnosis for women with T1c, or stage II or III hormone receptor negative breast cancer.	4,5	3	5	0,67	4,5	3	5	0,67	4,5	3	5	0,67	4,5	3	5	0,83
Treatment	Proportion of patients for whom tamoxifen or third generation aromatase inhibitor is considered or administered within 1 year (365 days) of diagnosis for women with T1c or stage II or III hormone receptor positive breast cancer.	3,5	3	5	0,50	3,5	3	5	0,50	3,5	3	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of > or= 50-55% who received chemotherapy and Trastuzumab	4,5	3	5	0,67	5	4	5	1,00	4,5	4	5	1,00	4,5	4	5	1,00
Treatment	Proportion of patients treated by Trastuzumab in whom cardiac function is monitored every 3 months	4	3	5	0,67	5	3	5	0,83	4	3	5	0,67	4,5	3	5	0,67
Treatment	Proportion of post-menopausal breast cancer women with positive/negative lymph node receiving adjuvant hormone therapy or chemotherapy	4,5	3	5	0,67	5	4	5	1,00	5	3	5	0,67	4,5	4	5	1,00
Treatment	Proportion of pre-menopausal breast cancer women with positive/negative lymph node receiving adjuvant chemotherapy and hormonal therapy	4,5	3	5	0,67	5	4	5	1,00	5	3	5	0,67	4,5	4	5	1,00
Treatment	Proportion of premenopausal patients with hormone receptor positive or hormone receptor unknown metastatic breast cancer who underwent suppression of ovarian function (e.g. with LHRH analogs, bilateral oophorectomy, irradiation of the ovaries) in combination with tamoxifen	3,5	3	5	0,50	5	3	5	0,83	5	3	5	0,83	4,5	2	5	0,83
Treatment	Proportion of postmenopausal patients with hormone receptor positive or hormone receptor unknown metastatic breast cancer who received third generation AI or Tamoxifen in first line	4	3	5	0,50	5	3	5	0,83	5	3	5	0,83	4,5	3	5	0,83
Treatment	Proportion of postmenopausal patients with hormone receptor positive or hormone receptor unknown metastatic breast cancer who received third generation AI or Fulvestrant in second line	3	3	5	0,33	5	3	5	0,67	5	3	5	0,67	4	3	5	0,67
Treatment	Proportion of women with metastatic breast cancer and bony metastases who received radiotherapy	3	3	5	0,33	3	3	5	0,33	4,5	3	5	0,67	3,5	3	5	0,50
Treatment	Proportion of patients with potentially resectable brain metastases who were treated with radiosurgery or with surgery followed by whole brain radiotherapy	3,5	3	5	0,50	3,5	3	5	0,50	5	3	5	0,83	3,5	3	5	0,50
Follow-up	Proportion of women who benefit from an annual mammography after a history of breast cancer	4,5	3	5	0,67	5	3	5	0,83	5	3	5	0,83	5	3	5	0,83
Treatment	Proportion of women who had CBC testing, chest x-ray, bone scans, liver ultrasound and/or computed tomography after an history of breast cancer	2	1	5	0,17	2	1	4	0,17	1,5	1	3	0,00	3	1	4	0,17
Treatment	Proportion of patients who had routine MRI after a treatment for early invasive breast cancer or DCIS	2,5	1	5	0,17	2,5	1	4	0,17	2,5	1	4	0,17	2,5	1	4	0,17

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Treatment	Proportion of women who received follow-up consultations every 3 months in the two years after diagnosis, every 6 months until 5 years after diagnosis, and every year after 5 years	2,5	1	5	0,33	3	1	4	0,33	2	1	4	0,33	2,5	1	4	0,33
Treatment	Proportion of women with metastatic breast cancer who received hormonal therapy, chemotherapy, and/or enrollment in a clinical trial with documentation of informed consent within 6 weeks of the identification of metastases	3	1	5	0,33	3	2	5	0,33	3	1	5	0,33	3	2	5	0,33
Treatment	Proportion of women with metastatic breast cancer who received anthracycline- and/or taxane based regimens as first-line treatment	3,5	3	5	0,50	3,5	3	5	0,50	3,5	3	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with metastatic breast cancer who received anthracycline but no taxane as first-line treatment, who received taxane-based regimens as second-line treatment	3,5	2	5	0,50	3,5	2	5	0,50	3,5	2	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with metastatic breast cancer who received anthracycline and taxanes as first-line treatment, who received capecitabine monotherapy as second-line treatment	3,5	2	5	0,50	3,5	3	5	0,50	3,5	2	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment	3,5	2	5	0,50	4,5	3	5	0,83	3,5	2	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab (or lapatinib) and capecitabine as second-line treatment	3,5	2	5	0,50	4	3	5	0,67	3,5	3	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with HER2 negative metastatic breast cancer who received Bevacizumab and taxane as first-line treatment	3,5	2	5	0,50	4	3	5	0,67	3,5	3	5	0,50	3,5	3	5	0,50
Treatment	Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates	4	2	5	0,50	4	2	5	0,50	4	3	5	0,50	4	3	5	0,50
Treatment	Proportion of women who received palliative radiotherapy after progression or recurrence	4	2	5	0,67	3,5	3	5	0,50	3,5	2	5	0,50	3,5	3	5	0,50
Treatment	Proportion of patients who received radiotherapy after BCS	4,5	3	5	0,83	5	4	5	1,00	4,5	3	5	0,67	5	4	5	1,00
Treatment	Proportion of patients who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND	4,5	3	5	0,83	5	4	5	1,00	4,5	3	5	0,67	5	4	5	1,00
Treatment	Proportion of patients treated with breast-conserving surgery should begin radiation therapy within 2 months of completing either of the following: the last surgical procedure on the breast (including reconstructive surgery that occurs within 6 weeks of primary resection) or chemotherapy, if patient receives adjuvant chemotherapy, unless wound complications prevent the initiation of treatment	4,5	1	5	0,67	4	2	5	0,50	4	1	5	0,50	4	2	5	0,50
Treatment	Proportion of patients with 4 or more positive axillary nodes having radiotherapy for internal mammary nodes	4,5	2	5	0,67	5	3	5	0,83	4	3	5	0,50	5	3	5	0,83

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Treatment	Proportion of patients with 4 or more positive axillary nodes having radiotherapy to whole breast with boost to tumor bed and supraclavicular area	4,5	2	5	0,67	5	3	5	0,83	4	3	5	0,50	5	3	5	0,83
Treatment	Proportion of patients with 1-3 positive axillary nodes having radiotherapy to supraclavicular area or to internal mammary nodes	4,5	2	5	0,67	5	3	5	0,83	4	3	5	0,50	5	3	5	0,83
Treatment	Proportion of patients with 1-3 positive axillary nodes having radiotherapy to whole breast with boost to tumor bed	4,5	2	5	0,67	5	3	5	0,83	4	3	5	0,50	5	3	5	0,83
Treatment	Proportion of patients with negative axillary nodes having radiotherapy to whole breast with boost to tumor bed	4,5	2	5	0,67	4,5	3	5	0,67	4	3	5	0,50	4	3	5	0,50
Treatment	Proportion of stage I-III patients with BCS and radiation therapy, for which radiation therapy was completed within a 7-wk interval from the start of XRT	4,5	1	5	0,67	4,5	1	5	0,67	4	2	5	0,50	4,5	3	5	0,83
Treatment	Proportion of patients receiving breast conserving surgery for breast cancer for whom radiation therapy is administered within 1 year of diagnosis	4	1	5	0,67	3	1	5	0,33	3	1	5	0,33	3,5	3	5	0,50
Treatment	Proportion of patients with mastectomy and radiation therapy, for which radiation therapy was completed within a 6-wk interval from the start of XRT	4	1	5	0,60	3	1	5	0,40	3	1	5	0,40	3	3	5	0,40
Treatment	Proportion of patients who had radiotherapy for breast conservation (pT1-3, any nodal staging, M0), during the 6 month time period, who had complete follow-up.	3	1	5	0,40	4	1	5	0,60	3	1	5	0,40	3	3	5	0,40
Treatment	Proportion of patients with pleomorphic lobular carcinoma in situ or lobular carcinoma in situ with comedonecrosis who were surgically treated	3,5	1	5	0,50	4	1	5	0,67	3	1	5	0,33	3,5	1	5	0,50
Treatment	Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)	4	3	5	0,83	5	4	5	1,00	4	3	5	0,67	5	4	5	1,00
Treatment	Proportion of women having immediate breast reconstruction after a mastectomy	4,5	3	5	0,83	5	3	5	0,83	4,5	3	5	0,67	5	3	5	0,83
Treatment	Proportion of patients with DCIS for which a sentinel lymph node biopsy was performed, whatever the surgical option (breast conserving surgery or mastectomy)	4	3	5	0,83	3,5	3	5	0,50	4	3	5	0,67	4	3	5	0,67
Treatment	Proportion of therapeutic operations (≤ 2) for women having breast-conserving surgery	4	3	5	0,50	4	3	5	0,50	4	3	5	0,50	4	3	5	0,50
Treatment	Proportion of breast cancer patients who underwent an ALND after positive SNLB > 0.2 mm	4,5	4	5	1,00	5	4	5	1,00	4,5	4	5	1,00	5	4	5	1,00
Treatment	Proportion of sentinel lymph nodes biopsy in cN1 patients	4,5	4	5	1,00	5	3	5	0,83	4	4	5	1,00	5	4	5	1,00
Treatment	Proportion of sentinel lymph nodes biopsy in cN0 patients without contraindications	4,5	4	5	1,00	5	4	5	1,00	4	4	5	1,00	5	4	5	1,00
Treatment	Benign to malignant open surgical biopsy ratio in women at initial and subsequent examinations	3	2	5	0,33	3	2	5	0,33	3	2	5	0,33	3	2	5	0,33

Category	Indicators	Reliability				Relevance				Interpretability				Actionability			
	Expert	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5	Med	Min	Max	%4-5
Treatment	Proportion of breast cancer patients having their initial breast cancer surgery within 30 days	3,5	2	5	0,50	3	1	5	0,33	3	2	5	0,33	3,5	2	5	0,50
Treatment	Proportion of women with metastatic disease who underwent breast conserving surgery or mastectomy	4	2	5	0,50	4	1	5	0,50	3,5	2	5	0,50	3	2	5	0,50
Treatment	Number of nodes examined following ALND	4,5	3	5	0,67	5	4	5	1,00	4	3	5	0,50	5	3	5	0,83
Treatment	Proportion of localised impalpable lesions successfully excised at the first operation	3	2	5	0,33	3	2	5	0,33	3	2	5	0,33	3	3	5	0,33
Treatment	Proportion of stage I and II patients who undergo breast-conserving surgery / mastectomy	5	4	5	1,00	5	4	5	1,00	5	4	5	1,00	5	4	5	1,00
Treatment	Proportion of reconstructions in the same operation and in a second operation	3,5	3	5	0,50	5	3	5	0,83	3,5	2	5	0,50	5	2	5	0,83
Treatment	Proportion of patients with a local recurrence who are treated with surgery and radiotherapy	4	2	5	0,50	4	3	5	0,50	4	2	5	0,50	4	2	5	0,50
Treatment	Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy	4,5	3	5	0,67	5	3	5	0,83	5	3	5	0,83	4,5	2	5	0,83

7.4 METHODS: CONSTRUCTION OF AN ALGORITHM TO ATTRIBUTE A PATIENT TO A HOSPITAL

7.4.1 Introduction

Description of the problem: how to identify the "main centre" for each patient, when the available data arise from three databases, each having different ways to identify the hospital?

This section will address different questions:

1. How to deal with hospital merging ?
2. How to identify centre in IMA data ?
3. How to identify centre in MCD data ?
4. Is there consistency between approaches to identify centres ?
5. What is the added value of MCD data compared to IMA data to identify centre ?
6. How to construct a valid algorithm ?

For this project, there are three sources of data:

1. **BCR dataset** (initial selection): there is no centre identifier (at least for this project)
   Unique key: patient – type of tumour – incidence date
2. **IMA Health dataset** (linked to BCR data): the centre is identified by a nomenclature code (if the MDT meeting and surgery are performed at two different places, the two centres are identified in the database)
   Unique key: patient (after regularizations) – nomenclature code – prestation date
   There are two variables which identify the institution in the IMA Health dataset:
   The variable **SS00075** indicates where the patient was hospitalized, but is often left blank, so does not provide reliable information.
   The variable **SS00085** is the location where the medical act (nomenclature code) was performed. This variable specifies the centre (hospital) in addition to the service (or lab centre). It requires a specific recoding by the data manager, who will group together all different codes/ identifiers from the same hospital (see 7.4.2.1.).
3. **MCD dataset** (linked to BCR data): the centre is the one where the patient was hospitalized.
   Unique key: patient- hospitalization (isnr).
   The variable **HOSPIDR_NEW** (in the MCD.STAYHOSP dataset) is the hospital where the patient was hospitalized. This variable also requires a recoding by the data manager, so that the same hospital is recoded by the same identifier in the IMA health dataset and in the MCD dataset

7.4.2 Methods

7.4.2.1 How to deal with hospital merging?

The table HOSPITAL (see a selection in Table 38) makes the link between the recoded ss00085 (ss00085r) and the hospital. Merges between hospitals are indicated by the "change" and "change_date" variables. This table has been created by the data manager, and is based on the 2009 situation. For the purpose of this project, all centres were merged retrospectively (in the past). For instance, centre A and centre B which merged into centre C in 2005 were labelled centre C during the whole study period (2001-2006). Hospitals which merged after the study period (2007-2009) were also retrospectively merged.

Table 38. Reference table for the link between the variable SS00085 and the hospital code in IMA data

SS75or85r	hospidr	hospidr_new	change_date	change	hosp_type
030479B	FF007		.		HOP-ZKH
03328B5	96361		.		HOP-ZKH
03341CB	7343B		.		HOP-ZKH
0341907	8DFB1	53359	01JAN2000	FUSION	HOP-ZKH

7.4.2.2 *How to select a centre in the IMA data?*

There are several possibilities to select a centre in the IMA data

- From the **MDT meetings** (see Table 71)
- From the **surgery** (see Table 81)
- From the **chemotherapy** (see Table 85)
- From the **lump sums for hospital admission and per diem price** (see Table 39)
- Endocrine therapy is not considered here as mainly given in an ambulatory setting.

Table 39. Nomenclature codes for lump sums (per diem) in IMA data

Code	Start Date	NL	FR
760001	01/01/1993	Heelkundige aandoeningen - Observatie en behandeling: Niet-universitaire inrichtingen	Affections chirurgicales - Observations et traitement : Etablissements non-universitaires
760060	01/01/1993	Heelkundige aandoeningen - Observatie en behandeling: Gemengde inrichtingen	Affections chirurgicales - Observations et traitement : Etablissements mixtes
760126	01/01/1993	Heelkundige aandoeningen - Observatie en behandeling: Universitaire inrichtingen	Affections chirurgicales - Observations et traitement : Etablissements universitaires
768003	7/01/2005	Ziekenhuisverpleging - variabel gedeelte op basis van ingediende facturen: Acute ziekenhuizen - bedrag per opname.	Hospitalisation - partie variable sur base des factures introduites : Hôpitaux aigus - forfait par admission.
768025	7/01/2002	Ziekenhuisverpleging - variabel gedeelte op basis van ingediende facturen: acute ziekenhuizen - bedrag per dag	Hospitalisation - partie variable sur base des factures introduites :hôpitaux aigus - forfait par jour

However, for each of these codes, time limits have to be set with regard to the incidence date of the cancer (see Table 40). This is to ensure that the treatment relates to the selected cancer. In general, a time limit of 1 month before and 6 months after the incidence date is chosen. A smaller time window has been chosen for the lump sums, because these are not specific for cancer (these codes are valid for any hospitalization, cancer or non cancer related). These limits are cancer specific and should be reviewed by experts for each type of cancer.

Table 40. Time windows applied to nomenclature codes in IMA (reference date: incidence date from BCR)

Category	Source of data	Time between nomenclature code date and incidence date (after)	Time between nomenclature code date and incidence date (before)
MDT meetings	IMA	6 months (180 days)	1 month (30 days)
Surgery	IMA	6 months (180 days)	1 month (30 days)
Chemotherapy	IMA	6 months (180 days)	6 months (180 days)
Lump sum any hospitalization	IMA	1 month (30 days)	1 month (30 days)

The last step is to check that the centre can be uniquely identified for each category. For instance, for patients having two MDT meetings in two different centres within the 6 months period after incidence date, the centre cannot be uniquely identified on this criterion.

The consistency between different approaches should be described.

7.4.2.3 How to select centre in the MCD data?

First, only hospitalizations with regard to the studied cancer have to be retained. One possibility is to select all the relevant APR-DRGs, or all the relevant stays with the appropriate primary diagnosis, but a first broad and easier selection can be done at the level of the Major Disease Classification (MDC). For breast cancer, the relevant MDC is MDC 09 "Diseases and Disorders of the Skin, Subcutaneous Tissue and Breast", which contains all stays classified in APR-DRGs reported in Table 41.

Table 41. APR-DRGs in MDC 09 "Diseases and Disorders of the Skin, Subcutaneous Tissue and Breast"

APR-DRG	M/P	NL	FR	ENG
360	P	huidgreffe en/of debridisatie voor ulcus of cellulitis	greffe de peau et/ou debridement pour ulcere ou cellulite	skin graft & wound debrid for skin ulcer & cellulitis
361	P	huidgreffe en/of debridisatie behalve voor ulcus of cellulitis	greffe de peau et/ou debridement excepte pour ulcere ou cellulite	skin graft & wound debrid exc for skin ulcer & cellulitis
362	P	mastectomie	mastectomie	mastectomy procedures
363	P	ingrepen op de borsten, behalve mastectomie	interventions sur les seins, excepte mastectomie	breast procedures except mastectomy
364	P	andere ingrepen op huid, subcutaan weefsel en borsten	autres interventions sur la peau, le tissu sous-cutane et les seins	other skin, subcutaneous tissue & breast procedures
380	M	huidulcus	ulcere de la peau	skin ulcers
381	M	belangrijke aandoeningen van de huid	affections majeures de la peau	major skin disorders
382	M	maligne aandoeningen van de borsten	affections malignes des seins	malignant breast disorders
383	M	cellulitis	cellulite	cellulitis
384	M	trauma van de huid, subcutaan weefsel en borsten	traumatisme de la peau, du tissu sous-cutane et des seins	trauma to the skin, subcutaneous tissue & breast
385	M	andere huid- en borstaandoeningen	autre affection de la peau et de seins	other skin & breast disorders

Another relevant MDC for all cancers is the MDC 17 "Lymphatic, Hematopoietic, Other Malignancies, Chemotherapy and Radiotherapy" but it includes radiotherapy stays, which can be given in a different centre than the "main" patient centre (where all the other treatments were given). Therefore we suggest not to include MDC 17 in the selection of stays to identify patient centre.

Once the selection on the MCD basis is done, a second selection has to be done on the time between the cancer incidence date (from BCR data) and the admission date, to avoid that recurrent cases are selected in place of primary tumour. As only admissions months and years are available in MCD, the selection retains all hospitalisations within 6 months of incidence month (Table 42).

Table 42. Time windows applied to admission month in MCD data (reference month: incidence month from BCR)

	Source of data	Number of months after the incidence date	Number of months before the admission date
Any hospitalisation in MCD of interest	MCD	6 months	6 months

7.4.2.4 Construction of the algorithm

Based on all pre-analyses discussed above, we propose the following algorithm to attribute each patient to a centre:

1. based on the centre where MDT meeting occurred (taking into account all MDT within 6 months after incidence date, and including those which occurred one month before the incidence date)
2. if there was no MDT, based on the centre where surgery occurred (taking into account all surgeries within 6 months after incidence date, and including also those which were performed one month before the incidence date)
3. if there was no MDT and no surgery, based on the centre where chemotherapy was given (including chemo within 6 months before or after incidence date)
4. if there was no MDT, no surgery and if no chemotherapy was given, based on the per diem lump sums from IMA data (within one month before or after incidence date)
5. if none of the above, based on centre where the patient was hospitalized for a cancer related hospitalisation (in MCD data, within 6 months before or after incidence date)

The fact that MCD data are used in the last step of this algorithm is due to the linkage problems that are specific to this project. When the linkage is good, MCD data could be used as a second or third step in the algorithm.

7.4.3 Results

Table 43 reports the percentage of patients for which the centre can be identified for breast cancer patients, by type of nomenclature code (on IMA data only). In 2006, the centre could be identified for 78% of the patients based on MDT meeting and for 88% on the surgery code. Chemotherapy, as not the most prevalent treatment, can only help to identify the centre in 41% of the cases. Finally, using the stringent criteria of an admission code within the month of the incidence date led the identification of the centre in 74% of the cases (in 2006).

Table 43. Comparison of different ways to identify centre of patients in IMA data.

	N	Centre can be unequivocally identified based on MDT meeting within 30 days before or 180 after ID (IMA)		Centre can be unequivocally identified based on breast cancer surgery code within 30 days before or 180 days after ID (IMA)		Centre can be unequivocally identified based on chemotherapy within 180 days before or after ID (IMA)		Centre can be unequivocally identified based on non specific hospital admission code within 30 days before or after ID (IMA)	
		yes		*yes*		*yes*		*yes*	
		N	*%*	*N*	*%*	*N*	*%*	*N*	*%*
Incidence year									
2001	7669	0	0	6332	82.57	3006	39.20	6113	79.71
2002	7686	180	2.34	6606	85.95	3084	40.12	6269	81.56
2003	8443	4851	57.46	7281	86.24	3371	39.93	6899	81.71
2004	8232	6156	74.78	7072	85.91	3309	40.20	6431	78.12
2005	8942	6682	74.73	7603	85.03	3534	39.52	6735	75.32
2006	9067	7119	78.52	7729	85.24	3675	40.53	6685	73.73
All	50039	24988	49.94	42623	85.18	19979	39.93	39132	78.20

Using this algorithm, 96% of the patients can be attributed to a centre based on IMA data exclusively (Table 44). There is an improvement of the performance of the algorithm over the years, due to the increase in the number of MDT meetings. One can hypothesize that it would even perform better now, when all patients (should) have a MDT meeting.

Table 44. Results of the algorithm to identify centre of patients based on IMA data.

		Centre can be identified based on IMA data (algorithm)			
		no		**yes**	
	N	**N**	**%**	**N**	**%**
Incidence year					
2001	7 669	536	6.99	7 133	93.01
2002	7 686	428	5.57	7 258	94.43
2003	8 443	337	3.99	8 106	96.01
2004	8 232	263	3.19	7 969	96.81
2005	8 942	340	3.80	8 602	96.20
2006	9 067	266	2.93	8 801	97.07
All patients	50 039	2 170	4.34	47 869	95.66

Table 45 reports the results of the attribution of centre based on MCD data only (data were only linked to MCD for the years 2002-2004). For 2001, some centres can be identified for those patients with incidence date at the end of the year and with hospitalizations in 2002. Globally, the percentages are very low (between 61% and 64%), and reflect the problems in the data linkage. One can hypothesize that these percentages would be much higher, would the linkage problems be resolved.

Table 45. Results of algorithm to identify centre of patients based on MCD data only

		Centre is unequivocally identified based on hospitalization for breast cancer within 6 months before or after ID (MCD)			
		no		yes	
	N	N	%	N	%
Incidence year					
2001	7 669	7 324	95.50	345	4.50
2002	7 686	2 888	37.57	4 798	62.43
2003	8 443	3 007	35.62	5 436	64.38
2004	8 232	3 204	38.92	5 028	61.08
2005	8 942	8 942	100.00	.	.
2006	9 067	9 067	100.00	.	.
All patients	50 039	34 432	68.81	15 607	31.19

Table 46 tests whether the different approaches to identify centres give the same results (based on patients for which the centre can be unequivocally identified, as explained above). In 98% of the cases, MDT and surgery occurred in the same centre. This percentage is slightly lower for chemotherapy (94%). Also, when centre can be identified based on MCD data, it matches the IMA algorithm in 98% of the cases. This confirms the validity of the IMA algorithm.

Table 46. Check consistency of approaches to identify centres based on administrative data

Consistency between	N of patients	N of consistent cases	% of consistency
MDT centre and surgery centre	22 659	22 293	98.38
MDT centre and chemotherapy	10 547	9 901	93.88
MDT centre and lump sum IMA	19 876	19 494	98.08
IMA algorithm versus MCD data	15 513	15 267	98.41

N = number of patients for which centre can be identified based on the two approaches compared

Table 47 presents what is the added information in the MCD data compared to IMA data (for the years 2002, 2003, 2004). As there are only 4.2% of the patients for whom centre could not be identified based on IMA data, the maximal potential gain from MCD data is 4.2%. For breast cancer, only 90 additional patients can have their centre identified thanks to MCD data (0.37%). This number obviously depends on the linkage percentage between MCD and BCR data.

Table 47. Extra information in MCD data compared to IMA data to identify centre

		Centre can be identified based on IMA data (algorithm)				Centre is unequivocally identified based on hospitalisation for breast cancer within 6 months before or after ID (MCD)				Extra info on centre data in available in MCD compared to IMA data			
		no		yes		no		yes		no		yes	
	N	N	%	N	%	N	%	N	%	N	%	N	%
Incidence year													
2002	7686	428	5.57	7258	94.43	2888	37.57	4798	62.43	7637	99.36	49	0.64
2003	8443	337	3.99	8106	96.01	3007	35.62	5436	64.38	8427	99.81	16	0.19
2004	8232	263	3.19	7969	96.81	3204	38.92	5028	61.08	8207	99.70	25	0.30
All	24361	1028	4.22	23333	95.78	9099	37.35	15262	62.65	24271	99.63	90	0.37

7.4.3.1 Volume of activity in centres for breast cancer

Table 48 reports the results of the above algorithm (only based on IMA data due to the linkage problems) for breast cancer.

Table 48. Summary measures of volume of centres for breast cancer

2001-2006	N hospitals	Mean	Median	SD	Min	Lower Quartile	Upper Quartile	Max
Total patients	112	427.4	284.0	443.7	13.0	164.5	532.0	3044.0
Annual volume	112	71.2	47.3	74.0	2.2	27.4	88.7	507.3

Annual volume (2001-2006) category	Frequency	Percent	Cumulative Frequency	Cumulative Percent
1-25 /year	26	23.21	26	23.21
26-50 /year	35	31.25	61	54.46
51-100/year	27	24.11	88	78.57
101-150/year	12	10.71	100	89.29
> 150 /year	12	10.71	112	100.00

7.4.3.2 How to link SS0085 to the hospital ? (details in from "2008-52 breast & testis cancer analysis log.pdf")

Author: Stephan Devriese

1.3.6 Recoding of institution ID [delivery 2]

All institution ID in variable SS00075 and SS00085 were recoded according to the following algorithm (see code on page 23).

1. Collect all institution ID from SS00075 and SS00085 that did not exist in the first delivery.
2. Convert numerical values to character and check that both variables have the same number of institutions (✓).
3. Recode the institution ID
4. Subdivide the ID according to the following rules:

Length of ID	Hospital ID	Check digit	Hospital Service
8	$1 \rightarrow 5$		$6 \rightarrow 8$
9	$1 \rightarrow 6$		$6 \rightarrow 8$
11	$1 \rightarrow 6$	$7 \rightarrow 8$	$9 \rightarrow 11$

5. Compare check digit to NIHDI reference table
6. Add correct recoded ID to institution of check digit wrong
7. Use same recoded ID for instutition ID with or without check digit
8. Add institutions from first delivery
9. Check for doubles (✓)

7.5 METHODS OF ANALYSIS

7.5.1 Descriptive statistics by type of outcome

Continuous variables

Continuous variables (such as the patient age, the number of mammographies …) were described with the mean, standard deviation (SD), median, 25th and 75th percentile of their distribution. For the quality indicators, these data were also presented with a box plot. The square of the box includes 50% of the observations (between the lower and the upper quartile, the interquartile range, IQR). The two whiskers (i.e. the vertical bars departing from the square) are drawn down till the last observation below Q1 (first quartile) - 1.5 x IQR and up above Q3 (third quartile) + 1.5 x IQR. The outliers outside those boundaries are located outside the box and indicated with an asterisk. The mean of the distribution is represented by a "+" sign and the median is the horizontal line dividing the box in 2 (if the median is different from Q1 or Q3).

Binary variables

Binary variables (the majority of the quality indicators) were described as percentages (denominator N, numerator n, %). The unit of analysis was most of the time the patient, otherwise explicitly mentioned.

Standardized Incidence Rates

Incidence rates by province were standardized for the age using the direct standardization method. The age structure of the European population was used as the standard[44].

5-year overall survival

Overall 5-year survival curves have been calculated using the Kaplan Meier method, stratifying the curves by pstage. The vital status of each patient at the end of December 2009 was available.

5 year relative survival

The calculation of the disease-specific survival is impossible at present, and the relative survival (i.e. observed survival / expected survival) is calculated as a proxy. Expected survival rates were retrieved from the mortality tables of 2006 (http://statbel.fgov.be/nl/statistieken/cijfers/bevolking/sterfte_leven/tafels/index.jsp) and were linked to the individual patient, taking into account age, gender and region.

7.5.2 Graphical description of the variability per centre (funnel plots)

The variability in processes and outcome results has been described graphically for all quality indicators. The algorithm to attribute a patient to a centre has been described in appendix 7.4. Patients who could not be attributed to a centre are not included in these graphics.

Definition of a funnel plot

The definition of funnel plots has four components. In each unit (hospital), r events are observed out of a sample size n (cross sectional binomial data).

1. An indicator (summary statistic) which is the observed proportion of event r/n.
2. A target proportion which is the average event rate θ_0. It is given by the sum of all events divided by the sum of all sample sizes.
3. A measure of the precision, in that case given by the unit sample size n.
4. The control limits that depend of the target θ_0, of the sample size n and of a given p-value. These limits are constructed such that the chance of exceeding these limits for a « in control » unit is p. Usual sets of values for p are p=0,001, p=0,999 corresponding to 3 SD (the usual limits in control charts framework), and p=0,025, p=0,975 corresponding to 2 SD (the usual limits set in the test of hypotheses framework). In the case of binomial cross sectional data, the limits are given by $y_p(\theta_0, n) = \theta_0 + z_p\sqrt{\frac{\theta_0(1-\theta_0)}{n}}$, with z_p as such that P(Z ≤ z_p)=p for a standard normal distribution Z ($_{z0.025}$=-1.96).

These charts aim to differentiate between « in control » units, showing a common cause of variation, and « out of control » units, exhibiting a special cause of variability, which has then to be investigated further. They show the outcome measure plotted against a measure of its precision, so that control limits form a funnel around the target outcome.

Funnel plots have many advantages: the axes are readily interpretable, so that additional information can be added by hand if desired, the eye is naturally drawn to important points that lie outside the funnels, there is no spurious ranking of institutions, and there is clear allowance of additional variability in institutions with small volume.

7.5.3 Volume outcome analyses

Cox proportional hazard models (PH) were used to assess the influence of the volume of patients treated within the hospital on the overall 5 year-mortality. Robust sandwich covariance matrix estimates were used to account for the intracluster (cluster = hospital) dependence of observations.

The volume of centres was based on the last three years of data available (2004, 2005, 2006). The annual volume was calculated based on these three years. Centres were categorized as follows:

- Low-volume centres: less than 100 patients treated per year
- Medium-volume centres: between 100 and 149 patients treated per year
- High-volume centres: at least 150 patients treated annually

Three risk factors were taken into account in the regression models. These factors are

- The patient's age (as a linear variable)
- The tumour's stage: pStage (and if missing, cStage).
- The tumour differentiation (grade)
  - Grade I : well differentiated
  - Grade II : moderately differentiated
  - Grade III : poorly differentiated
  - Grade IV : undifferentiated

- Unknown differentiation.

The severity of illness (SOI) which is encoded in the MCD was not used for risk adjustment. The reason for this decision is the fact that SOI is encoded at the end of the admission which implies that the patient's complications are taken into account.

7.6 QUALITY INDICATORS: GENERAL INDICATORS

7.6.1 BC1: overall 5-year survival rate by stage

7.6.1.1 Rationale

In Belgium, 9 405 new breast cancers were diagnosed in 2005. In Belgium as in Europe, breast cancer is the most frequent cause of death by cancer in women (20.6% of all cancer deaths)[19]. The health care system can improve the prognosis of breast cancer through early detection and appropriate treatment. A favourable pattern in breast cancer mortality in the EU-25 was observed after 1989, leading to a fall in overall rates from 21.3/100 000 in 1990 to 18.9/100 000 in 2000[45].

Survival rates depend on the stage of disease at diagnosis. At stage 0 (carcinoma in situ), the five-year survival rate is 100%. Five-year survival rates for women with stage IV (cancer has spread beyond the breast) are only 16%[46]. This indicator is essential to evaluate treatment effectiveness.

7.6.1.2 Numerator

All women diagnosed with breast cancer in a given year, surviving 5 years after diagnosis, by stage

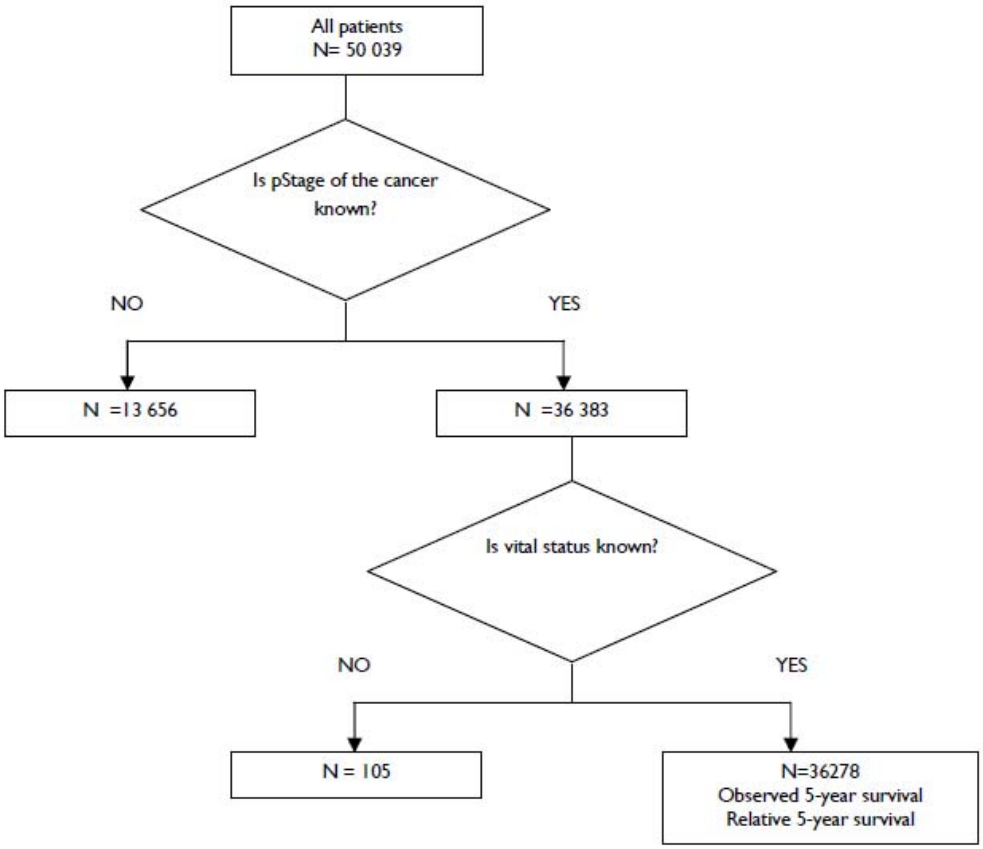
7.6.1.3 Denominator

All women diagnosed with breast cancer in a given year, by stage

7.6.1.4 Elaboration

For the calculation of survival statistics, it is essential to include only those women with a follow-up of the date of death (Figure 23). Mortality data are collected from the mortality database of the sickness funds, and are available until December 31st 2009 for the present study. To calculate the period between the incidence and mortality date, it is of course essential to have the incidence date.

Figure 23. Flowchart of indicator BC1 and BC2



7.6.1.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- Banque Carrefour for mortality data

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50 (BCR)
- Stage: BCR
- Incidence date: algorithm BCR
- Mortality date: Banque Carrefour

7.6.1.6 *Results*

To determine the survival rates for the selected patient group, the vital status at the close-out date of December 31st 2009 was considered. For all patients with recorded pStage and vital status (36 278 patients or 72.5%), we calculated observed survival rates.

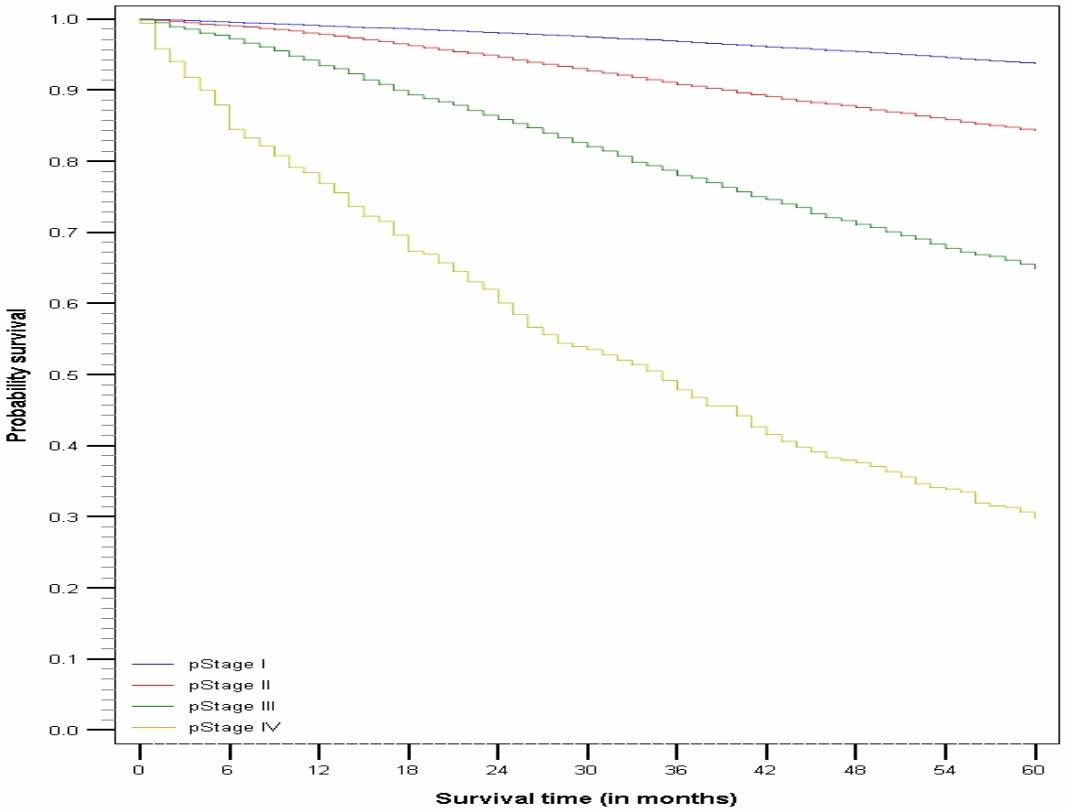
Taken all incidence years together, the 5-year observed survival probability was 0.93 for pStage I and decreased to 0.28 for pStage IV. For pStage X, survival was 0.93 after one year, 0.85 after three years and 0.79 after five years. The evolution of the 5-year observed survival according to the incidence year was relatively stable (Table 49 and Figure 24).

Of all women, 6 233 women died during a 5-year time frame (17.2% of this sample) 7.5% were in pStage I, 18.4% in pStage II, 37.2% in pStage III and 73.6% in pStage IV. The 5-year overall survival is logically lower for advanced pStages (II and IV), due to the disease extension but also because patients were older in these groups.

Table 49. Observed survival probability by pStage

		N	# deaths	Survival time				
				1 year	2 years	3 years	4 years	5 years
pStage	I	15 437	1 165	0.99	0.97	0.96	0.95	0.93
	II	15 617	2 877	0.96	0.93	0.89	0.86	0.83
	III	4 553	1 697	0.89	0.82	0.75	0.69	0.64
	IV	671	494	0.68	0.54	0.42	0.35	0.28

Figure 24. Observed survival probability by pStage



As demonstrated in Table 50, the evolution of 5-year survival probability remained relatively stable according to incidence year, with a slight increase for pStages II and III.

Table 50. Evolution of 5-year observed survival probability by pStage according to incidence year

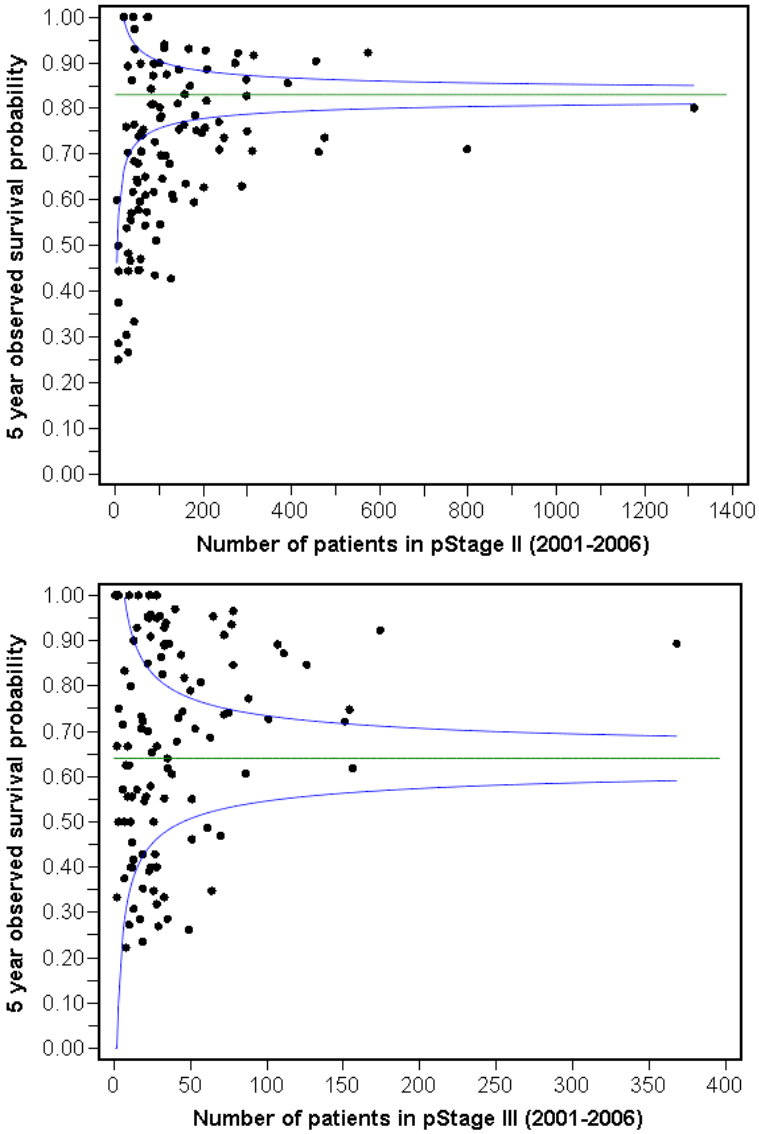
		Incidence year			
		2001	**2002**	**2003**	**2004**
pStage	I	0.93	0.93	0.92	0.93
	II	0.81	0.82	0.83	0.84
	III	0.59	0.57	0.63	0.64
	IV	0.30	0.24	0.30	0.27

Variability between centres was large for pStage I-III (Figure 25). This might indicate that within each pStage, the differences in breast cancer patients' characteristics (such as age and socio-economical status) could be large. However, this figure also reflects a large variability in 5-year survival according to the volume of breast cancer women treated by medical centre.

Variability in diagnostic and therapeutic practices between hospitals could be correlated to volumes of patients, explaining a part of these survival results.

For pStage IV, a variability between centres was also observed. Because only few women having a metastatic breast cancer were treated by centre (maximal volume of 18 women in the highest volume centre between 2001 and 2006), a graph is useless to illustrate such variability.

Figure 25. 5-year observed survival probability per pStage, analyzed per centre



7.6.2 BC2: disease specific 5 year survival by stage

7.6.2.1 Rationale

See overall 5-year survival rate by stage

7.6.2.2 Numerator

All women diagnosed with breast cancer in a given year, surviving 5 years after diagnosis or dying due to a non breast cancer-related cause, by stage.

7.6.2.3 Denominator

All women diagnosed with breast cancer in a given year, by stage.

7.6.2.4 Elaboration

For the calculation of survival statistics, it is essential to include only those women with a follow-up of the date of death (Figure 23).

7.6.2.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- Banque Carrefour for mortality data

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50
- Stage: BCR
- Incidence date: algorithm BCR
- Mortality date: Banque Carrefour
- Expected survival: mortality tables (StatBel)

7.6.2.6 Results

Since no accurate data are available on the cause of death in databases, disease-specific survival as such is not measurable at this moment. However, relative survival is a frequently used parameter in cancer epidemiology and can be used as a proxy of the disease-specific survival[21]. For the calculation of the relative survival, the numerator was defined as the observed rate of breast cancer women surviving 5 years after diagnosis, while the denominator was defined as the expected survival rate of a comparable group (age, gender and region) from the general population.

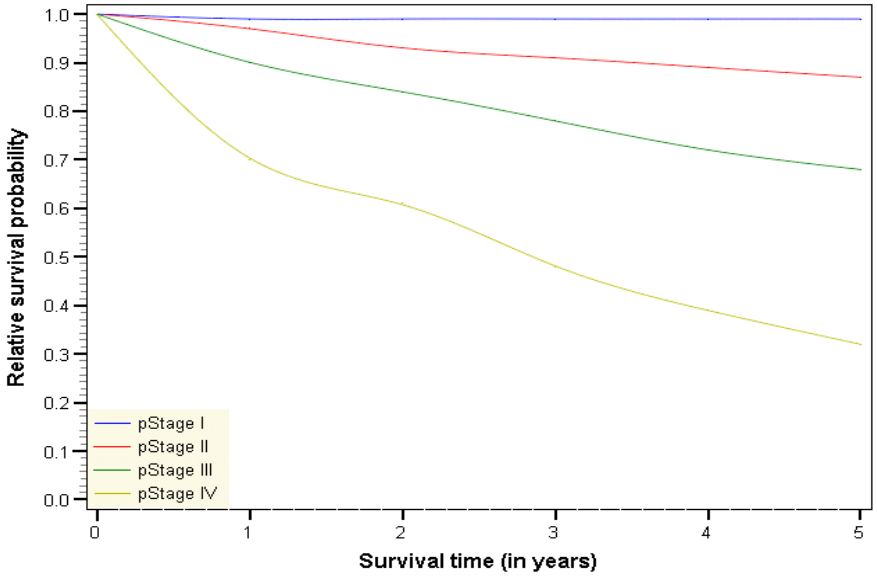
To determine the survival rates for the selected patient group, the vital status at the close-out date of December 31st 2009 was considered. For all patients with recorded pStage and vital status (36 278 patients or 72.5%), we also calculated relative survival rates.

The calculated relative survival probabilities were slightly higher than the observed survival rates (BC1). This difference can be due to the methodology used to determine relative survival, in which the observed survival rate is divided by the expected survival rate of a comparable group from the general population. The current analyses showed a 5-year relative survival of between 0.32 for pStage IV disease and 0.98 for pStage I (Table 51 and Figure 26). Relative survival for pStage X was 0.96 after one year, 0.90 after 3 years and 0.86 after five years.

Table 51. Relative survival probability by pStage

		N	# deaths	Survival time				
				1 year	2 ears	3 years	4 years	5 years
pStage	I	15 437	1 165	1	1	0.99	0.99	0.98
	II	15 617	2 877	0.97	0.93	0.91	0.89	0.87
	III	4 553	1 697	0.90	0.84	0.78	0.72	0.68
	IV	671	494	0.70	0.61	0.48	0.39	0.32

Figure 26. Relative survival probability by pStage



7.6.3 BC3: disease-free 5-year survival rate by stage

7.6.3.1 Rationale

Numerous clinical studies have conclusively demonstrated the effectiveness of breast cancer treatment in improving disease-free survival[23, 47-52]. This indicator is essential to evaluate treatment effectiveness.

7.6.3.2 Numerator

All women diagnosed with breast cancer in a given year, surviving 5 years after diagnosis and free of disease, by stage.

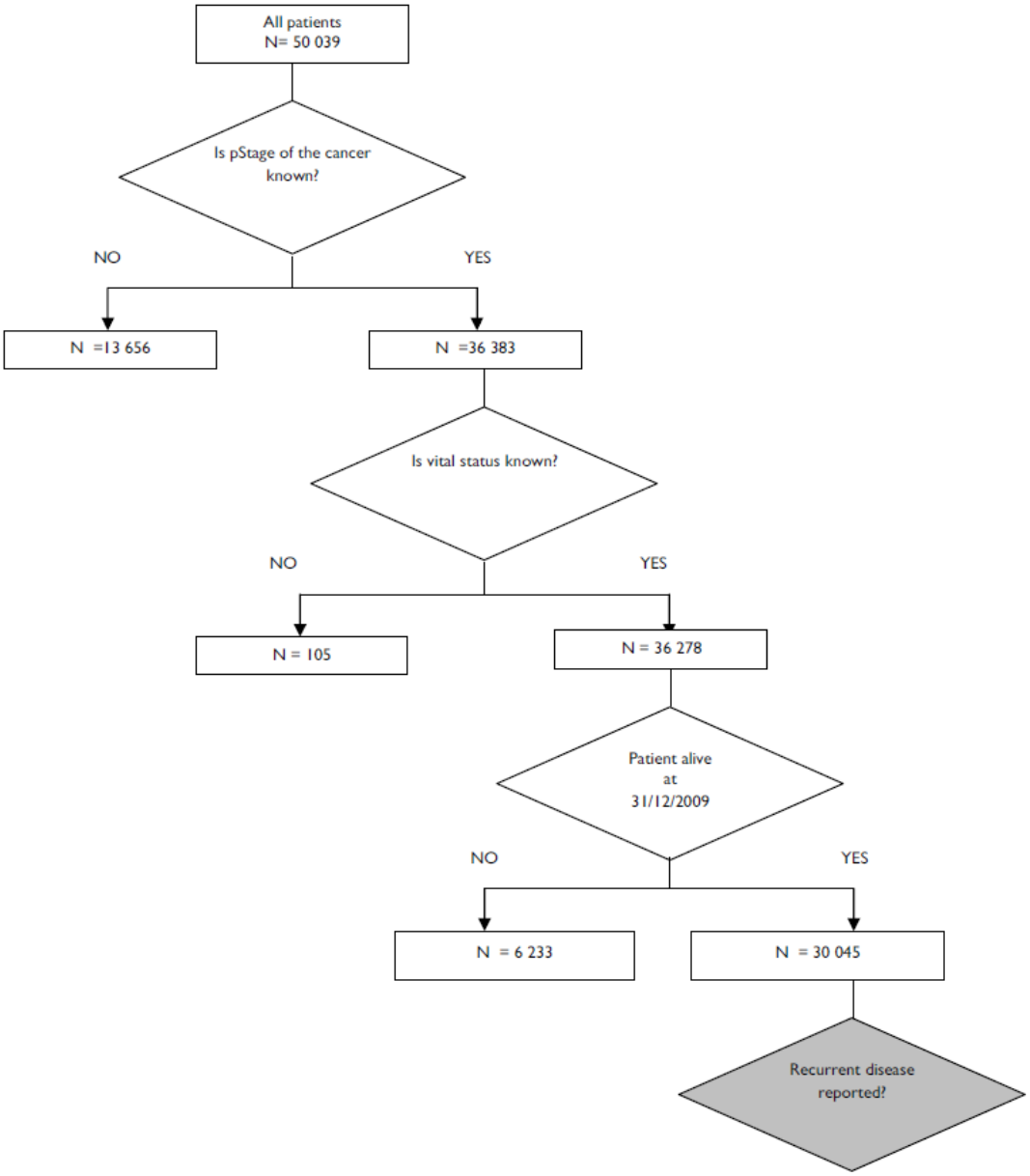
7.6.3.3 Denominator

All women diagnosed with breast cancer in a given year, by stage.

7.6.3.4 Elaboration

The same logic is followed as for indicators BC1 and BC2. However, to calculate the disease-free survival, the disease status is a necessary parameter.

Figure 27. Flowchart of indicator BC3



7.6.3.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- Banque Carrefour for mortality data

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50 (BCR)
- Stage: BCR
- Incidence date: algorithm BCR
- Mortality date: Banque Carrefour
- Disease activity: not measurable

7.6.3.6 *Results*

Disease free survival could not be determined exactly since registration data as an administrative code for recurrent disease were lacking. An indirect measurement of this indicator by investigating the number of retreatments also seemed invalid for this cancer type. Indeed, a retreatment can only be determined if there is a clear interval between the first line and the second line treatment. Endocrine therapy may be a long term treatment which makes a treatment-free interval difficult to determine.

Consequently, the only finding that could be reported concerning this indicator, was that vital status was known for 36 278 patients (72.5%). Of these patients, 30 045 survivors and 6 233 deaths were counted at December 31st 2009.

7.6.4 BC4: 5-year local recurrence rate after curative surgery, by stage

7.6.4.1 *Rationale*

Numerous clinical studies have conclusively demonstrated the effectiveness of breast cancer surgery in reducing local recurrence[37, 47, 53-55]. This indicator is essential to evaluate treatment effectiveness.

7.6.4.2 *Numerator*

All pStage I-IIIB women with a R0 resection who developed a local recurrence, by stage

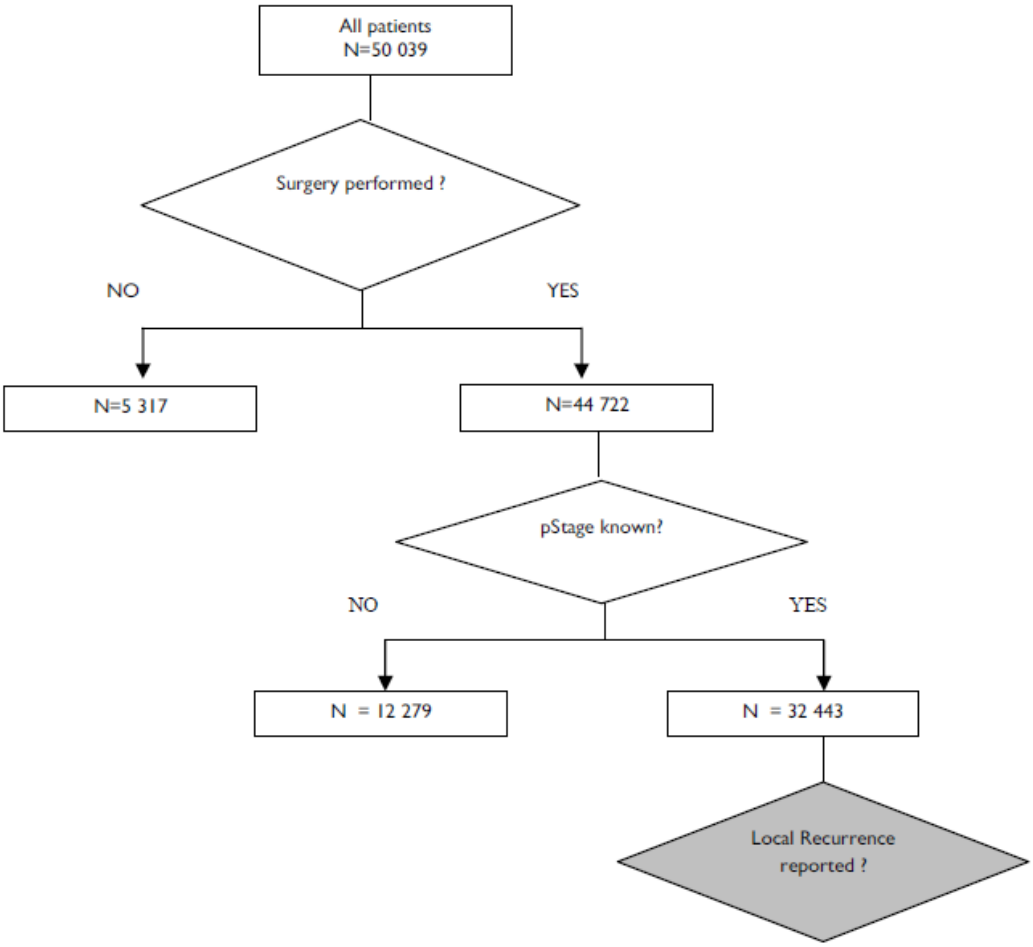
7.6.4.3 *Denominator*

All pStage I-IIIB women with a R0 resection, by stage

7.6.4.4 *Elaboration*

As for the flowchart drawn for BC3, the potential relapses cannot be determined and the indicator BC4 cannot be measured (Figure 28).

Figure 28. Flowchart for indicator BC4



7.6.4.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50 (BCR)
- Stage: BCR
  - *Surgery :* nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.6.4.6 *Results*

As the BCR database did not contain information on local recurrences, this indicator could not be determined as such. Moreover, an indirect measurement by considering retreatment rates was not possible for this tumour type (cfr. indicator BC3).

The only finding that could be derived from the algorithm was that from 44 722 patients in whom surgery was performed (89.4%), 32 443 (72.5%) had a reported pStage. This information should be reported in all patients records, since it orientates the adjuvant treatment, and be communicated to the BCR.

7.6.5 BC5: Proportion of breast cancer women discussed at the multidisciplinary team meeting

7.6.5.1 Rationale

The multidisciplinary approach was considered to be an efficient, cost-effective way to taking care for breast cancer women[56]. The benefits of the multidisciplinary team approach included increased survival, increased patient satisfaction with care, improved perception of management of care, and increased access to information, including psychosocial and practical support[57]. Specific nomenclature codes for a multidisciplinary oncologic consultation are available since February 1st 2003.

7.6.5.2 Numerator

All women diagnosed with breast cancer in a given year discussed at the MDT meeting within 6 months after incidence date, by stage.

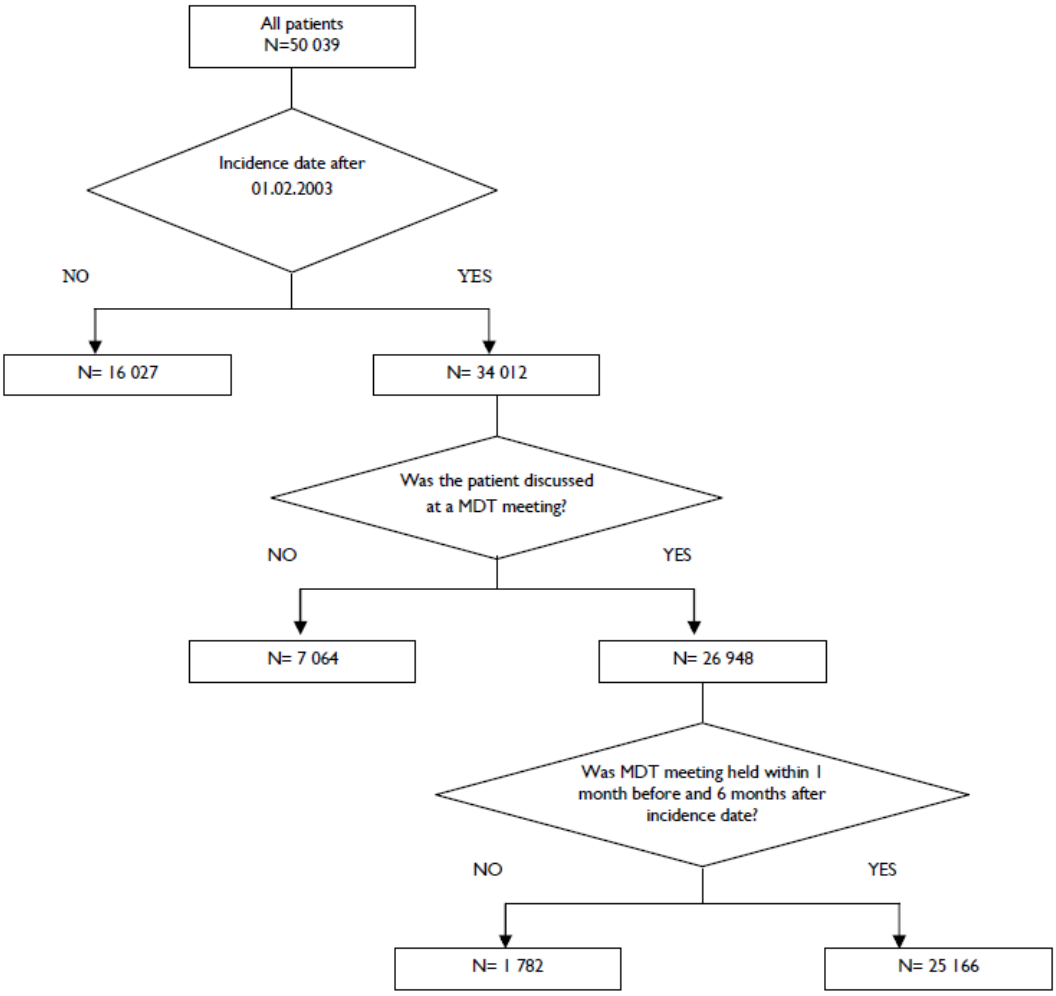
7.6.5.3 Denominator

All women diagnosed with breast cancer in a given year, by stage.

7.6.5.4 Elaboration

Figure 29 provides the algorithm for indicator BC5. Since a specific code for a MDT meeting only became available since February 1st 2003, women with incidence date before were excluded. Since there is always a possibility of more than one primary tumour (other than the breast tumour) and in order to increase the likelihood that the MDT was linked to the breast tumour, a timeframe of 6 months after the incidence date was chosen. From all women diagnosed with breast cancer (denominator), only those who were discussed at the MDT meeting within 6 months after incidence date (numerator) were selected.

Figure 29. Flowchart of indicator BC5



7.6.5.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50 (BCR)
- MDT meeting: nomenclature code (IMA) (Table 71)
  - MDT meeting 1 month before to 6 months after incidence date

7.6.5.6 *Results*

Of the 34 012 patients with breast cancer diagnosed after February 1st 2003, 79.2% have been discussed at a MDT meeting. In 74% of the cases, the discussion was held within 1 month before and 6 months after the incidence date. The proportion of patients, discussed at a MDT, increased over time. In the first year the MDT nomenclature codes were introduced, only 61.4% of the patients were discussed. This percentage rose to more than 80% in 2006, indicating that a multidisciplinary approach is gaining interest in breast cancer treatment (Table 52).

One barrier to organize MDT is the high cost, which is about six times greater than originally foreseen; however, this is balanced by a more standardized management of breast cancer women and a higher quality of care that patients now receive. Indeed, every new event (relapse, progression of disease, unexpected side-effects, etc.) experienced by the individual is discussed in multidisciplinary meetings[31].

Table 52. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per year (2003-2006)

	Numerator	Denominator	Proportion (%)
2003	4 770	7 771	61.4
2004	6 285	8 232	76.3
2005	6 831	8 942	76.4
2006	7 280	9 067	80.3
Total	**25 166**	**34 012**	**74.0**

Numerator: All women diagnosed with breast cancer in a given year (after February 1st 2003) discussed at the MDT meeting within one month before and 6 months after incidence date
Denominator: All women diagnosed with breast cancer in a given year (after February 1st 2003)

The analysis per centre indicated that in 2004, 7 centres (6.4%) discussed no patients at a MDT meeting according to the nomenclature codes, while 8 centres (7.2%) discussed all patients in a multidisciplinary setting (Figure 30). Comparable numbers were noticed for 2006, with 7 centres (6.3%) holding no multidisciplinary consults and 10 centres (9.0%) discussing all patients multidisciplinary (Figure 31). In fact, it is still possible to exclude patients from this system as it remains a voluntary act to present a patient's case to the MDT[31]. Importantly, these figures must be interpreted with caution as they refer only to recorded nomenclature codes and may not reflect the true numbers of multidisciplinary patient discussions.

Figure 30. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per centre (2004)

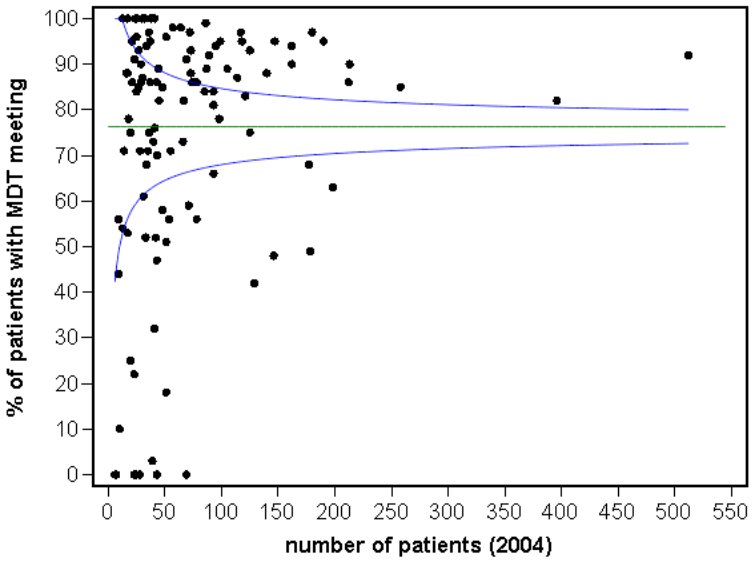
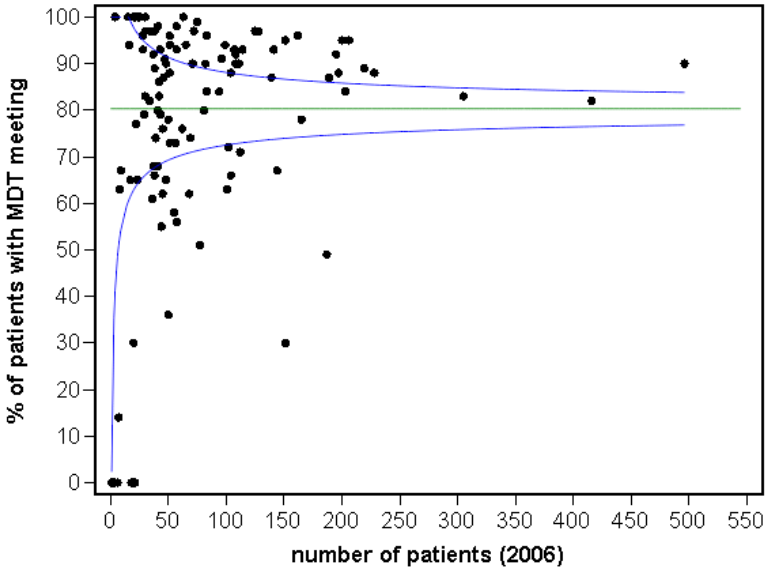


Figure 31. Proportion of breast cancer patients discussed at a multidisciplinary team meeting, analyzed per centre (2006)



7.6.6 BC6: Proportion of women with breast cancer who participate in clinical trials

7.6.6.1 Rationale

It is widely recognized that clinical trials are a major component of the whole process aiming to find better treatments for breast cancer. There is indirect evidence that women who participate in clinical trials have better outcomes than women given similar treatments outside trials[57, 58].

7.6.6.2 Numerator

All women diagnosed with breast cancer in a given year who were recruited in a clinical trial

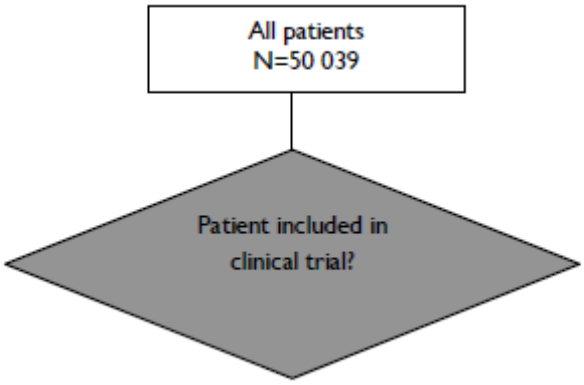
7.6.6.3 Denominator

All women diagnosed with breast cancer in a given year

7.6.6.4 Elaboration

Figure 32 provides the algorithm for indicator BC6. From all women diagnosed with breast cancer (denominator), only those who were recruited in a clinical trial (numerator) were selected.

Figure 32. Flowchart of indicator BC6



7.6.6.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)

7.6.6.6 *Results*

Till now, no administrative code exists to identify patients who are included in clinical trials. As a consequence, this indicator could not be assessed.

It would be particularly interesting that patients who were included in clinical trials be prospectively registered, as they receive specific therapeutic products (chemotherapy, endocrine therapy, biological therapy) and are submitted to specific surveillance procedures. Both are not recorded in general databases which leads to an underestimation of treatments administered.

7.7 QUALITY INDICATORS: DIAGNOSIS AND STAGING

7.7.1 BC7: Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography

7.7.1.1 *Rationale*

Minimal delays must exist between taking a mammogram, film reading and the availability of the report, the provision of an assessment appointment for women with screen detected abnormalities or a clinic appointment for women with substantial breast symptoms[15]. AHRQ proposed a process/access indicator related to the recommendation that women with breast cancer detected by screening should attend an assessment centre within 3 weeks of mammography[16]. Our GDG considered this delay too short and proposed that a maximal 2 months delay was reasonable. The priority aim addressed by this indicator is to reduce the length of time between first knowledge of a breast abnormality and a specific assessment made by a specialist.

7.7.1.2 *Numerator*

All women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography in a given year

7.7.1.3 *Denominator*

All women with class 3, 4 or 5 abnormal mammograms in a given year

7.7.1.4 *Elaboration*

From all women who had a class 3, 4 or 5 abnormal mammogram (denominator), women who obtained an assessment with a specialist were selected. To allow the identification of this consultation for diagnostic purpose, a time limit of 2 months after the first mammography was set (numerator).

Firstly, no specific codes exist for class 3, 4 or 5 abnormal mammograms. Secondly, only women who were diagnosed 'breast cancer' are recorded in the BCR, introducing a selection bias. Women having an abnormal mammogram that was not a cancer are not included in the dataset.

7.7.1.5 *Data source(s)*

Source database(s)

- IMA
- MCD

Administrative codes

- *Mammography or mammotest:* nomenclature codes (IMA) (Table 72) or ICD-9-CM codes (MCD) (Table 73)
- *Consultation with a specialist for an assessment:* nomenclature codes (IMA) (Table 74)

7.7.1.6 *Results*

This indicator has to consider all women with class 3, 4 or 5 abnormal mammograms. Firstly, no specific codes exist to identify class 3, 4 or 5 abnormal mammograms. Secondly, only women who finally received a diagnostic confirmation of breast cancer are recorded in the BCR, introducing a selection bias. Women having an abnormal mammogram that was not cancer related are not included in the dataset. For both reasons, this indicator was not measurable.

Moreover, the identification of a consultation in senology was difficult as the code 102012 is used in senology but also in many other specialties. Other specialities such as geriatrics, hematology, oncology have their own nomenclature code.

7.7.2 BC8: Proportion of women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration, or percutaneous biopsy

7.7.2.1 *Rationale*

Women with abnormal mammograms detected after a screening mammography have to be referred to a specialized breast centre for diagnosis. The diagnosis of breast cancer relies on the so-called triple assessment, including clinical examination, imaging (comprising mammography and ultrasonography [US])[59,60] and sampling of the lesion with a needle for histological/cytological assessment[37,61]. The choice between core biopsy and/or a fine needle aspiration cytology (FNAC) depends on the clinician's, radiologist's and pathologist's experience. The priority aim addressed by this indicator is to reduce the length of time between first knowledge of a breast abnormality and a diagnostic confirmation.

7.7.2.2 *Numerator*

All women with class 3, 4 or 5 abnormal mammograms who have at least one of the following procedures within 2 months after communication of the screening result: mammography, ultrasound, fine-needle aspiration or percutaneous biopsy, in a given year

7.7.2.3 *Denominator*

All women with class 3, 4 or 5 abnormal mammograms, in a given year

7.7.2.4 *Elaboration*

From all women who had a class 3, 4 or 5 abnormal mammogram (denominator), women who underwent a second mammography or an ultrasound or a fine-needle aspiration or a percutaneous biopsy were selected. To allow the identification of these imaging tests performed for diagnostic reasons, a time limit of 2 months after the first mammography was set (numerator). Firstly, no specific codes exist for class 3, 4 or 5 abnormal mammograms. Secondly, only women who were diagnosed 'breast cancer' are recorded in the BCR, introducing a selection bias. Women having an abnormal mammogram that was not a cancer are not included in the dataset.

7.7.2.5 *Data source(s)*

Source database(s)

- IMA
- MCD

Administrative codes

- *Mammography or mammotest:* nomenclature codes (IMA) (Table 72) or ICD-9-CM codes (MCD) (Table 73)
- *Two-view mammography or breast sonography:* nomenclature codes (IMA) (Table 75) or ICD-9-CM codes (MCD) (Table 73)
- *FNAC*: nomenclature codes (IMA) (Table 76)
- *Percutaneous biopsy:* nomenclature codes (IMA) (Table 77)

7.7.2.6 *Results*

As for BC7, this indicator has to consider all women with class 3, 4 or 5 abnormal mammograms. For the same reasons, this indicator was not measurable.

7.7.3 BC9: Proportion of newly diagnosed cStage I-III breast cancer women who underwent two-view mammography or breast sonography within 3 months prior to surgery

7.7.3.1 *Rationale*

Mammography remains one of the primary tools used to evaluate a palpable breast mass or other signs of breast disease. Ultrasound has emerged as an important tool to assess a palpable mass in women with dense breast tissue and/or to complement mammography[16]. Two-view mammography should be performed as part of triple assessment (clinical assessment, imaging and tissue sampling) in a unit specialized in breast imaging (1C evidence)[37].

7.7.3.2 *Numerator*

All women diagnosed with breast cancer (cStage I-III) in a given year undergoing two-view mammography or breast sonography within 3 months before surgery

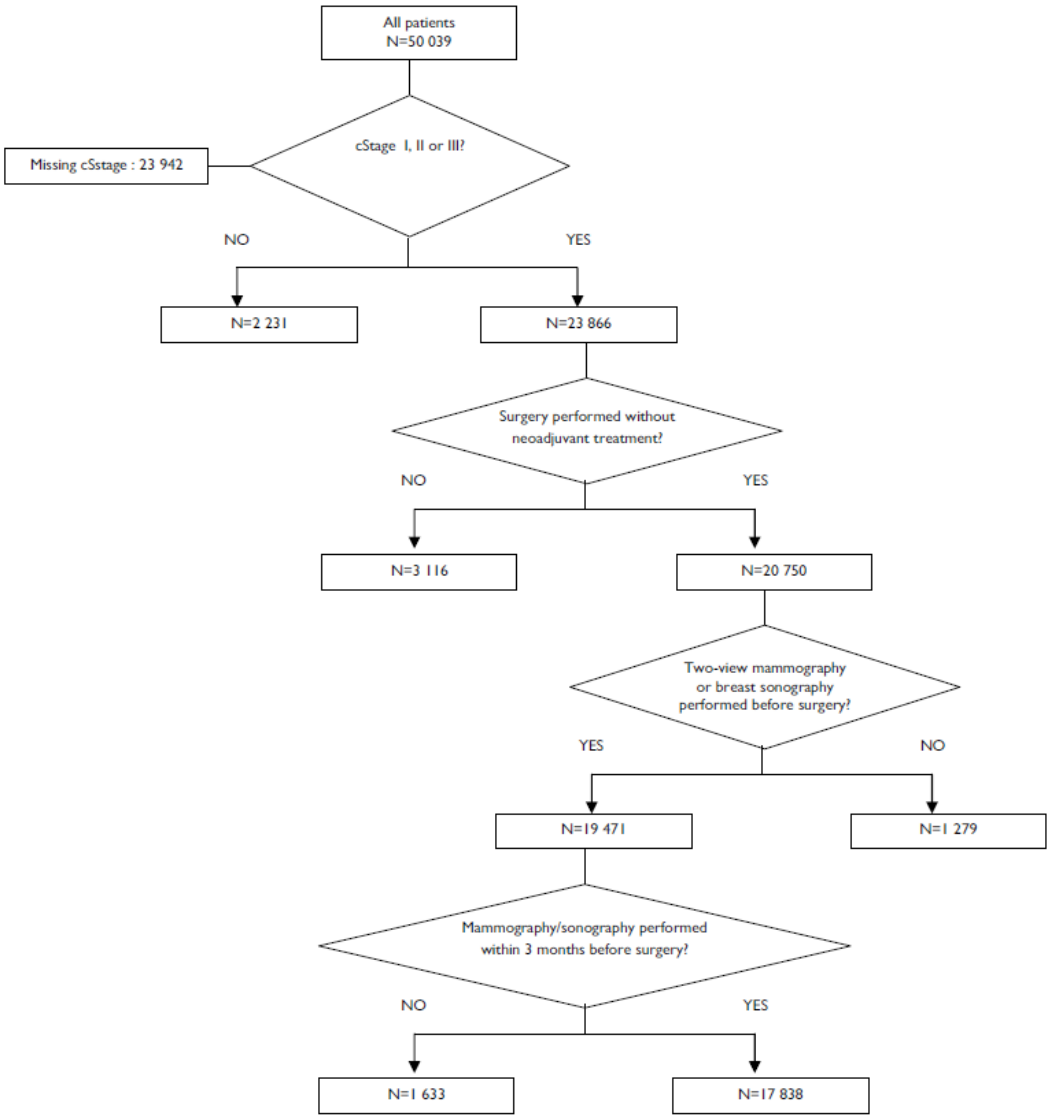
7.7.3.3 *Denominator*

All women diagnosed with breast cancer (cStage I-III) in a given year who were surgically treated (breast conserving surgery or mastectomy)

7.7.3.4 *Elaboration*

Figure 33 provides the algorithm for indicator BC9. From the breast cancer population who had a cStage I-III and who were surgically treated (denominator), women who underwent a two-view mammography or breast sonography within 3 months before surgery were selected (numerator). The delay of 3 months can only be ensured if women do not receive neo-adjuvant treatment. So, women who received a neo-adjuvant treatment were excluded from this analysis.

Figure 33. Flowchart of indicator BC9



7.7.3.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Two-view mammography or breast sonography: nomenclature codes (IMA) (Table 75) or ICD-9-CM codes (MCD) (Table 73)
- Surgery: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.7.3.6 *Results*

Of all patients, 23 866 were diagnosed with cStage I, II or III breast cancer (91.5% of known cStage). Of those patients, a surgical intervention not preceded by a neoadjuvant treatment was performed in 20 750 cases (86.9%). Most of the surgically treated patients (93.8%) also had a two-view mammography or breast sonography before surgery. In 86% of the cases (17 838 patients), examinations were performed within 3 months prior to surgery (Table 53).

The proportion of patients with a breast mammography or sonography within the 3-months timeframe stayed relatively stable between 2001 and 2003, with the highest proportion being observed in 2002 and 2003. The last three years of our observation, the proportion slightly decreased. One possible explanation could be the increase in delay between the diagnostic work-up and the surgical intervention due to the increase in the number of women who were diagnosed cStage I-III and who were surgically treated (from 2 405 in 2001 to 3 686 in 2006), creating a longer waiting delay than 3 months between diagnostic workup ad surgical treatment. However, proportions of women who underwent a breast mammography or sonography within a 6-months interval before surgery are only slightly higher (Table 54).

Adding the MCD data did not change proportions to a large extent (Table 55). The funnel plots for 2001 and 2006 appeared very similar (Figure 34 and Figure 35). In 2001, nine (8.0%) centres performed imaging for all cases within 3 months prior to surgery, compared with eight centres (7.1%) in 2006.

Table 53. Proportion of newly diagnosed cStage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	2 042	2 405	84.9
2002	2 339	2 667	87.7
2003	3 486	3 969	87.8
2004	3 543	4 144	85.5
2005	3 296	3 879	85.0
2006	3 132	3 686	85.0
Total	**17 838**	**20 750**	**86.0**

Numerator: All women diagnosed with breast cancer (cStage I-III) in a given year undergoing two-view mammography or breast sonography within 3 months before surgery
Denominator: All women diagnosed with breast cancer (cStage I-III) in a given year who were surgically treated (breast conserving surgery or mastectomy)

Table 54. Proportion of newly diagnosed cStage I-III breast cancer patients who underwent two-view mammography or breast sonography within 6 months prior to surgery (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	2 078	2 405	86.4
2002	2 431	2 667	91.2
2003	3 620	3 969	91.2
2004	3 682	4 144	88.9
2005	3 338	3 879	86.1
2006	3 250	3 686	88.2
Total	**18 399**	**20 750**	**88.7**

Numerator: All women diagnosed with breast cancer (cStage I-III) in a given year undergoing two-view mammography or breast sonography within 6 months before surgery
Denominator: All women diagnosed with breast cancer (cStage I-III) in a given year who were surgically treated (breast conserving surgery or mastectomy)

Table 55. Proportion of newly diagnosed cStage I-III breast cancer patients who underwent two-view mammography or breast sonography within 3 months prior to surgery (MCD data, 2002-2004)

	Numerator	Denominator	Proportion (%)
2002	1 870	2 119	88.2
2003	2 756	3 151	87.5
2004	2 673	3 138	85.2
Total	**7 299**	**8 408**	**86.8**

Numerator: All women diagnosed with breast cancer (cStage I-III) in a given year undergoing two-view mammography or breast sonography within 3 months before surgery
Denominator: All women diagnosed with breast cancer (cStage I-III) in a given year who were surgically treated (breast conserving surgery or mastectomy)

Figure 34. Proportion of newly diagnosed cStage I-III breast cancer patients undergoing two-view mammography or breast sonography within 3 months prior to surgery, analyzed per centre (2001)

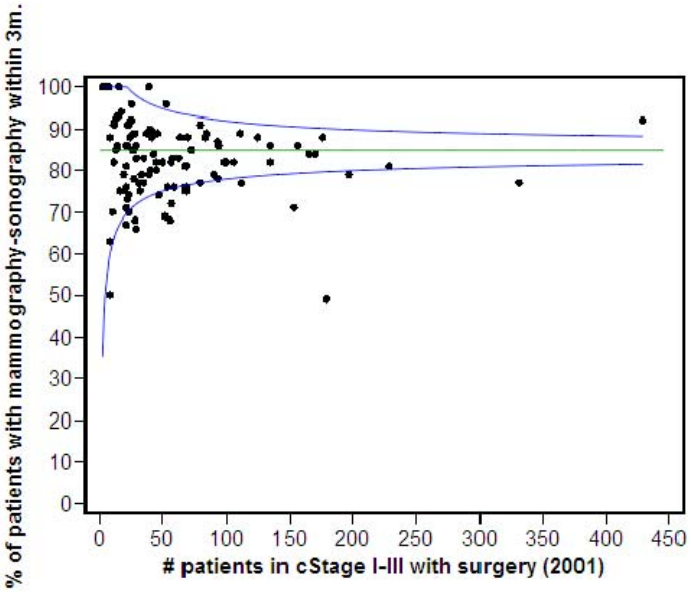
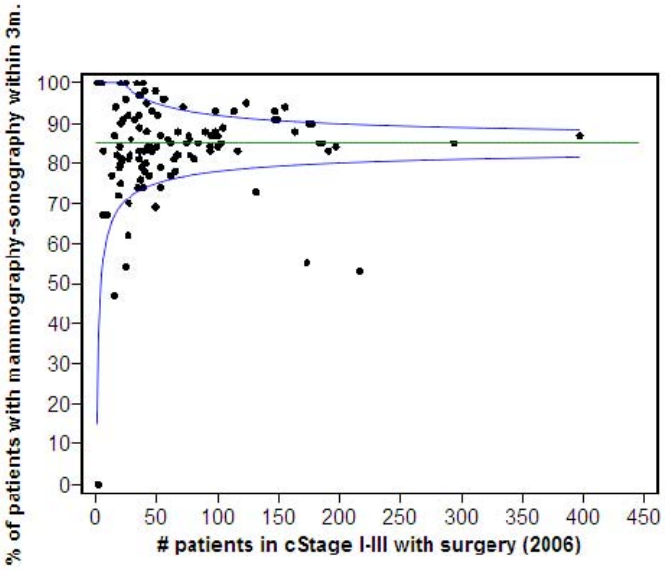


Figure 35. Proportion of newly diagnosed cStage I-III breast cancer patients undergoing two-view mammography or breast sonography within 3 months prior to surgery, analyzed per centre (2006)



7.7.4 BC10: Proportion of women who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment

7.7.4.1 Rationale

For women with early invasive breast cancer, staging of the ipsilateral axilla is essential for deciding what local and systemic treatments are subsequently required[52]. Axillary ultrasonography with fine needle aspiration cytology of axillary lymph nodes suspicious for malignancy is recommended before preoperative systemic treatment (2C evidence).

7.7.4.2 Numerator

All women diagnosed with breast cancer in a given year undergoing axillary ultrasonography with FNAC of the axillary lymph nodes before any treatment

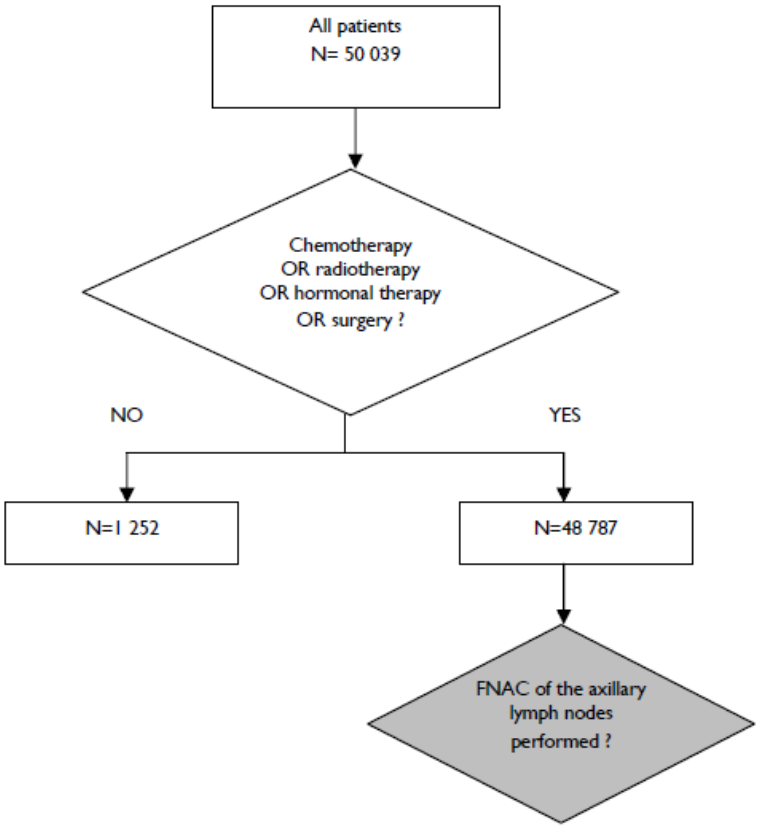
7.7.4.3 Denominator

All women diagnosed with breast cancer who receive any treatment in a given year

7.7.4.4 Elaboration

Figure 36 provides the algorithm for indicator BC10. From the breast cancer population who received a treatment (surgery, radiotherapy, chemotherapy or endocrine therapy) (denominator), women who underwent an axillary ultrasonography with FNAC of the axillary lymph nodes before this treatment were selected (numerator).

Figure 36. Flowchart of indicator BC10



7.7.4.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Axillary US with FNAC: nomenclature codes (IMA) (Table 76)
- Chemotherapy or hormonal therapy: CNK codes (IMA) (Table 85 to Table 88)
- Trastuzumab: CNK codes (IMA) (Table 89)
- Surgery: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)
- Radiotherapy: nomenclature codes (IMA) (Table 91) and codes ICD-9-CM (Table 92)

7.7.4.6 *Results*

Of all women with breast cancer, 48 787 (97.5%) were treated with chemotherapy, endocrine therapy, radiotherapy or surgery. However, as a specific nomenclature code for FNAC of the axillary lymph nodes does not exist, the indicator could not be evaluated. Using a general code for a cytopathological examination (codes 588416-588420), 38.5% of the patients were identified to have received a cytopathological examination prior to treatment.

7.7.5 BC11: Proportion of women in whom human epidermal growth factor receptor 2 (HER2) status was assessed before any systemic treatment

7.7.5.1 Rationale

The amplification of the HER2 gene or the overexpression of its protein is observed in 20% to 30% of human breast cancers and is associated with a poor prognosis in women with primary breast cancer[62]. Amplification and/or overexpression of HER2 in breast cancer is associated with a number of adverse prognostic factors. HER2 status is of great clinical value in breast tumours for the identification of those patients who are eligible for trastuzumab or lapatinib therapy. Moreover, level II evidence suggests that overexpression of HER2 identifies patients who have greater benefit from anthracycline-based adjuvant therapy[62, 63]. HER2 protein expression, and if positive confirmed with gene amplification, should be evaluated in every primary invasive breast cancer at the time of diagnosis and at the time of recurrence whenever possible (1B evidence).

7.7.5.2 Numerator

All women diagnosed with breast cancer in a given year undergoing HER2 assessment before any systemic treatment

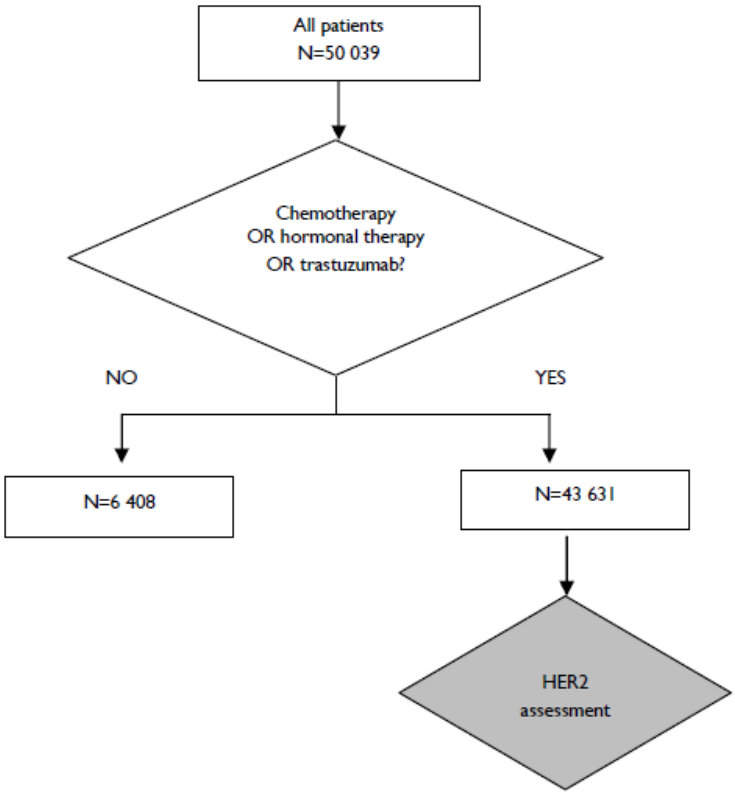
7.7.5.3 Denominator

All women diagnosed with breast cancer receiving systemic treatment in a given year

7.7.5.4 Elaboration

Figure 37 provides the algorithm for indicator BC11. The HER2 assessment is important to choose the more adapted systemic treatment. From all breast cancer women receiving systemic treatment (denominator), only those who underwent an HER2 assessment before this systemic treatment were selected (numerator).

Figure 37. Flowchart of indicator BC11



7.7.5.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- HER2 assessment: nomenclature codes (IMA) (Table 78)
- Chemotherapy or hormonal therapy: CNK codes (IMA) (Table 85 to Table 88)
- Trastuzumab: CNK codes (IMA) (Table 89)

7.7.5.6 *Results*

The data used for the analysis of all indicators encompass the period 2001-2006. Before 2007, FISH HER2 was not reimbursed, and no nomenclature code existed before this moment. First codes for HER2 assessment were introduced respectively on August 1st 2007 and July 1st 2009. Consequently, this indicator was not measurable for the period considered. Since January 1st 2011, a prospective registration will be conducted including all hormonal receptors assessments, but also the result of these assessments (e.g. status of HER2 receptors).

Nevertheless, some results can be calculated using the available administrative data. Indicator BC4 reported that 94.2% of breast cancer women were treated with chemotherapy, hormonal therapy, radiotherapy or surgery. Indicator BC11 reported that, of all women with breast cancer whatever their cancer stage, 62.3% were specifically treated with chemotherapy, hormonal therapy and/or trastuzumab. This result is slightly lower than proportion of breast cancer women who received chemotherapy and/or hormonal therapy in Nederland in 2009, i.e. 70%[20].

7.7.6 BC12: Proportion of women in whom a ER and PgR status assessment were performed before any systemic treatment

7.7.6.1 Rationale

ER and PgR status are predictive of benefit from endocrine treatment (tamoxifen, chemical ovarian ablation, aromatase inhibitors and fulvestrant) in both the adjuvant and metastatic settings[22]. The potential role of hormone receptor determination in the management of DCIS is currently an emerging topic. Breast cancer women with tumours that are ER-positive and/or PgR-positive have lower risks of mortality after their diagnosis compared to women with ER- and/or PgR-negative disease[64]. Estrogen receptors and progesterone receptors (ER/PgR) should be measured on all ductal carcinomas in situ (DCIS) and primary invasive breast cancers (1B evidence). Metastatic lesions should be biopsied whenever accessible and ER and PgR reassessed (1B evidence).

7.7.6.2 Numerator

All women diagnosed with breast cancer in a given year undergoing ER and PgR status assessment before any systemic treatment.

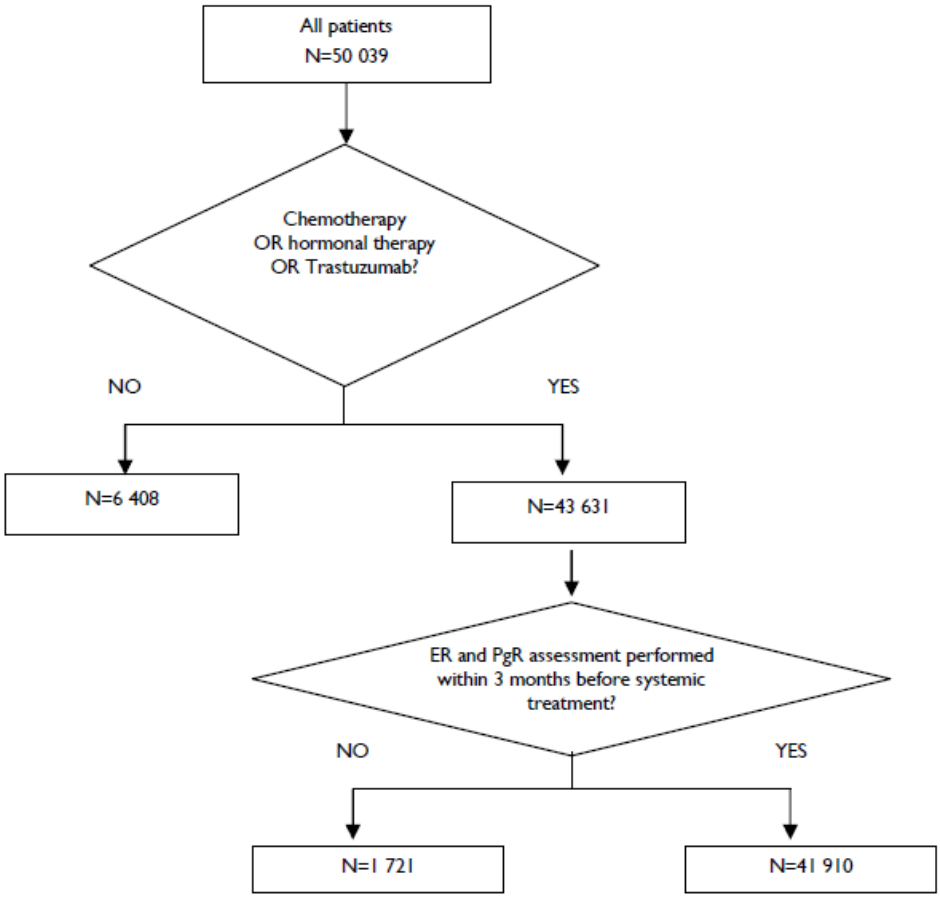
7.7.6.3 Denominator

All women diagnosed with breast cancer receiving systemic treatment in a given year.

7.7.6.4 Elaboration

Figure 38 provides the algorithm for indicator BC13. The ER/PgR assessment is important to choose the more adapted systemic treatment. From all breast cancer women receiving systemic treatment (denominator), only those who underwent a ER/PgR assessment before this systemic treatment were selected (numerator).

Figure 38. Flowchart of indicator BC12



7.7.6.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50
- ER and PgR status assessment: nomenclature codes (IMA) (Table 79)
- Chemotherapy: CNK codes (IMA) (Table 85)
- Hormonal therapy: CNK codes (IMA) (Table 86 to Table 88)

7.7.6.6 *Results*

The proportion of breast cancer patients who received chemotherapy or endocrine treatment was 87.2%. Of those 43 631 patients with systemic treatment, 41 910 (96.1%) had an immunohistological examination within three months prior to treatment start (Table 56). The number of patients with an immunohistological examination may be slightly overestimated, since a combination of the general nomenclature codes (588070 – 588081) and the specific codes for ER and PgR (435831 – 435842) was used. However, when only using the specific codes for ER and PgR (435831 – 435842), only 145 patients (0.3%) were withdrawn.

The proportion of patients with an immunohistological examination three months prior to systemic treatment increased over the years. In 2001, 90.5% was assessed by immunohistology, while this was true for 98% in 2006.

This difference is also reflected in the funnel plots (Figure 39 and Figure 40). In 2006, almost all centres underwent an immunohistological examination in all their patients.

Table 56. Proportion of patients with assessment of ER and PgR status before any systemic treatment (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	5 935	6 555	90.5
2002	6 367	6 684	95.3
2003	7 130	7 360	96.9
2004	7 042	7 230	97.4
2005	7 629	7 839	97.3
2006	7 807	7 963	98.0
Total	**41 910**	**43 631**	**96.1**

Numerator: All women diagnosed with breast cancer in a given year undergoing ER and PgR status assessment before any systemic treatment.
Denominator: All women diagnosed with breast cancer receiving systemic treatment in a given year.

Figure 39. Proportion of patients with assessment of ER and PgR status before any systemic treatment: analysis per centre (2001)

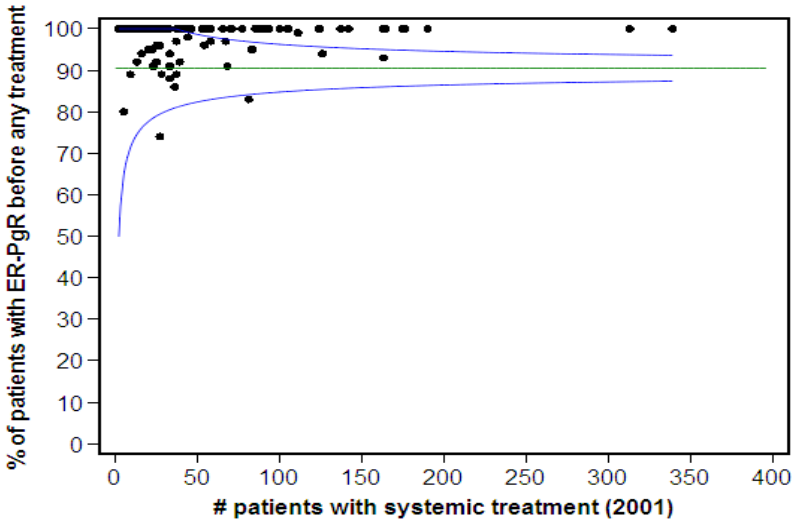
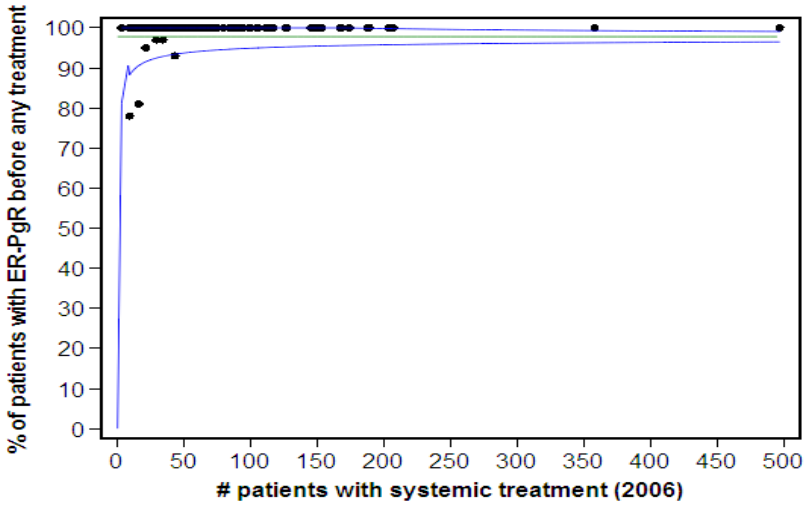


Figure 40. Proportion of patients with assessment of ER and PgR status before any systemic treatment: analysis per centre (2006)



7.7.7 BC13: Proportion of breast cancer women with cytological and/or histological assessment before surgery

7.7.7.1 Rationale

A lesion considered malignant following clinical examination, imaging or cytology alone should, where possible, have histopathological confirmation of malignancy before any surgical procedure takes place (1C evidence). This confirmation performed respecting a sufficient delay before surgery allows to have patient's fully understanding and consent[26].

7.7.7.2 Numerator

All women diagnosed with breast cancer in a given year undergoing cytological and/or histological assessment before surgery.

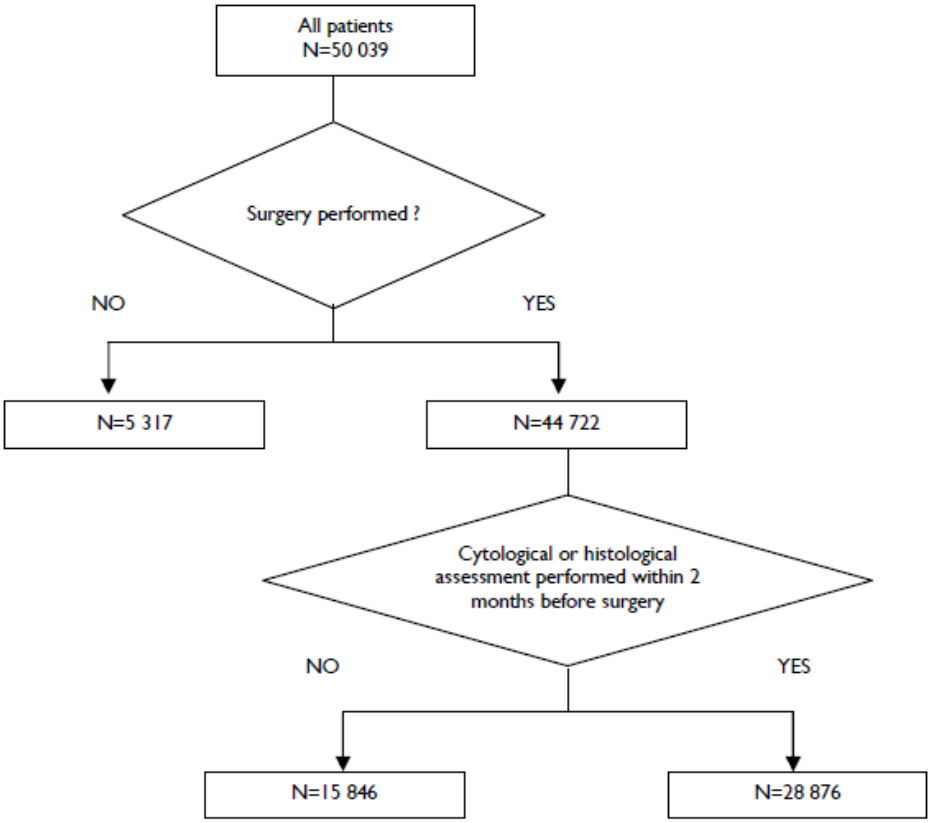
7.7.7.3 Denominator

All women diagnosed with breast cancer in a given year.

7.7.7.4 Elaboration

Figure 41 provides the algorithm for indicator BC13. From all breast cancer women (denominator), only those who underwent a cytological and/or histological assessment before surgery were selected (numerator).

Figure 41. Flowchart of indicator BC13



7.7.7.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 codes C50 (BCR)
- Cytology and histology: nomenclature codes (IMA) (Table 80)
- Surgery: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.7.7.6 *Results*

Histological and/or cytological assessment performed within 2 months before surgery should give an accurate estimation of this quality indicator although the nomenclature codes used for these medical acts are not exclusively reserved for breast pathology examination.

Of all patients who had a nomenclature code for breast surgery (44 722 or 89.4%), 28 876 (64.6%) had a histological and/or cytological examination within 2 months before surgery. There is a clear increase over the years: while in 2001, about 50% of the patients had a histological examination, the proportion raised to more than 60% in 2003 and more than 70% in 2006 (Table 57). Adding the MCD data caused only a minor change in proportions (Table 58).

In 2001, there was a large spread between centres, which decreased in 2006 (Figure 42 and Figure 43). Moreover, in 2006 fewer centres are under the lower limit line.

Table 57. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	3 324	6 596	50.4
2002	4 156	6 976	59.6
2003	4 939	7 629	64.7
2004	5 053	7 400	68.3
2005	5 612	8 021	70.0
2006	5 792	8 100	71.5
Total	**28 876**	**44 722**	**64.6**

Numerator: All women diagnosed with breast cancer in a given year undergoing cytological and/or histological assessment within 2 months before surgery.
Denominator: All women diagnosed with breast cancer and treated with surgery in a given year.

Table 58. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery (BCR-IMA-MCD data, 2002-2004)

	Numerator	Denominator	Proportion (%)
2002	3 199	5 410	59.1
2003	3 818	5 981	63.8
2004	3 750	5 526	67.9
Total	**10 767**	**16 917**	**63.6**

Numerator: All women diagnosed with breast cancer in a given year undergoing cytological and/or histological assessment within 2 months before surgery.
Denominator: All women diagnosed with breast cancer and treated with surgery in a given year.

Figure 42. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery, analyzed per centre (2001)

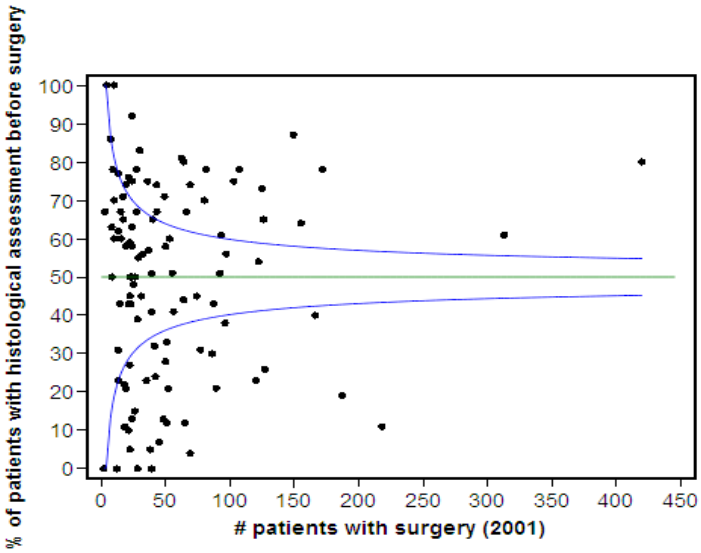
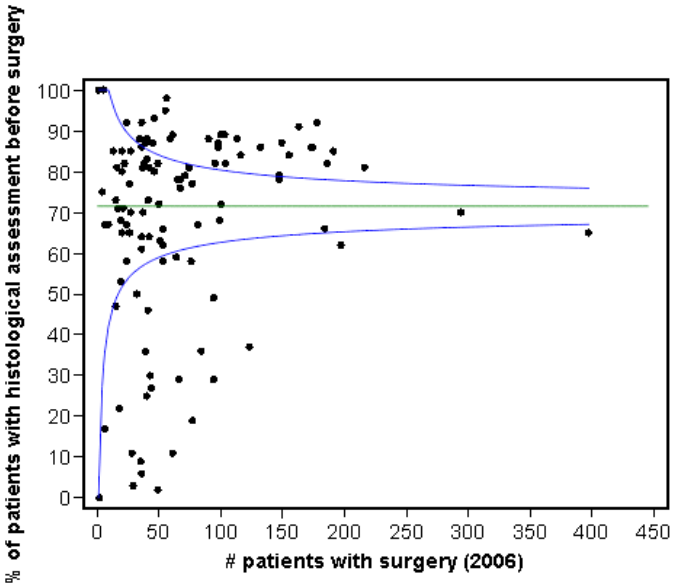


Figure 43. Proportion of breast cancer patients with cytological and/or histological assessment within 2 months prior to surgery, analyzed per centre (2006)



7.7.8 BC14: Proportion of sentinel lymph nodes biopsy in cN0 women without contraindications

7.7.8.1 Rationale

In women with primary breast cancer less than 3 cm and with clinically and ultrasonographically negative nodes, a sentinel lymph node biopsy should be performed (1A evidence).[36, 65, 66]. However, sentinel lymph node biopsy is not recommended for (1A evidence):

1. large T2 (i.e. > 3 cm) or T3-4 invasive breast cancers;
2. inflammatory breast cancer;
3. in the presence of suspicious palpable axillary lymph nodes;

4. multiple tumours; and possible disturbed lymph drainage after recent axillary surgery or a large biopsy cave after tumour excision.

7.7.8.2 *Numerator*

All cN0 women without contraindications who underwent a SLNB, in a given year

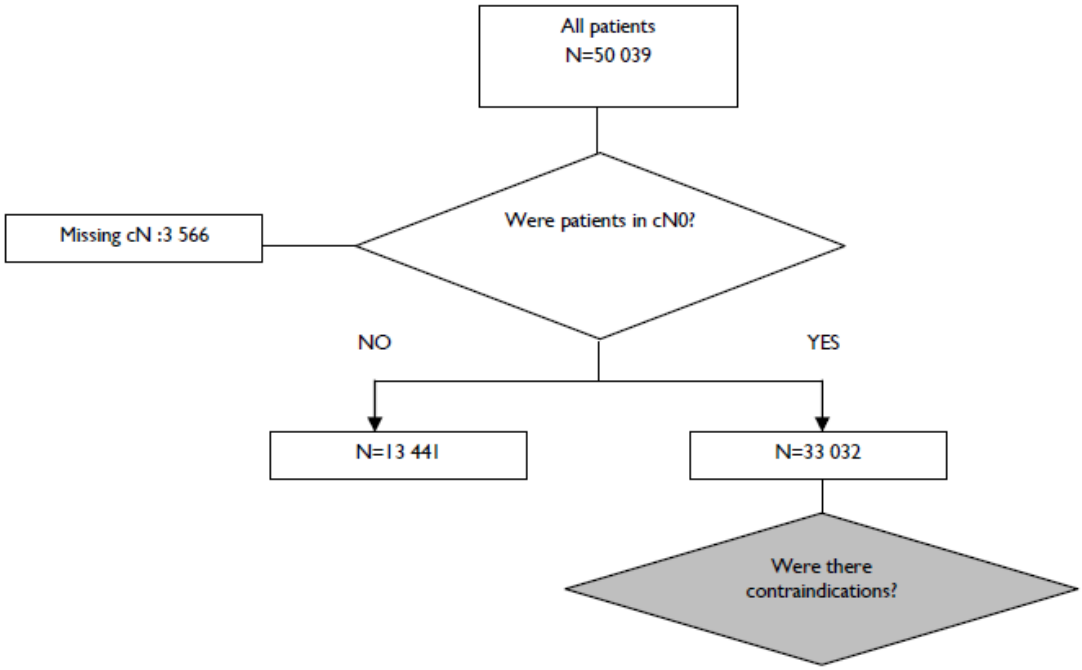
7.7.8.3 *Denominator*

All cN0 women in a given year

7.7.8.4 *Elaboration*

Figure 44 provides the algorithm for indicator BC14. From all women who had a cN0 breast cancer (denominator), only those having no contraindications for SLNB who underwent a SNLB were selected (numerator).

Figure 44. Flowchart of indicator BC14



7.7.8.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Sentinel lymph node biopsy: no specific nomenclature code

7.7.8.6 *Results*

This indicator could not be assessed, as no code was available to determine the presence of contraindications that may have lead to omitting a SLNB. The only feasible step in the calculation of this quality of care indicator was determining the number of cN0 patients, resulting in 33 032 patients (66.0%).

7.8 QUALITY INDICATORS: NEO-ADJUVANT TREATMENT

7.8.1 BC15: Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy

7.8.1.1 Rationale

Preoperative treatment increases the possibility for breast conserving surgery because of shrinkage of the tumour before surgical intervention, yet at the associated cost of increased locoregional recurrence rates[23]. In women with unifocal operable tumours too large for breast conserving surgery, downstaging with neoadjuvant systemic therapy should be considered (1A evidence).

7.8.1.2 Numerator

All women diagnosed with cT2-T3 breast cancer in a given year who received neoadjuvant systemic treatment.

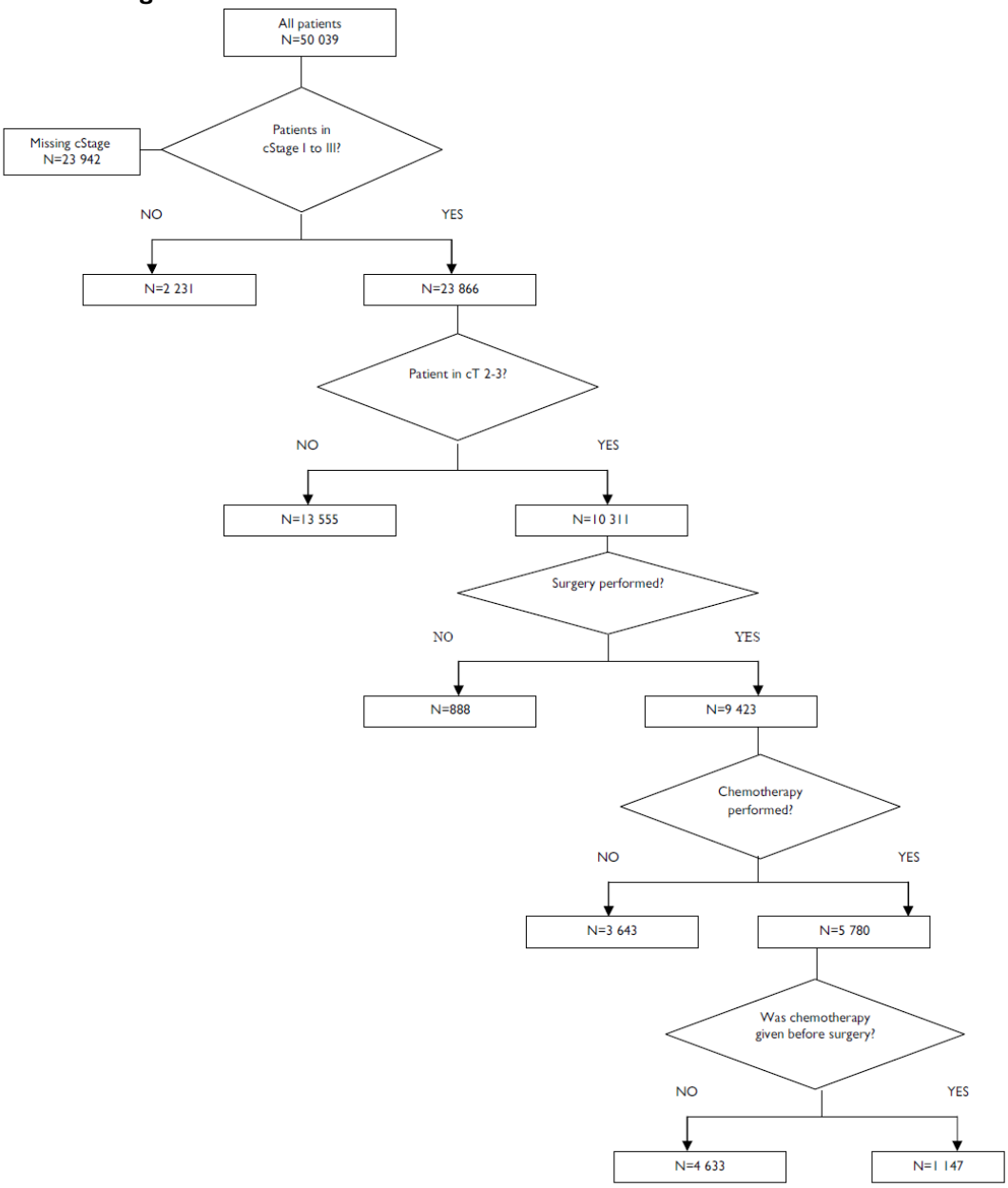
7.8.1.3 Denominator

All women diagnosed with cT2-T3 breast cancer in a given year who underwent surgical resection.

7.8.1.4 Elaboration

Figure 45 provides the algorithm for indicator BC15. From all women diagnosed with a cT2-T3 breast cancer who were planned to be treated by surgery (denominator), only those who received a neoadjuvant systemic therapy were selected (numerator).

Figure 45. Flowchart of indicator BC15



7.8.1.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Chemotherapy: CNK codes (IMA) (Table 85)
- Surgery: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.8.1.6 Results

The number of patients considered as operable (cStage I-III) was 23 866 (91.5% of all patients with known cStage). Of those patients, 10 311 (43.2%) had a tumour size larger than 2 cm without direct extension to the chest wall or skin (cT2 or cT3).

From the operable cT2 and cT3 tumours, 9 423 (93.9%) were surgically treated and from this group, 61.3% received chemotherapy. A total of 1 147 patients (11.8%) received systemic treatment in a neoadjuvant setting (Table 59).

The analyses per year showed a clear increase in the proportion of patients treated by neoadjuvant chemotherapy, but also a sharp increase in the number of cT2-cT3 women who benefited from surgery. Whereas in 2001 only 5.5% of the patients had neoadjuvant treatment (chemotherapy), this percentage increased above 13% in 2004 and above 18% in 2006. The same analysis conducted on the coupled BCR-IMA and MCD databases obtained congruent results (Table 60).

The analyses per centre revealed few outliers for both extreme years (Figure 46 and Figure 47).

Table 59. Proportion of operable cT2-cT3 patients who received neoadjuvant systemic therapy (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	59	1 065	5.5
2002	85	1 145	7.4
2003	155	1 758	8.8
2004	242	1 809	13.4
2005	265	1 846	14.4
2006	341	1 800	18.9
Total	**1 147**	**9 423**	**12.2**

Numerator: patients with operable cT2-cT3 disease receiving chemotherapy between incidence and surgery date
Denominator: patients with operable cT2-cT3 disease who were surgically treated

Table 60. Proportion of operable cT2-cT3 patients who received neoadjuvant systemic therapy (BCR-IMA-MCD data, 2002-2004)

	Numerator	Denominator	Proportion (%)
2002	68	939	7.2
2003	117	1 442	8.1
2004	176	1 420	12.4
Total	**361**	**3 801**	**9.5**

Numerator: patients with operable cT2-cT3 disease receiving chemotherapy between incidence and surgery date
Denominator: patients with operable cT2-cT3 disease who were surgically treated

Figure 46. Proportion of operable cT2-cT3 patients who received neoadjuvant systemic therapy: analysis per centre (2001)

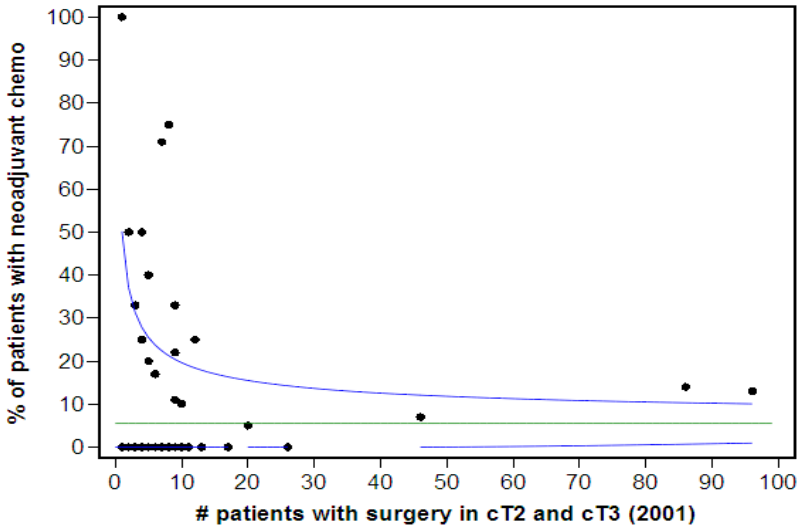
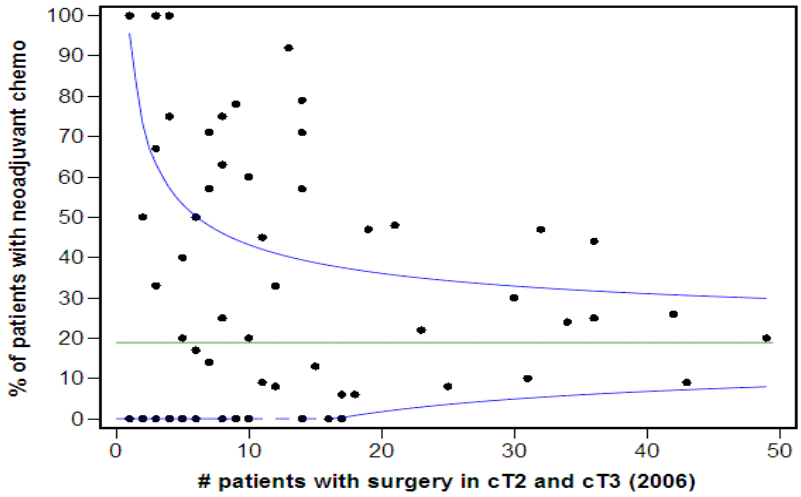


Figure 47. Proportion of operable cT2-cT3 patients who received neoadjuvant systemic therapy: analysis per centre (2006)



7.9 QUALITY INDICATORS: SURGERY

7.9.1 BC16: Proportion of breast cancer women who underwent an ALND after positive SNLB > 2 mm

7.9.1.1 Rationale

SLNB is indicated in women with primary breast cancer less than 3 cm and clinically and ultrasonographically negative nodes[36, 65, 66]. Peri-operative pathology examination of SLN is recommended. For macrometastases (>2 mm), axillary lymph node dissection level I and II is indicated (1A evidence)[52, 67]. For micrometastases (0.2-2 mm) until final results of ongoing prospective clinical trials are available (AMAROS trial and IBCSG-23-01 trial), axillary dissection is recommended taking into consideration other risk factors (for example used as a nomogram) (expert opinion).[36]. Patients found to have only isolated tumour cells in their sentinel lymph nodes should not be offered further axillary treatment

7.9.1.2 *Numerator*

All breast cancer women having a positive SLNB > 2 mm who underwent an ALND, in a given year

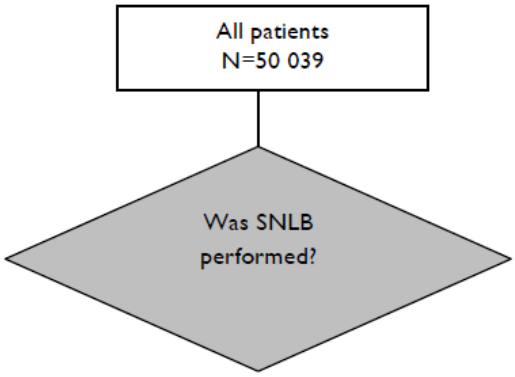
7.9.1.3 *Denominator*

All breast cancer women having a positive SLNB > 2 mm, in a given year

7.9.1.4 *Elaboration*

Figure 48 provides the algorithm for indicator BC16. From all women who had a positive SLNB > 2 mm (denominator), only those who underwent an ALND were selected (numerator).

Figure 48. Flowchart of indicator BC16



7.9.1.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Sentinel lymph node biopsy: no specific nomenclature code
- Axillary lymph node dissection: nomenclature codes (IMA) (Table 83) and codes ICD-9-CM) (Table 84)

7.9.1.6 *Results*

This quality of care indicator could no be determined, as no specific nomenclature code exists to record a sentinel lymph node biopsy. Only general codes for anatomo-pathological examinations and cytopathological examination were available in the IMA database.

7.9.2 BC17: Proportion of women with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, whatever the surgical option (local wide excision or mastectomy)

7.9.2.1 Rationale

Women with high-grade and/or palpable and/or large DCIS of the breast should be offered the choice of local wide excision or mastectomy after the patient is correctly informed. The best available evidence for the optimal surgical resection margin was reported in the NICE guideline[52]. Most studies agree that margins containing tumour cells are associated with local recurrence or bear the risk of residual cancer. There is agreement that the risk of local recurrence is reduced with very wide margins, e.g. more than 10 mm of tumour-free tissue. When margins of 2 mm or more are achieved, local recurrence rates of 2% (with radiotherapy) to 11% (without radiotherapy) were reported[52].

7.9.2.2 Numerator

All women diagnosed with high-grade and/or palpable and/or large DCIS of the breast who had negative margins after surgery, in a given year

7.9.2.3 Denominator

All women diagnosed with high-grade and/or palpable and/or large DCIS of the breast who underwent a surgical treatment, in a given year

7.9.2.4 Elaboration

This quality of care indicator could not be determined, because the DCIS patients were not selected in the cancer registry database

7.9.2.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code D05 for DCIS of the breast (BCR)
- *Surgery:* nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.9.2.6 Results

This quality of care indicator could not be determined, because the DCIS patients were not selected in the cancer registry database. Furthermore, the R-status after surgery could not be determined, because the resection margins were not reported in any of the databases.

In the future, such indicator could be measured since the ICD-10 code D05 for DCIS of the breast is recorded in BCR, and has to be selected to conduct the adequate analysis. The prospective registration of patients with breast cancer could include the status of resection margins after surgery, allowing the measurement of this indicator.

7.9.3 BC18: Proportion of cStage I and II women who undergo breast-conserving surgery / mastectomy

7.9.3.1 Rationale

Breast-conserving surgery followed by radiotherapy offers the same benefits regarding local tumour control, recurrence free survival and overall survival as modified radical mastectomy in women with stage I or II breast cancer who are candidates for breast-conserving surgery (1A evidence)[37, 47, 53-55]. The choice of surgery must be tailored to the individual patient with stage I or II breast cancer, who should be fully informed of the options (1A evidence).

7.9.3.2 Numerator

All cStage I and II breast cancer women who underwent a breast conserving surgery or mastectomy in a given year

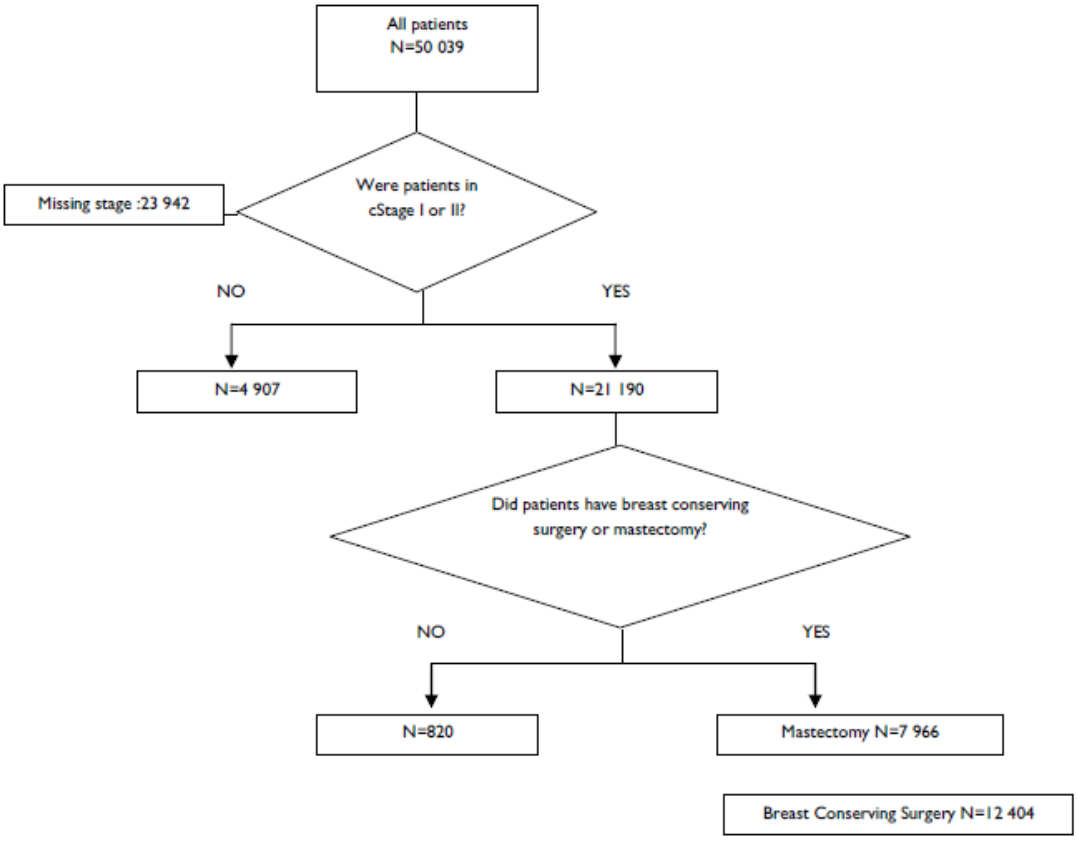
7.9.3.3 Denominator

All cStage I and II breast cancer women in a given year

7.9.3.4 Elaboration

Figure 49 provides the algorithm for indicator BC18. From all cStage I and II breast cancer women (denominator), only those who underwent a breast conserving surgery or mastectomy were selected (numerator).

Figure 49. Flowchart of indicator BC18



7.9.3.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- Diagnosis of breast cancer: ICD-10 code C50 (BCR)
- Surgery: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)

7.9.3.6 *Results*

For all patients in cStage I or II (21 190 or 42.3%), the number of patients with mastectomy and breast conserving surgery was investigated. In total, 12 404 patients (58.5%) were treated with breast conserving surgery and 7 966 patients (37.6%) with mastectomy. The observed ratio breast conserving surgery/mastectomy stayed relatively stable over time (Table 61). Same results were obtained using the coupled BCR-IMA-MCD databases, without added-value (Table 62).

Between centres, this ratio varied between 0 and 8 in 2001 (Figure 50) and between 0 and 7 in 2006 (Figure 51). For both extreme years, outliers in the surgical ratio were preferentially observed in smaller centres.

Table 61. Proportion of cStage I and II patients who undergo breast conserving surgery/mastectomy (IMA data, 2001-2006)

Year	Number of surgically treated women	% of surgically treated women	Number of women with BCS	% of women with BCS	Number of women with mastectomy	% of women with mastectomy	Ratio BCS/ mastectomy
2001	2 276	93.0	1 352	55.3	924	37.8	1.463
2002	2 574	97.0	1 595	60.1	979	36.9	1.629
2003	3 824	96.8	2 362	59.8	1 462	37.0	1.616
2004	4 116	96.8	2 538	59.7	1 578	37.1	1.608
2005	3 842	96.4	2 280	57.2	1 562	39.2	1.460
2006	3 738	95.8	2 277	58.4	1 461	37.4	1.559
Total	**20 370**	**96.1**	**12 404**	**58.5**	**7 966**	**37.6**	**1.463**

Table 62. Proportion of cStage I and II patients who undergo breast conserving surgery/mastectomy (BCR-IMA-MCD data, 2002-2004)

Year	Number of surgically treated women	% of surgically treated women	Number of women with BCS	% of women with BCS	Number of women with mastectomy	% of women with mastectomy	Ratio BCS/ mastectomy
2002	2 057	98.4	1 277	61.1	780	37.3	1.637
2003	3 041	98.0	1 882	60.6	1 159	37.3	1.624
2004	3 124	98.1	1 930	60.6	1 194	37.5	1.616
Total	**8 222**	**90.3**	**5 089**	**61.6**	**3 133**	**28.7**	**1.624**

Figure 50. Proportion of cStage I and II patients who undergo breast conserving surgery/mastectomy: analysis per centre (BCS/mastectomy ratio) - 2001

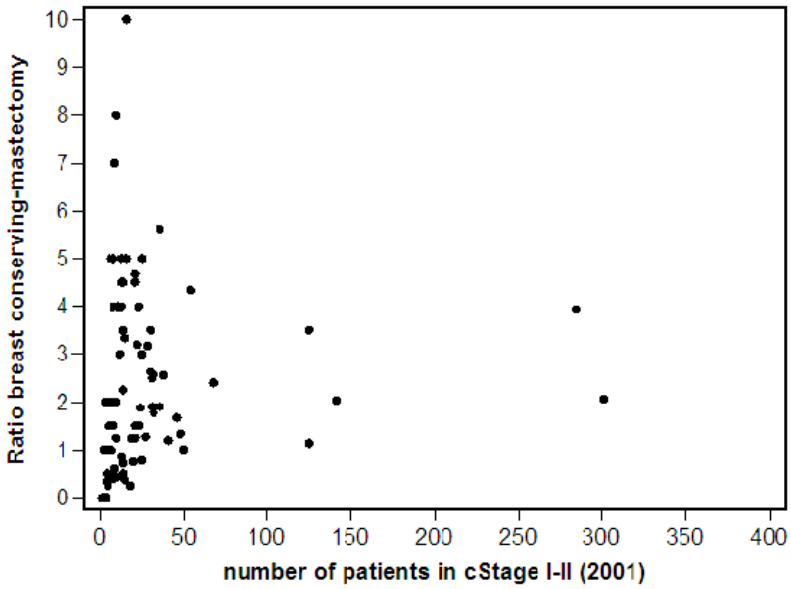
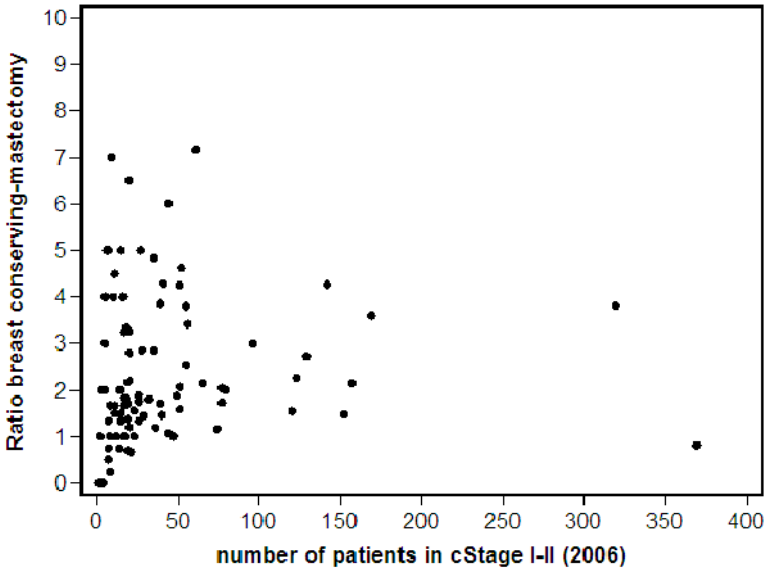


Figure 51. Proportion of cStage I and II patients who undergo breast conserving surgery/mastectomy: analysis per centre (BCS/mastectomy ratio) - 2006



Moreover, it is possible to calculate the rate of re-interventions after a breast conserving surgery, whatever the reason for this re-intervention (recurrence, positive resection margins,…). All women who underwent a surgical reintervention (mastectomy or other breast surgery) within respectively 6 months and 1 year after the breast conserving surgery were identified (Table 63). The rate of reinterventions decreased overtime from 12% to 10% in the year following BCS. This decrease is particularly sharp for mastectomy whose rates fell 1 year after BCS from 8.5% in 2001 to 5% in 2006 (Table 64).

Table 63. Number and proportion of women who underwent a surgical reintervention 6 months or 1 year after a BCS (2001-2006).

	Denominator	New surgery within 6 months	Proportion (%)	New surgery within 1 year	Proportion (%)
2001	2 232	258	11.6	265	11.9
2002	2 504	281	11.2	296	11.8
2003	3 463	308	8.9	324	9.4
2004	3 840	342	8.9	363	9.5
2005	4 069	350	8.6	371	9.1
2006	4 268	341	8.0	362	8.5
Total	**20 376**	**1 880**	**9.2**	**1 981**	**9.7**

Table 64. Number and proportion of women who underwent a mastectomy 6 months or 1 year after a BCS (2001-2006).

	Denominator	Mastectomy within 6 months	Proportion (%)	Mastectomy within 1 year	Proportion (%)
2001	2 232	184	8.2	190	8.5
2002	2 504	197	7.9	208	8.3
2003	3 463	213	6.2	225	6.5
2004	3 840	228	5.9	243	6.3
2005	4 069	197	4.8	207	5.1
2006	4 268	197	4.6	212	5.0
Total	**20 376**	**1 216**	**6.0**	**1 285**	**6.3**

7.9.4 BC19: Proportion of women with breast cancer recurrence after breast conserving surgery who are treated by a mastectomy

7.9.4.1 Rationale

In women with a local recurrence after breast conserving treatment, salvage mastectomy is recommended[36].

7.9.4.2 Numerator

All stage I-III breast cancer women who underwent a mastectomy for a recurrence after a breast conserving surgery in a given year

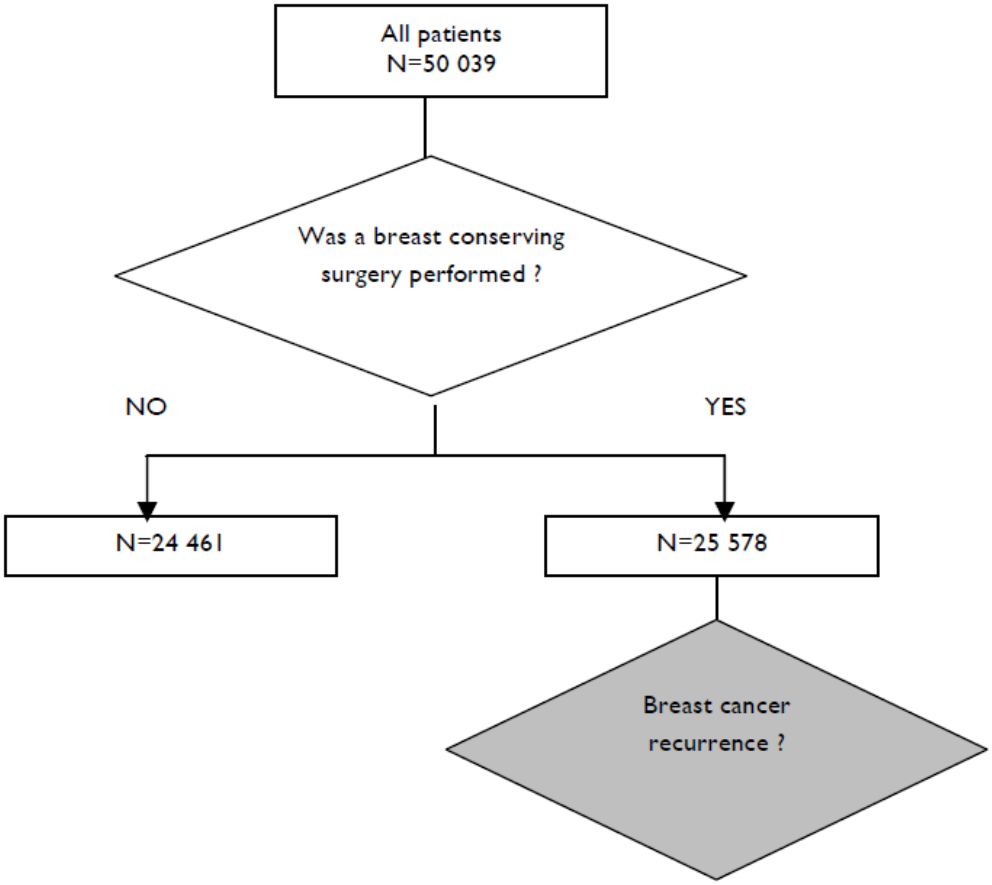
7.9.4.3 Denominator

All stage I-III breast cancer women who have a recurrence after a breast conserving surgery in a given year

7.9.4.4 Elaboration

Figure 52 provides the algorithm for indicator BC19. From all stage I-III breast cancer women who have a recurrence after a breast conserving surgery (denominator), only those who underwent a mastectomy (numerator) were selected.

Figure 52. Flowchart of indicator BC19



7.9.4.5 *Data source(s)*

Source database(s)

- BCR for source population

IMA administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 (BCR)
- *Breast conserving surgery*: nomenclature codes (IMA) (Table 81) and codes ICD-9-CM (Table 82)
- *Mastectomy after recurrence*: nomenclature codes (IMA) (Table 81) and codes ICD-9-CM (Table 82)

7.9.4.6 *Results*

As up till now no code nor registration for breast cancer recurrence exists, this indicator could not be determined directly. An indirect measurement of this indicator by investigating the number of retreatments also seemed invalid for this cancer type. Indeed, a retreatment can only be determined if there is a clear interval between the first line treatment and the second line treatment. Endocrine therapy may be a long term treatment which makes a treatment-free interval difficult to determine. In conclusion, it remained impossible to calculate how many of the 24 578 patients with breast conserving surgery (49.1%) experienced recurrent disease.

7.10 QUALITY INDICATORS: ADJUVANT TREATMENT

7.10.1 BC20: Proportion of women with a breast cancer who are receiving intravenous chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen

7.10.1.1 Rationale

A detailed plan for the chemotherapy regimen is a critical component of ensuring safety and high quality care for women[68]. ASCO specifies that a treatment plan should include the following information about the planned chemotherapy regimen: chemotherapy regimen and starting dosages; duration of treatment and number of planned cycles. Abbreviated documentation is acceptable only if: a) there is a standard, written definition for the abbreviation that includes details of the medications, dose and duration, that is physically available at the practice or in the practice Electronic System or b) the abbreviated documentation includes a reference to a published regimen[68].

7.10.1.2 Numerator

All women diagnosed with a breast cancer who received a chemotherapy for whom the planned chemotherapy regimen (which includes, at a minimum: drug[s] prescribed, dose, and duration) is documented prior to the initiation, and at each administration of the treatment regimen, in a given year.

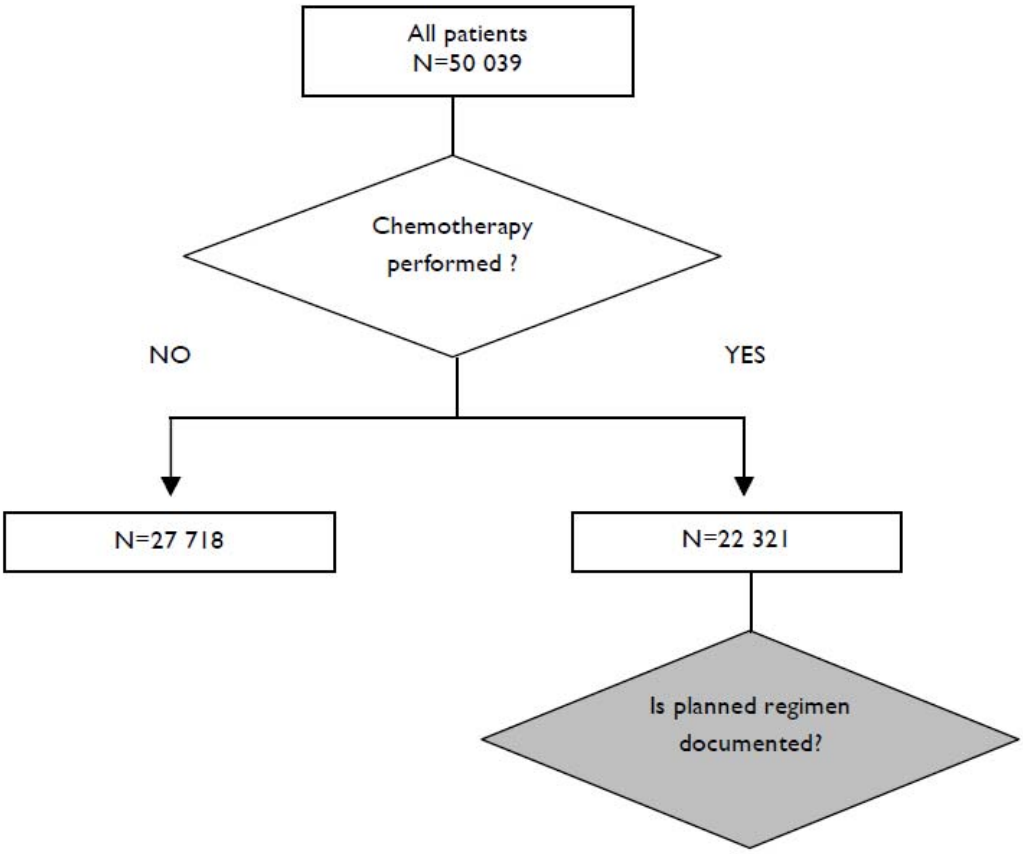
7.10.1.3 Denominator

All women diagnosed with a breast cancer who received a chemotherapy in a given year

7.10.1.4 Elaboration

Figure 53 provides the algorithm for indicator BC20. From all breast cancer women treated with chemotherapy (denominator), only those for whom the planned chemotherapy regimen is actually documented prior to the initiation, and at each administration of the treatment regimen were selected (numerator).

Figure 53. Flowchart of indicator BC20



7.10.1.5 Data source(s)

Source database(s)

- BCR for source population
- IMA

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 (BCR)
- *Chemotherapy*: CNK codes (IMA) (Table 85)

7.10.1.6 Results

From all breast cancer women, 44.6% were treated with a chemotherapy regimen. However, in the administrative databases, no code allowed to check the documentation of the planned chemotherapy regimen. This information could only be obtained in studying each patient medical record or care plan at hospital. As a consequence, this indicator could not be measured at a national level.

7.10.2 BC21: Proportion of women receiving adjuvant systemic therapy after breast surgery for invasive breast cancer

7.10.2.1 Rationale

The choice of the adjuvant systemic treatment for invasive breast cancer should be driven by the hormonal sensitivity, risk profile of the tumour, age, menopausal status and comorbidities of the patient (1A evidence). For patients with Stage I-III breast cancer, preferred regimens are standard anthracycline-based regimens with or without a taxane (1A evidence). A better 10-year disease-free survival was reported in early breast cancer patients (stage I – III) treated with adjuvant anthracycline-based chemotherapy compared to patients not treated with chemotherapy (65% vs. 60%, p=0.01)[51]. Also, the 10-year distant metastasis rates were significantly better in the active treatment group (23% vs. 28%, p=0.02). For patients with lymph node-positive breast cancer, preferred regimens are standard anthracycline and taxane-based regimens (2A evidence)[69].

The measure requires chemotherapy to begin within 120 days of diagnosis. This time frame allows for completion of surgery and appropriate consultation regarding adjuvant treatment options[10]. As hormonal therapy is generally prescribed after the completion of the chemotherapy, the panel of experts proposed an interval of 9 months between the surgical intervention and the start of the endocrine therapy.

7.10.2.2 Numerator

All women diagnosed with pT2-T3 breast cancer in a given year who received adjuvant systemic treatment within 4 months (for chemotherapy) and within 9 months (for hormonal therapy) after a surgical resection.

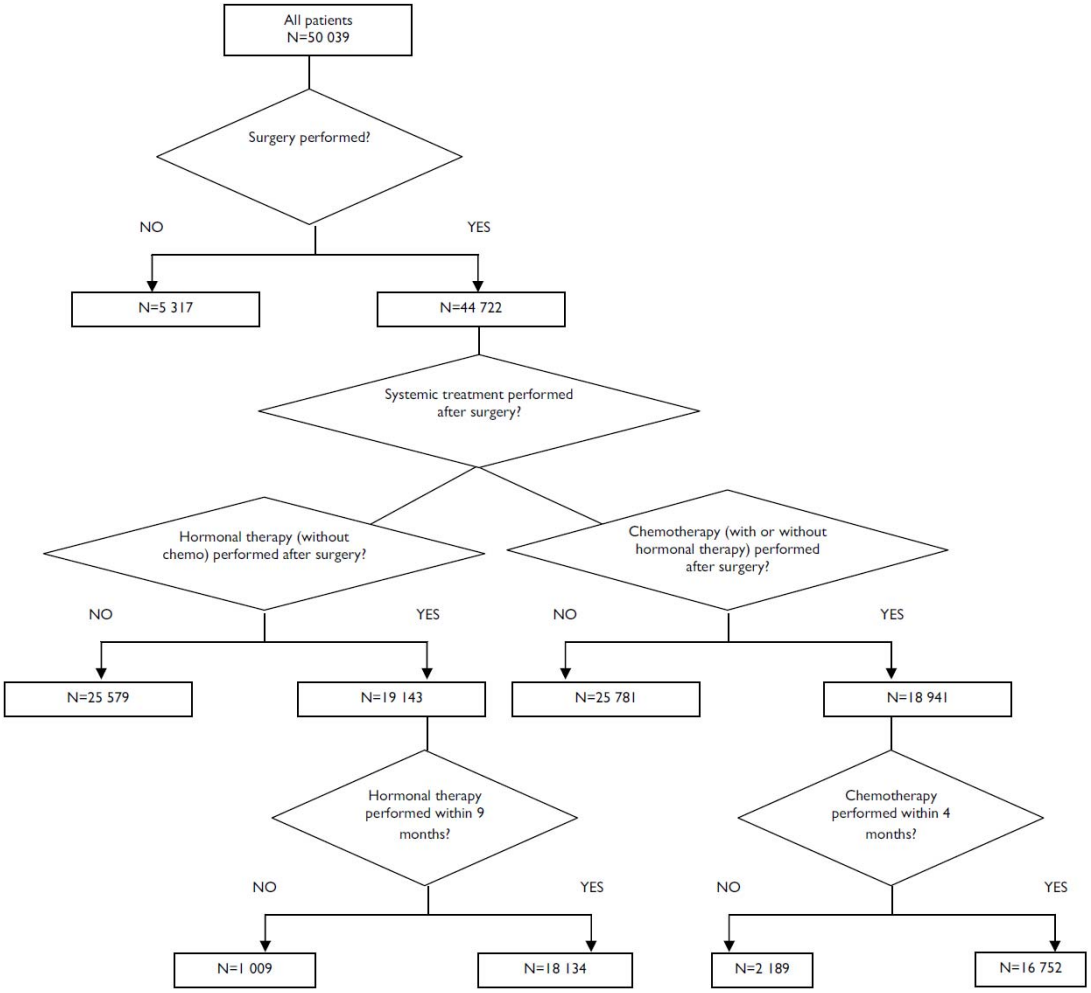
7.10.2.3 Denominator

All women diagnosed with pT2-T3 breast cancer in a given year who underwent a surgical resection.

7.10.2.4 Elaboration

Figure 54 provides the algorithm for indicator BC21. From all women diagnosed with pT2-T3 breast cancer who underwent a surgical resection (denominator), only those who received adjuvant systemic treatment (numerator) were selected.

Figure 54. Flowchart of indicator BC21



7.10.2.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 (BCR)
- *Surgery*: nomenclature codes (IMA) (Table 81) or ICD-9-CM codes (MCD) (Table 82)
- *Chemotherapy or hormonal therapy*: CNK codes (IMA) (Table 85 to Table 88)
- *Trastuzumab*: CNK codes (IMA) (Table 89)
  - Date of surgery + 4 months (maximum) to be considered as adjuvant chemotherapy
  - Date of surgery + 9 months (maximum) to be considered as adjuvant hormonal therapy

7.10.2.6 Results

From the 44 722 operated patients (89.4% of all patients), 18 941 (42.4%) had additional chemotherapy (with or without endocrine therapy) and 19 143 (42.8%) had additional endocrine treatment (without chemotherapy), administered in the time frame 2001-2006. So, at least 38 084 operated women received an adjuvant systemic treatment (85.1%). The chemotherapy was administered within four months after surgery for 16 752 women (88.4%) and the hormonal therapy was administered within 9 months for 18 134 patients (94.7%) (Table 65). The adjuvant treatment was administered in the recommended delays in 91.6% of all patients who received such treatment.

It is also important to note that some patients, diagnosed and surgically treated in the time frame 2001-2006 could receive an adjuvant systemic treatment in the beginning of 2007. Those patients are not identifiable with the dataset considered. Moreover, a certain proportion of breast cancer women entered in clinical trials or received chemotherapy for 'compassionate use'. The exact number of these women is currently unknown. In conclusion, it is possible that the number of patients who received adjuvant systemic therapy is underestimated.

Variability between centres appeared to be limited, showing no extreme outliers for both examined years and for both types of adjuvant systemic treatment (Figure 55 to Figure 58).

Table 65. Proportion of women receiving adjuvant endocrine therapy within 9 months or chemotherapy within 4 monhts after breast surgery for invasive breast cancer (IMA data, 2001-2006).

	# surgery	# adjuvant chemo	# adjuvant hormonal	% adjuvant chemo	% adjuvant hormonal
2001	6 596	2 553	2 438	38.7	37.0
2002	6 976	2 657	2 688	38.1	38.5
2003	7 629	2 862	2 982	37.5	39.1
2004	7 400	2 779	3 001	37.6	40.6
2005	8 021	2 914	3 479	36.3	43.4
2006	8 100	2 987	3 546	36.9	43.8
Total	**44 722**	**16 752**	**18 134**	**37.5**	**40.5**

Figure 55. Proportion of women receiving adjuvant chemotherapy within 4 months after breast surgery for invasive breast cancer: analysis per centre (2001)

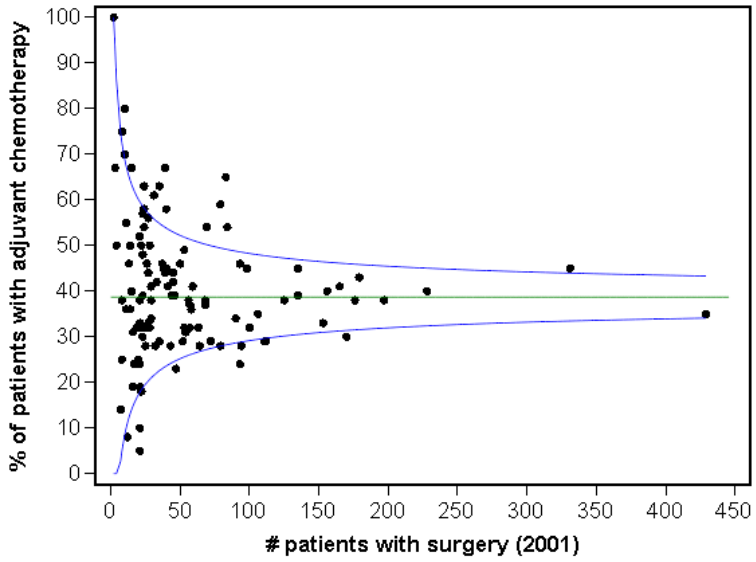


Figure 56. Proportion of women receiving adjuvant chemotherapy within 4 months after breast surgery for invasive breast cancer: analysis per centre (2006)

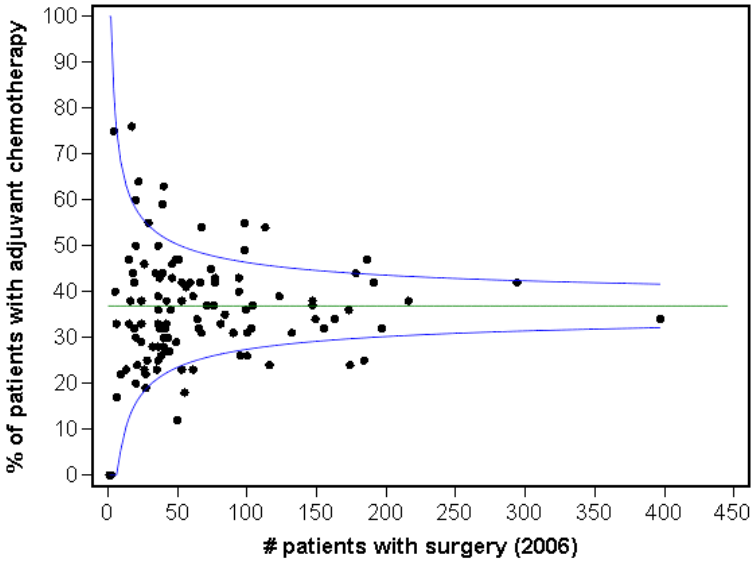


Figure 57. Proportion of women receiving adjuvant hormonal therapy within 9 months after breast surgery for invasive breast cancer: analysis per centre (2001)

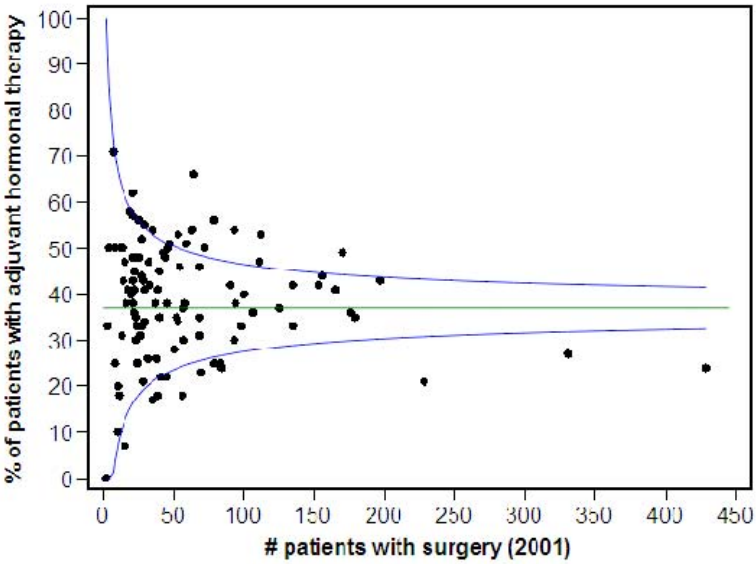
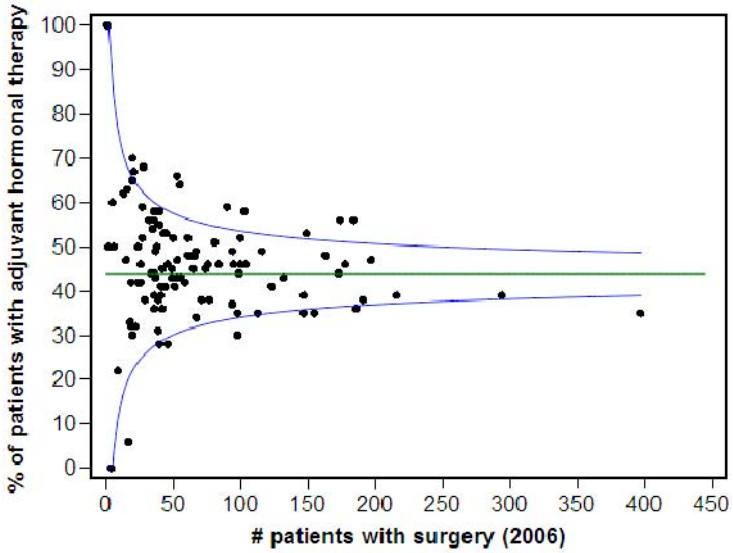


Figure 58. Proportion of women receiving adjuvant hormonal therapy within 9 months after breast surgery for invasive breast cancer: analysis per centre (2006).



7.10.3 BC22: Proportion of women with hormone receptor positive invasive breast cancer or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI)

7.10.3.1 Rationale

Adjuvant treatment with tamoxifen substantially improves the 15-year survival of premenopausal women with ER-positive tumours and of women whose tumours are of unknown ER status[70]. Aromatase inhibitors (anastrozole, exemestane and letrozole) are alternative options to tamoxifen for ER-positive invasive breast cancer in postmenopausal women[52, 71]. Despite the impressive evidence reporting the role of adjuvant endocrine therapy in reducing the risk of tumour recurrence, many women who should be receiving this therapy are not. It is important to document all medical, patient or system instances in which a patient with stage I-III, ER/PgR+ may not be a candidate for the therapy[68].

7.10.3.2 Numerator

All women diagnosed with ER+ or PgR+ invasive breast cancer or DCIS in a given year who received adjuvant endocrine treatment with Tamoxifen or an aromatase inhibitor.

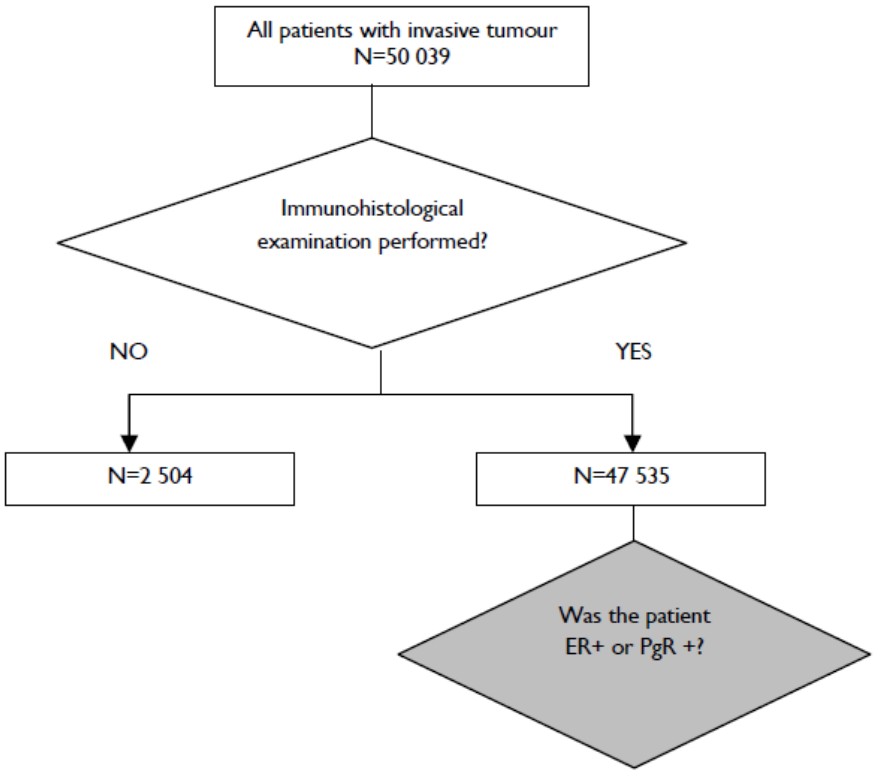
7.10.3.3 Denominator

All women diagnosed with ER+ or PgR+ invasive breast cancer or DCIS in a given year

7.10.3.4 Elaboration

Figure 59 provides the algorithm for indicator BC22. From all women diagnosed with ER+ or PgR+ invasive breast cancer or DCIS (denominator), only those who received adjuvant endocrine treatment with Tamoxifen or an aromatase inhibitor (numerator) were selected.

Figure 59. Flowchart of indicator BC22



7.10.3.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *ER and PgR status assessment*: nomenclature codes (IMA) (Table 79)
- *Hormonal therapy:* CNK codes (IMA) (Table 86 and Table 88)

7.10.3.6 Results

The nomenclature code for an immunohistological examination was found in 47 535 (95.0%) patients. However, the findings or results of this examination (whether ER or PgR receptors are positive) were not available in the administrative databases, rendering this quality of care indicator inassessable. Since January 1st 2011, a prospective registration will be conducted including all hormonal receptors assessments, but also the result of these assessments (e.g. status of ER/PgR receptors). In the future, such indicator could be measured since the status of ER/PgR receptors status will be recorded and the ICD-10 code D05 for DCIS of the breast will be selected to conduct the adequate analysis.

7.10.4 BC23: Proportion of women with HER2 positive, node positive or high-risk node negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of ≥ 55% who received chemotherapy and Trastuzumab

7.10.4.1 Rationale

Trastuzumab is an adjuvant therapy of HER2-positive breast cancer that reduces the risk of relapse by about 50% and the risk of death by about 30%[52]. However, with trastuzumab, women had a higher risk for congestive heart failure and for left ventricular ejection fraction decline. One year treatment with adjuvant trastuzumab is indicated for women with HER2-positive, node-positive or high-risk node-negative breast cancer (tumour size > 1 cm), having a left ventricular ejection fraction of ≥ 55% and without important cardiovascular risk factors who received chemotherapy (1A evidence) [25].

7.10.4.2 Numerator

All women diagnosed with HER2+ node positive or high-risk node negative breast cancer (tumour size > 1 cm) having a left ventricular ejection fraction ≥ 55% who received Trastuzumab and chemotherapy in a given year

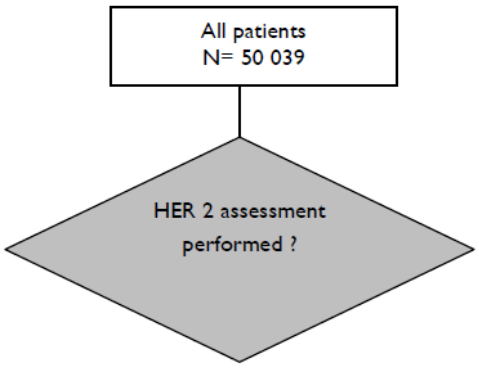
7.10.4.3 Denominator

All women diagnosed with HER2+ node positive or high-risk node negative breast cancer (tumour size > 1 cm) in a given year

7.10.4.4 Elaboration

Figure 60 provides the algorithm for indicator BC23. From all women diagnosed with HER2+ node positive or high-risk node negative breast cancer (tumour size > 1 cm) (denominator), only those who have a left ventricular ejection fraction ≥ 55% who received Trastuzumab and chemotherapy (numerator) were selected.

Figure 60. Flowchart of indicator BC23



7.10.4.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *HER2 assessment*: nomenclature codes (IMA) (Table 78)
- *Cardiac assessment:* nomenclature codes (IMA) (Table 90)
- *Chemotherapy*: CNK codes (IMA) (Table 85)
- *Trastuzumab:* CNK codes (IMA) (Table 89)

7.10.4.6 *Results*

Firstly, the data used for the analysis of all indicators concern the period 2001-2006. First codes for HER2 assessment were introduced on August 1st 2007 and July 1st 2009. Consequently, in alignment with indicator BC5, this indicator was not measurable for the period considered. Moreover, even if the code for HER 2 assessment would have been available before 2007, it would remain impossible to assess whether women were HER2 positive, based on the nomenclature code. Since January 1st 2011, a prospective registration will be conducted including all hormonal receptors assessments, but also the result of these assessments (e.g. status of HER2 receptors).

Secondly, nomenclature codes for cardiac assessment exist in the IMA database, but the level of the left ventricular ejection fraction remains unreported in an administrative database. Without a prospective registration that would include such result, this indicator could not be measurable.

7.10.5 BC24: Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months

7.10.5.1 *Rationale*

An increased risk of grade III-IV congestive heart failure and asymptomatic left ventricular ejection fraction was reported with trastuzumab, along with prolonged disease-free survival, prolonged distant disease-free survival and prolonged overall survival[24]. In view of the safety profile of trastuzumab, cardiac function should be monitored during treatment with trastuzumab[25].

7.10.5.2 *Numerator*

All women diagnosed with breast cancer in a given year who received Trastuzumab in whom cardiac function is monitored every 3 months

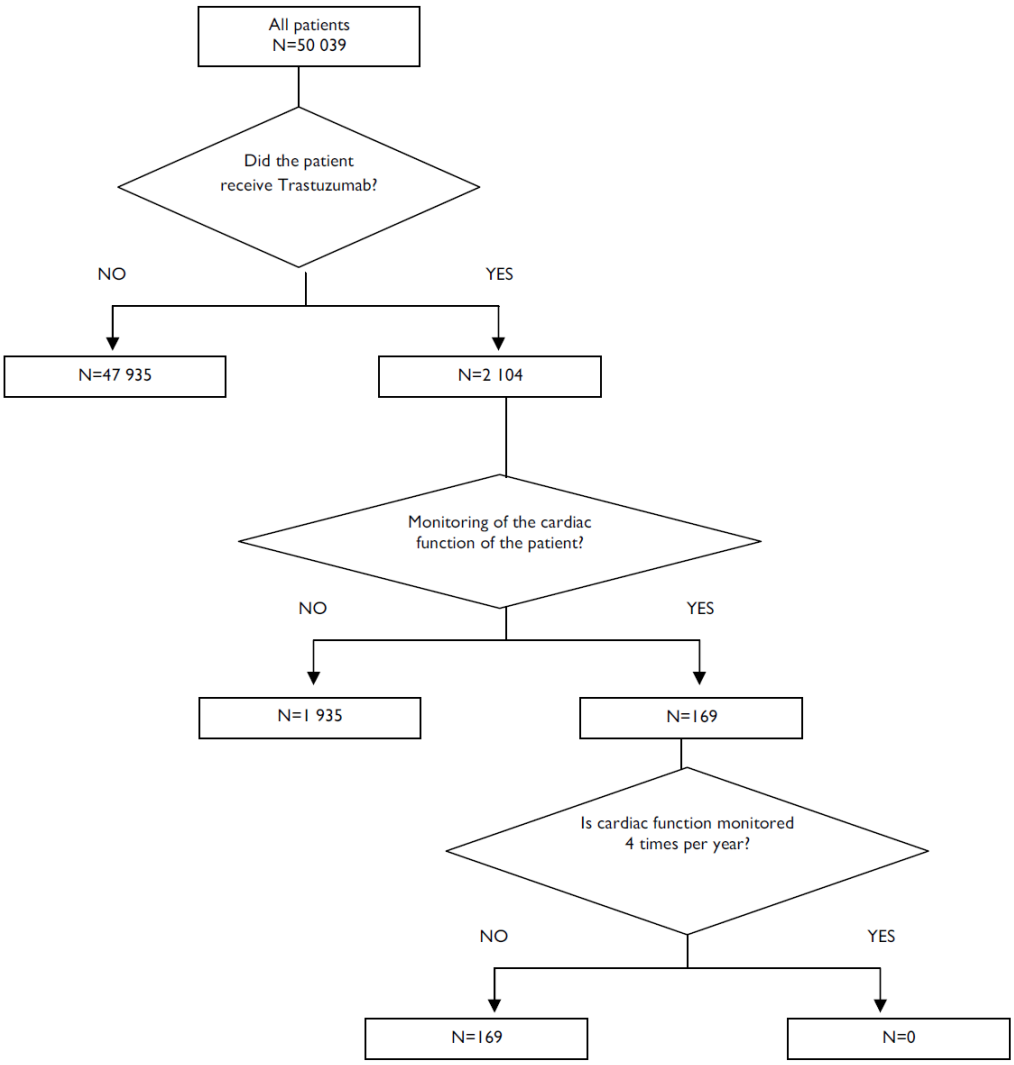
7.10.5.3 *Denominator*

All women diagnosed with breast cancer in a given year who received Trastuzumab

7.10.5.4 *Elaboration*

Figure 61 provides the algorithm for indicator BC24. From all breast cancer women treated with Trastuzumab (denominator), only those in whom cardiac function is monitored every 3 months (numerator) were selected.

Figure 61. Flowchart of indicator BC24



7.10.5.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *Trastuzumab:* CNK codes (IMA) (Table 89)
- *Cardiac assessment:* nomenclature codes (IMA) (Table 90)

7.10.5.6 Results

As trastuzumab was not reimbursed before July 1st 2006, it was impossible to trace trastuzumab treatments before this date. Consequently, it was impossible to determine when patients, with incidence date before July 1st 2006, started their trastuzumab treatment. More results will be obtained in a future evaluation of this indicator.

However, it is possible to see that 2 104 patients received at least one trastuzumab based treatment after July 1st 2006. Cardiac function was monitored in only 169 patients (8%). No patient benefited from a cardiac function assessment 4 times a year. However, the follow-up period is too short to draw conclusions, based on the available data.

7.10.6 BC25: Proportion of women who received radiotherapy after breast conserving surgery

7.10.6.1 Rationale

In women with early breast cancer, adjuvant irradiation is indicated after breast conserving surgery (1A evidence). This recommendation is based on the systematic review of the Early Breast Cancer Trialists Collaborative Group (EBCBCG) and subsequent RCTs[36, 37, 50], that reported a substantial and significant reduction in local recurrence (mainly in the conserved breast) after adjuvant radiotherapy.

7.10.6.2 Numerator

All women diagnosed with invasive breast cancer in a given year who received radiotherapy after breast conserving surgery without further mastectomy

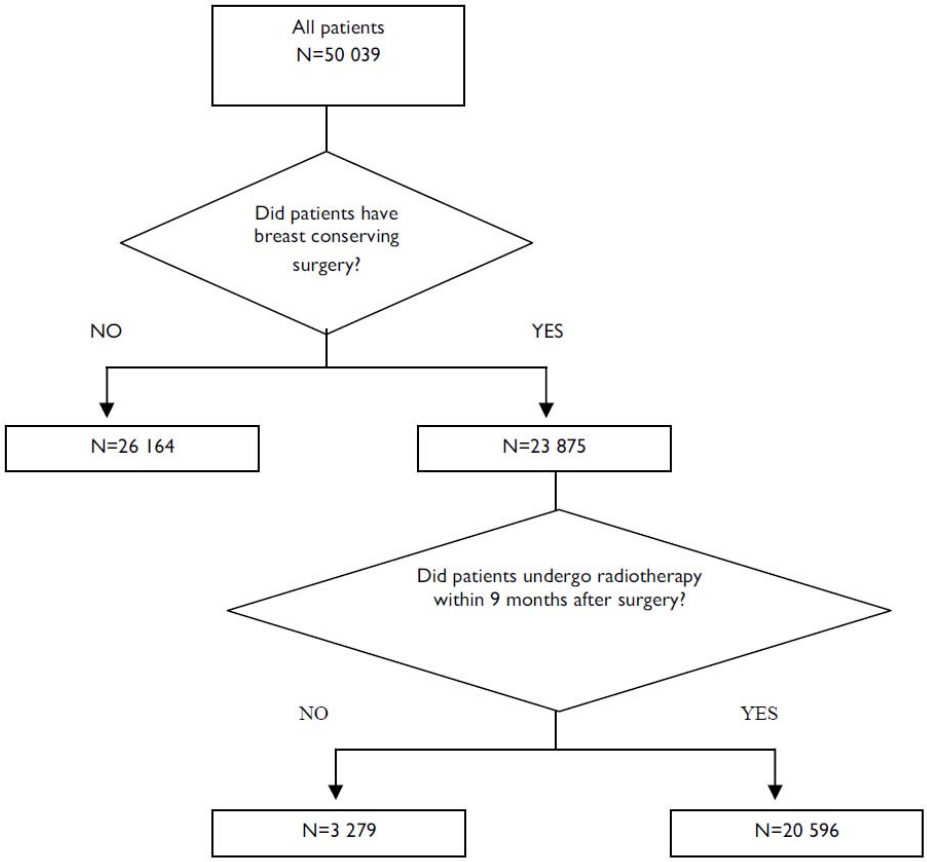
7.10.6.3 Denominator

All women diagnosed with invasive breast cancer in a given year who underwent breast conserving surgery, without further mastectomy

7.10.6.4 Elaboration

Figure 62 provides the algorithm for indicator BC25. From all invasive breast cancer women who underwent breast conserving surgery without further mastectomy (denominator), only those who received adjuvant radiotherapy (numerator) were selected.

Figure 62. Flowchart of indicator BC25



7.10.6.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *Breast conserving surgery:* nomenclature codes (IMA) (Table 81) and codes ICD-9-CM (Table 82)
- *Radiotherapy:* nomenclature codes (IMA) (Table 91) and codes ICD-9-CM (Table 92)

7.10.6.6 Results

From the 50 039 patients, 23 875 (47.7%) had breast conserving surgery without further mastectomy. From these patients 20 596 (86.3%) were irradiated postoperatively. Over the years, an increase in the number of patients with radiotherapy after breast saving surgery was reported. In 2001, this proportion was about 82.3%, while in 2006 it had increased to 89.8% (Table 66). The use of MCD data had no added-value to measure and to interpret this indicator (Table 67). The variability between centres was similar for 2001 and 2006 (Figure 63 and Figure 64).

Table 66. Proportion of patients who received RT after breast conserving surgery (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	2 716	3 302	82.3
2002	3 003	3 608	83.2
2003	3 525	4 131	85.3
2004	3 550	4 039	87.9
2005	3 780	4 318	87.5
2006	4 022	4 477	89.8
Total	**20 596**	**23 875**	**86.3**

Numerator: All women diagnosed with invasive breast cancer in a given year who received radiotherapy after breast conserving surgery
Denominator: All women diagnosed with invasive breast cancer in a given year who underwent breast conserving surgery

Table 67. Proportion of patients who received RT after breast conserving surgery (BCR-IMA-MCD data, 2002-2004)

	Numerator	Denominator	Proportion (%)
2002	2 573	3 091	83.2
2003	3 028	3 511	86.2
2004	2 891	3 311	87.3
Total	**8 492**	**9 913**	**85.7**

Numerator: All women diagnosed with invasive breast cancer in a given year who received radiotherapy after breast conserving surgery
Denominator: All women diagnosed with invasive breast cancer in a given year who underwent breast conserving surgery

Figure 63. Proportion of patients who received RT after breast conserving surgery: analysis per centre (2001)

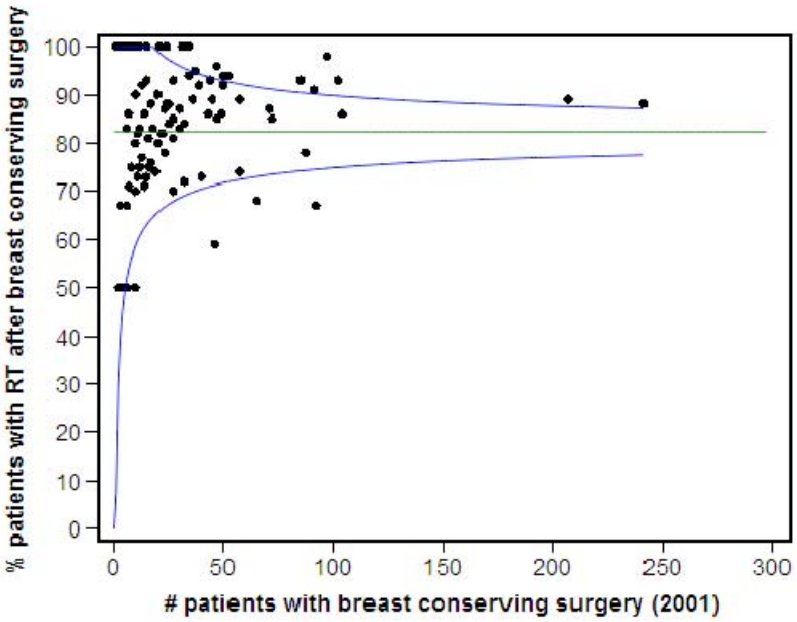
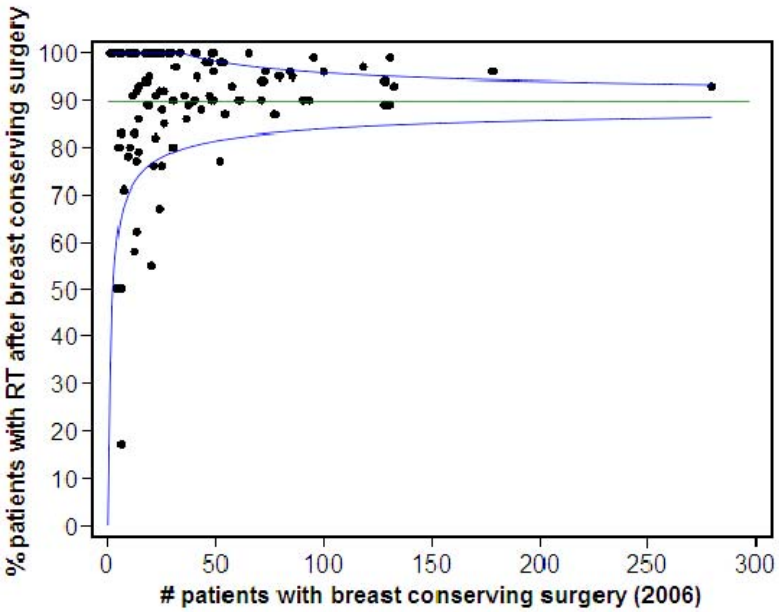


Figure 64. Proportion of patients who received RT after breast conserving surgery: analysis per centre (2006)



7.10.7 BC26: Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND

7.10.7.1 Rationale

The EBCBCG meta-analysis[72] provided strong evidence of a significant increase in overall survival with post-mastectomy radiotherapy, with a 5% reduction in 15-year mortality in women with 4+ involved nodes having received an axillary clearance. Moreover, Overgaard et al.[73] concluded that post-mastectomy radiotherapy significantly and substantially improved loco-regional control in all women with node-positive disease. Adjuvant chest wall radiotherapy after mastectomy should be offered to patients with early invasive breast cancer and a high risk of local recurrence including four or more positive axillary lymph nodes or involved resection margins (1A evidence).

7.10.7.2 Numerator

All women diagnosed with invasive breast cancer who underwent a mastectomy and having ≥ 4 positive nodes that received radiotherapy on axilla following ALND in a given year

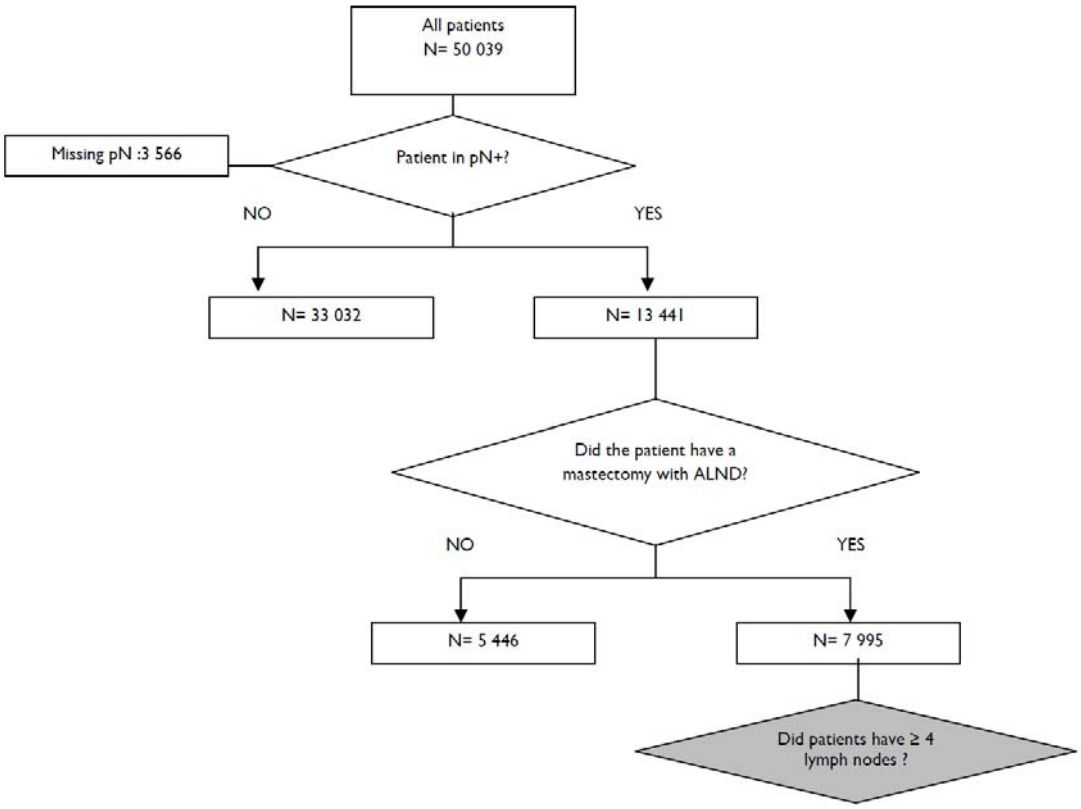
7.10.7.3 Denominator

All women diagnosed with invasive breast cancer who underwent a mastectomy and having ≥ 4 positive nodes in a given year

7.10.7.4 Elaboration

Figure 65 provides the algorithm for indicator BC26. From all women diagnosed with invasive breast cancer who underwent a mastectomy and having ≥ 4 positive nodes (denominator), only those who received radiotherapy on axilla following ALND (numerator) were selected.

Figure 65. Flowchart of indicator BC26



7.10.7.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *Mastectomy:* nomenclature codes (IMA) (Table 81) and codes ICD-9-CM (Table 82)
- *ALND:* nomenclature codes (IMA) (Table 83) and codes ICD-9-CM (Table 84)
- *Radiotherapy:* nomenclature codes (IMA) (Table 91) and codes ICD-9-CM (Table 92)

7.10.7.6 Results

From all women with breast cancer, 26.9% (n=13 441) were diagnosed with pN+. The proportion of breast cancer patients who underwent a mastectomy with ALND in this specific group could be measured and was 59.5% (n=7 995).

However, this quality of care indicator could not be measured for two reasons. First of all, no code was available in any of the administrative databases concerning the number of positive lymph nodes. Secondly, it seemed impossible to distinguish between chest wall radiotherapy and radiotherapy on axilla, as only a general radiotherapy nomenclature code existed in the IMA database.

7.11 QUALITY INDICATORS: TREATMENT OF METASTATIC CANCER

7.11.1 BC27: Proportion of women with HER2 positive metastatic breast cancer who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment

7.11.1.1 Rationale

Trastuzumab with/without non-anthracycline-based chemotherapy or endocrine therapy is the treatment of choice for first-line therapy of all HER2 positive metastatic breast cancer except in the presence of cardiac contra-indications for the use of Trastuzumab (1A evidence)[37, 74].

7.11.1.2 Numerator

All women diagnosed with HER2+ cStage/pStage IV breast cancer in a given year who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment

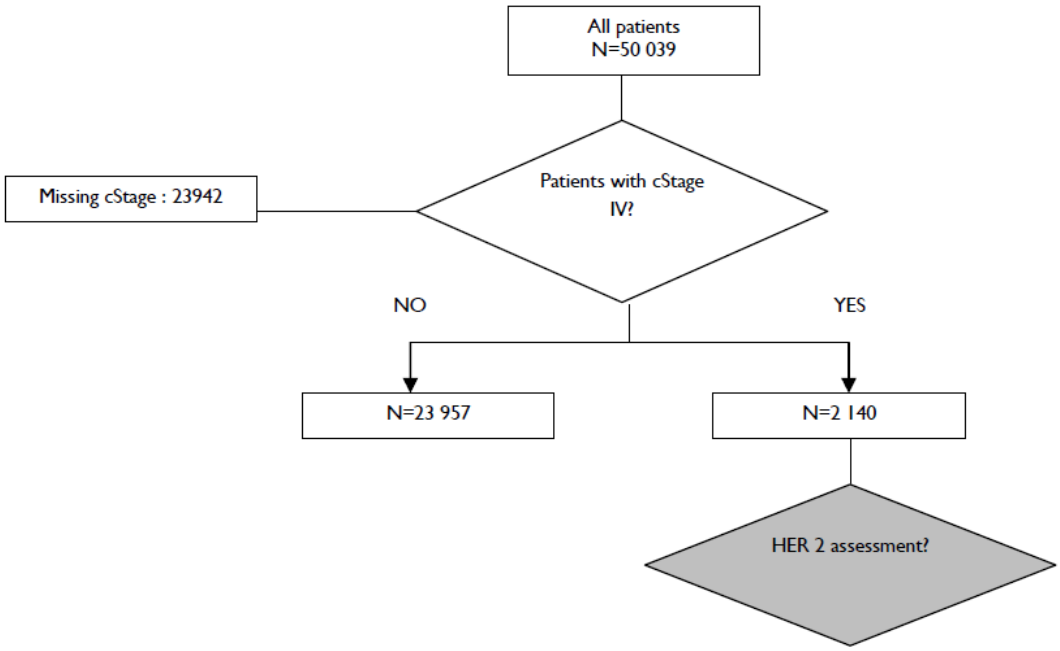
7.11.1.3 Denominator

All women diagnosed with HER2+ cStage/pStage IV breast cancer in a given year

7.11.1.4 Elaboration

Figure 66 provides the algorithm for indicator BC27. From all women diagnosed with HER2+ cStage/pStage IV breast cancer (denominator), only those who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment (numerator) were selected.

Figure 66. Flowchart of indicator BC27



7.11.1.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *HER2 assessment*: nomenclature codes (IMA) (Table 78)
- *Trastuzumab:* CNK codes (IMA) (Table 89)
- *Non-anthracycline based chemotherapy:* CNK codes (IMA) (Table 85 ; column 'NA')
- *Aromatase inhibitors:* CNK codes (IMA) (Table 88)

7.11.1.6 Results

The data used for the analysis of all indicators concern the period 2001-2006. First codes for HER2 assessment were introduced on August 1st 2007 and July 1st 2009. Moreover, even if the code for HER2 assessment would have been available before 2007, it would remain impossible to assess the result of the HER2 assessment, based on the nomenclature code. Therefore, in alignment with indicators BC5 and BC19, the current indicator was not measurable for the period considered. Since January 1st 2011, a prospective registration will be conducted including all hormonal receptors assessments, but also the result of these assessments (e.g. status of HER2 receptors).

The only step in the algorithm that could be determined was the number of patients in cStage IV, resulting in 2 140 patients (4.3%).

7.11.2 BC28: Proportion of metastatic breast cancer women who receive systemic therapy as 1st and/or 2nd line treatment

7.11.2.1 Rationale

Chemotherapy is indicated for women with hormone refractory or HR-negative metastatic breast cancer, rapidly progressive disease or symptomatic disease, or with life-threatening disease (e.g. diffuse lung or liver metastases, massive bone marrow metastases with pancytopenia)[36]. Multiple systematic reviews exist evaluating different chemotherapy regimens for women with metastatic breast cancer[75-78].

7.11.2.2 Numerator

All women diagnosed with cStage/pStage IV breast cancer in a given year who received systemic therapy as first-line treatment and/or 2nd line treatment

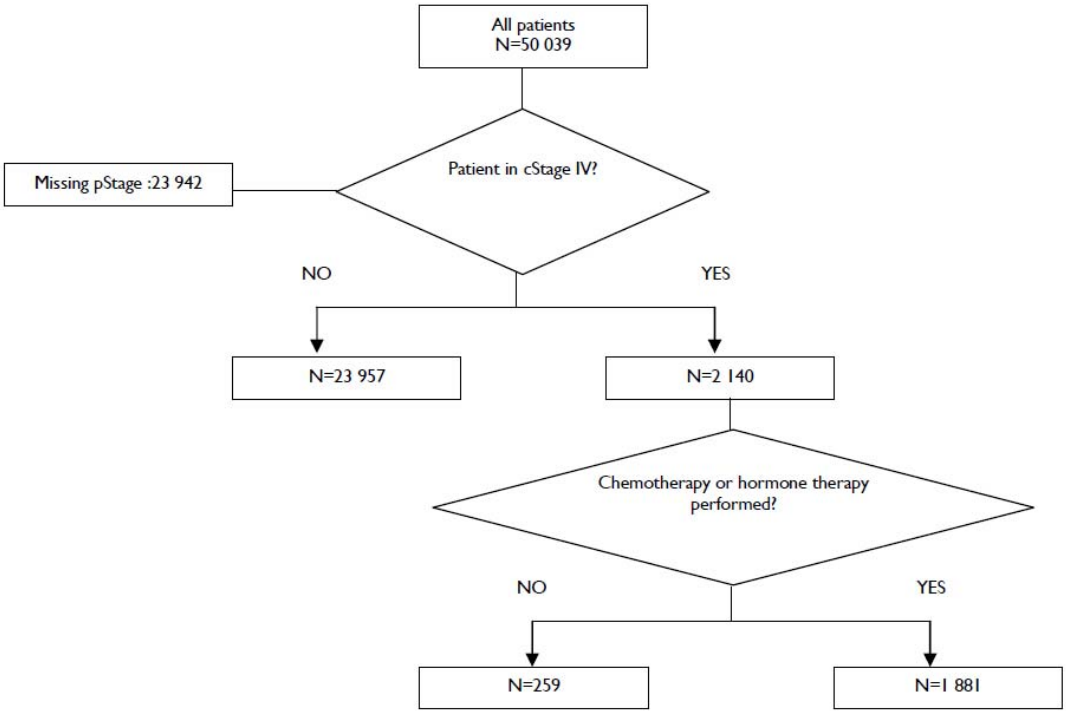
7.11.2.3 Denominator

All women diagnosed with cStage/pStage IV breast cancer in a given year

7.11.2.4 *Elaboration*

Figure 67 provides the algorithm for indicator BC28. From all women diagnosed with cStage/pStage IV breast cancer (denominator), only those who received systemic therapy as first-line treatment and/or 2nd line treatment (numerator) were selected.

Figure 67. Flowchart of indicator BC28



7.11.2.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *Chemotherapy or hormonal therapy*: CNK codes (IMA) (Table 85 to Table 88)
- *Trastuzumab:* CNK codes (IMA) (Table 89)

7.11.2.6 *Results*

The number of patients with metastatic breast cancer or, in other words, the number of patients witch cStage/pStage IV breast cancer was 2 140 (4.3%). From those patients, 1 881 (87.9%) received chemotherapy or endocrine treatment in first or second line. The proportion of cStage/pStage IV patients with systemic therapy slightly increased over time, reaching a maximum of 91.2% in 2005 (Table 68). The observed decrease in proportion in 2006 can be explained by the fact that treatments administered in 2007 to breast cancer patients were not identifiable according to the current available database (2001-2006).

The variability plots need to be interpreted with caution, as the number of patients per centre with cStage/pStage IV was very low. No major differences in variability per centre were noted when comparing 2001 with 2006 (Figure 68 and Figure 69).

Table 68. Proportion of metastatic breast cancer women who receive systemic therapy (IMA data, 2001-2006)

	Numerator	Denominator	Proportion (%)
2001	246	283	86.9
2002	260	296	87.8
2003	335	379	88.4
2004	400	453	88.3
2005	333	365	91.2
2006	307	364	84.3
Total	**1 881**	**2 140**	**87.9**

Numerator: All women diagnosed with cStage/pStage IV breast cancer in a given year who received systemic therapy as first-line treatment and/or 2nd line treatment

Denominator: All women diagnosed with cStage/pStage IV breast cancer in a given year

Figure 68. Proportion of metastatic breast cancer women who receive systemic therapy: analysis per centre (2001)

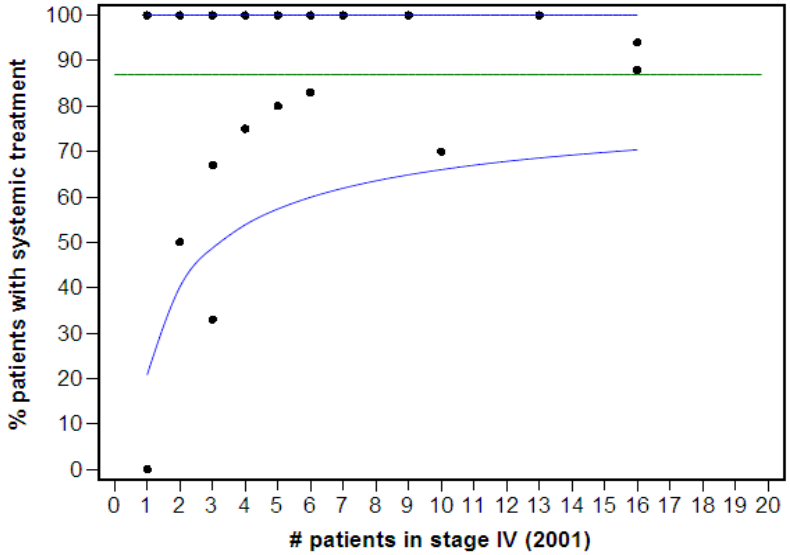
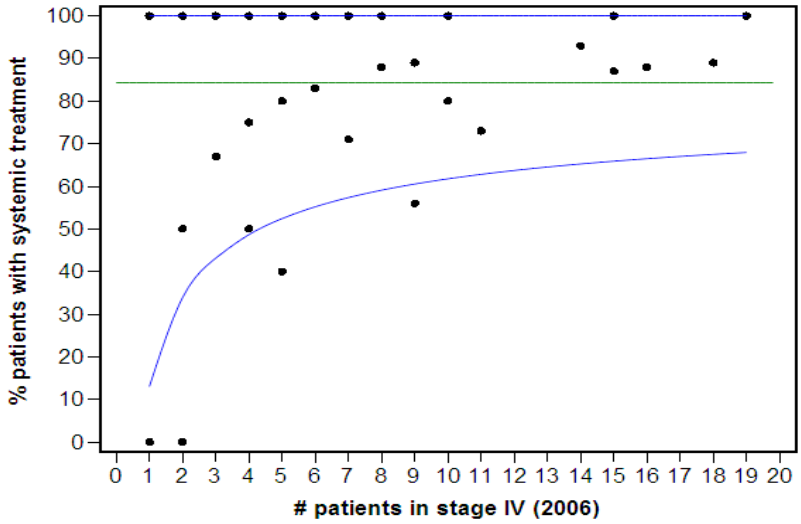


Figure 69. Proportion of metastatic breast cancer women who receive systemic therapy: analysis per centre (2006)



7.11.3 BC29: Proportion of women with metastatic breast cancer and lytic bone metastases who received biphosphonates

7.11.3.1 Rationale

Extensive evidence has shown the effectiveness of bisphosphonates in women with breast cancer and multiple lytic bone metastases in terms of pain reduction, reduction of skeletal events, improvement of the quality of life, and time-to-progression[36, 37, 79]. Bisphosphonates should be routinely used in combination with other systemic therapy in women with metastatic breast cancer with multiple or symptomatic lytic bone metastases (1A evidence). The use of biphosphonates is a palliative care measure, and has no impact on overall survival.

7.11.3.2 Numerator

All women diagnosed with cStage/pStage IV breast cancer and bone mestastases in a given year who received biphosphonates

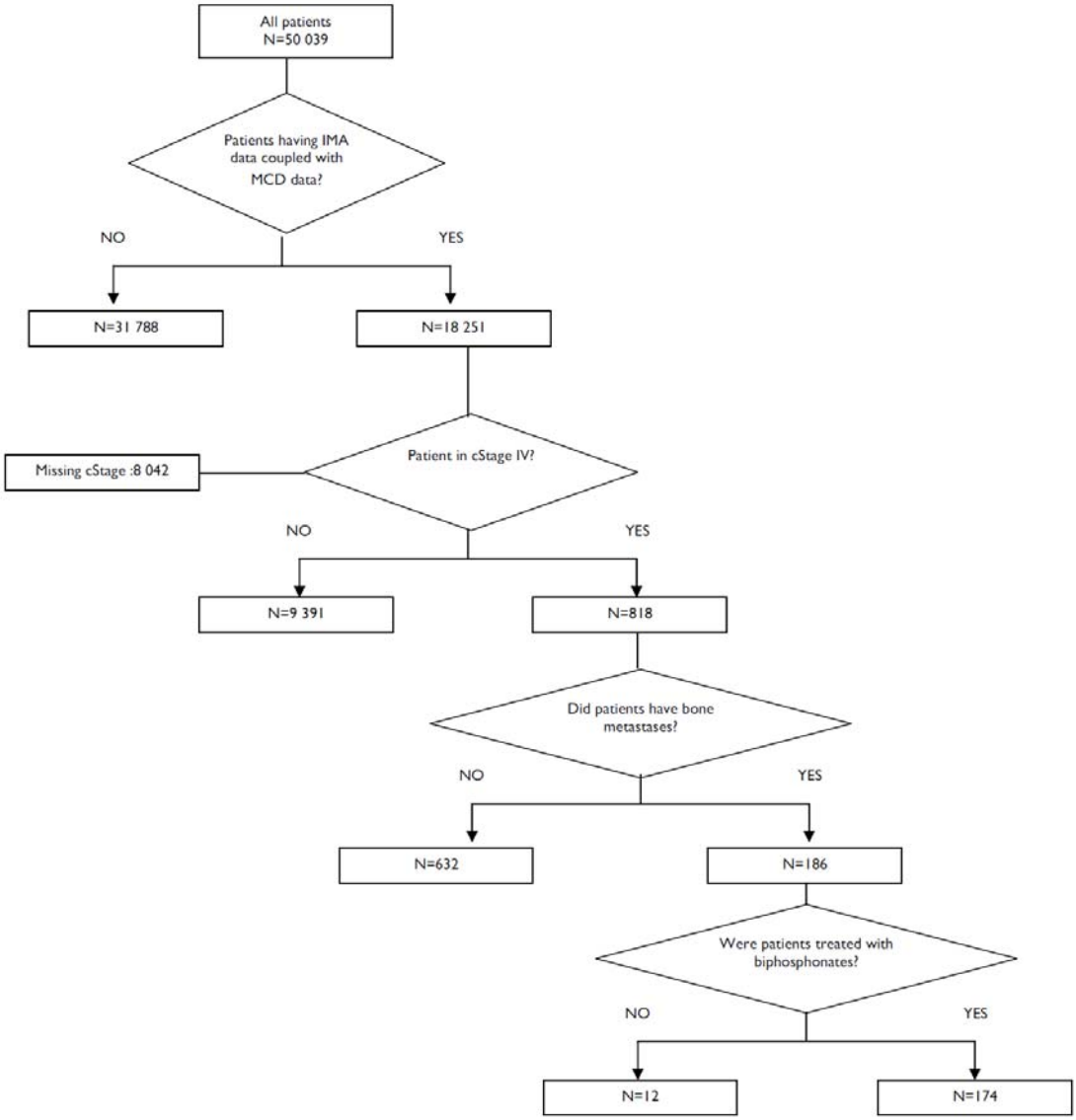
7.11.3.3 Denominator

All women diagnosed with cStage/pStage IV breast cancer and bone mestastases in a given year

7.11.3.4 Elaboration

Figure 70 provides the algorithm for indicator BC29. From all women diagnosed with cStage/pStage IV breast cancer and bone mestastases (denominator), only those who received biphosphonates (numerator) were selected.

Figure 70. Flowchart of indicator BC29



7.11.3.5 Data source(s)

Source database(s)

- BCR for source population
- IMA
- MCD

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 for breast cancer (BCR)
- *Diagnosis of bone metastases* : ICD-10 code C79.5 for secondary malignant neoplasm of bone and bone marrow; ICD-9-CM code 198 (Secondary malignant neoplasm of other specified sites - 198.5 Bone and bone marrow)
- *Biphosphonates*: CNK codes (IMA) (Table 93)

7.11.3.6 *Results*

The number of patients with lytic bone metastases could not be determined, based on the cancer registry database. Therefore, this indicator was calculated with those patients that were in the coupled IMA-MCD databases and who were registered between 2002 and 2004. For this indicator, using MCD database has clearly an added-value. The ICD-9 code for bone and bone marrow metastasis (198.5) could be used as proxy to determine the patients with lytic bone metastases.

A total number of 18 251 (36.4%) patients, were included in the analysis. From these patients, 818 (4.5%) were in cStage/pStage IV; 186 (22.7%) of them had bone or bone marrow metastasis (ICD9 198.5). Most of these patients (n=174 or 93.5%) were treated with biphosphonates, with a relatively stable proportion over time (Table 69). Only one centre did not treat all bone metastatic patients with biphosphonates.

Table 69. Proportion of women with metastatic breast cancer and lytic bone metastases who received bisphosphonates (BCR-MCD- IMA, 2002-2004).

	Numerator	Denominator	Proportion (%)
2002	44	50	88.0
2003	64	65	98.5
2004	66	71	93.0
Total	**174**	**186**	**93.5**

Numerator: All women diagnosed with cStage/pStage IV breast cancer and bone mestastases in a given year who received biphosphonates
Denominator: All women diagnosed with cStage/pStage IV breast cancer and bone mestastases in a given year

7.12 QUALITY INDICATORS: FOLLOW-UP

7.12.1 BC30: Proportion of women who benefit from an annual mammography after a history of breast cancer

7.12.1.1 *Rationale*

Mammography is the gold standard method of imaging to detect local recurrences or second primaries in the treated breast, but no evidence was identified to suggest the optimal frequency of this procedure[35-37, 79]. Yearly mammography with/without ultrasound should be used during the first 10 years to detect recurrence or second primaries in patients who have undergone previous treatment for breast cancer, including DCIS (1C evidence). In current practice, mammography is offered once yearly after treatment for breast cancer to detect ipsilateral or contralateral breast cancer[26].

7.12.1.2 *Numerator*

All women with a history of pStage I-III breast cancer who underwent an annual mammography

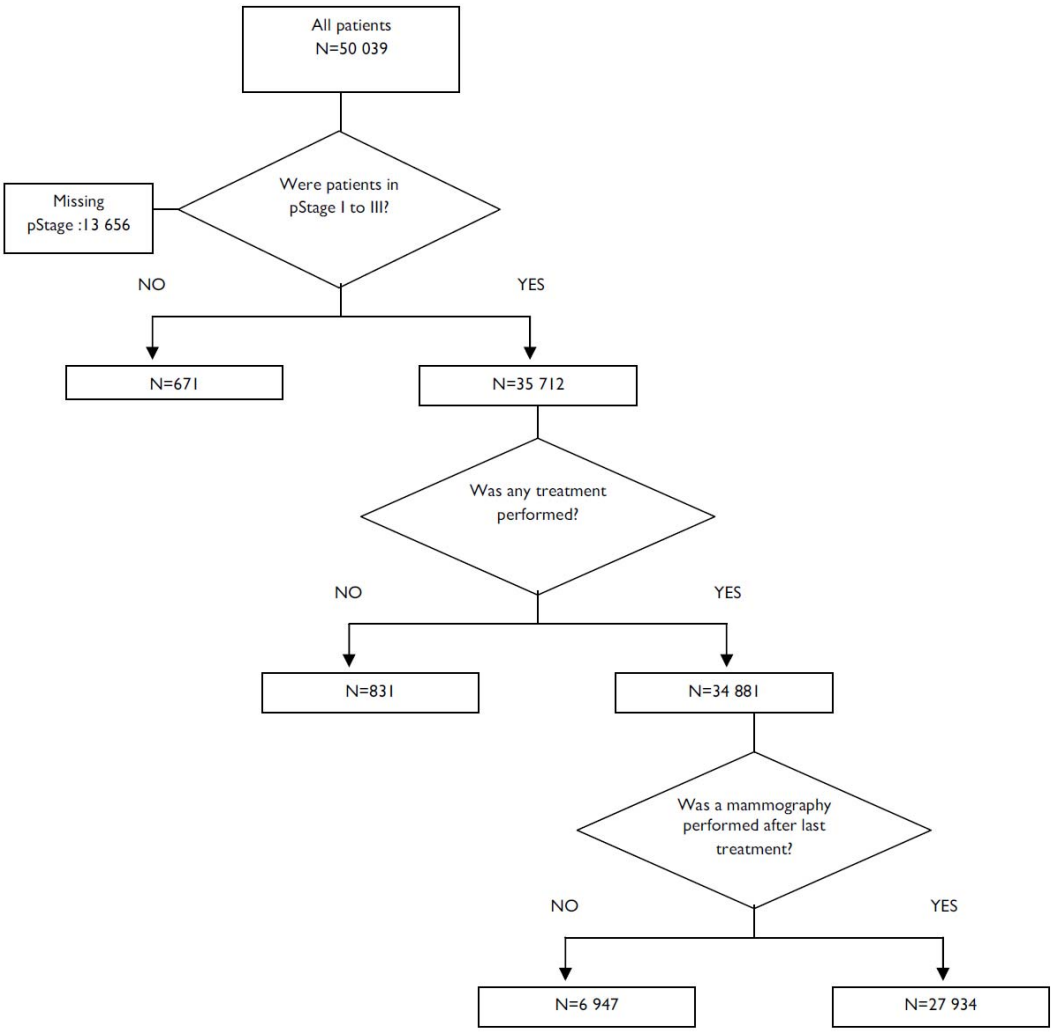
7.12.1.3 *Denominator*

All women with a history of pStage I-III breast cancer

7.12.1.4 *Elaboration*

Figure 71 provides the algorithm for indicator BC30. From all women with a history of pStage I-III breast cancer (denominator), only those who underwent an annual mammography (numerator) were selected.

Figure 71. Flowchart of indicator BC30



7.12.1.5 Data source(s)

Source database(s)

- BCR for source population
- IMA

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 (BCR)
- *Chemotherapy*: CNK codes (IMA) (Table 85): Date of end of last chemotherapy
- *Mammography*: nomenclature codes (IMA) (Table 94): Date of mammography (1 year after the last chemotherapy until a new chemotherapy is implemented) – one mammography/year during 5 years

7.12.1.6 Results

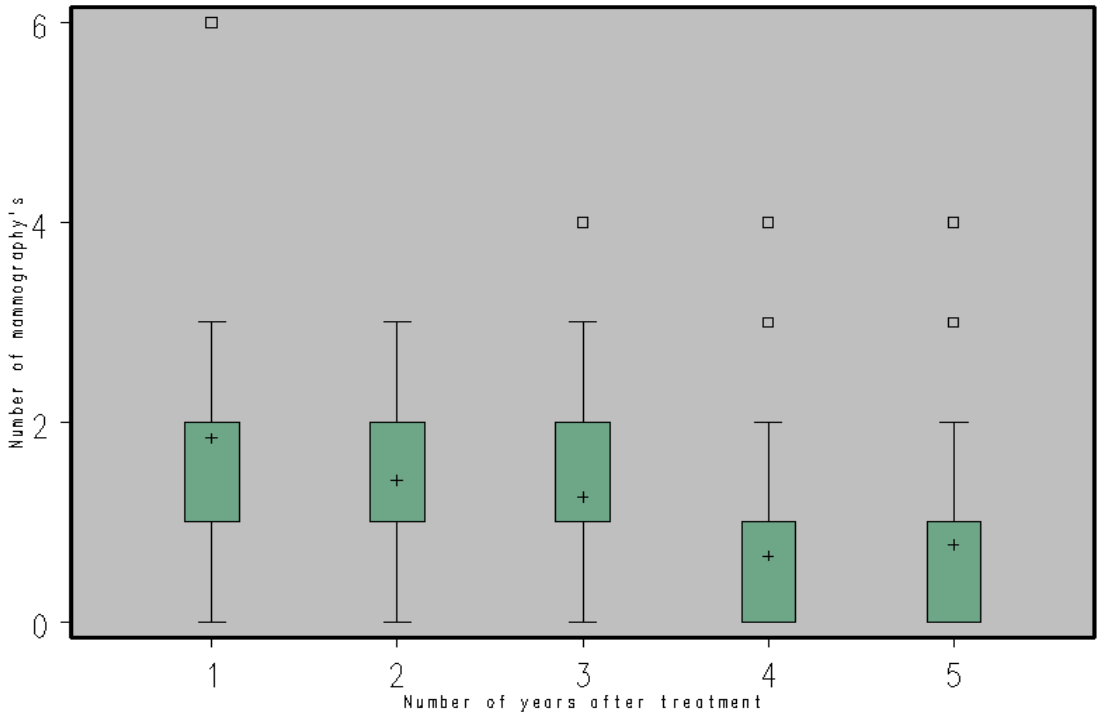
From the patients in pStage I-III (n=35 712 or 71.4%), 34 881 have a known treatment (97.7%). In 27 934 (80.1%) of these patients, at least one mammography after treatment was performed.

The analysis of the number of mammograms performed per patient according to the year of treatment and the follow-up period shows that patients who were more recently treated underwent more mammograms during follow-up. Furthermore, the annual number of mammograms decreased slightly with time after treatment, as expected (Table 70 and Figure 72).

Table 70. Mean and median number of mammograms per patient after last treatment: analysis per year of treatment and per year of follow-up (IMA, 2001-2006)

Variable	Mean	SD	Median	25th pct	75th pct
Year of treatment=2001 (n=2 047)					
mammo after 1 year of treatment	1.35	1.21	1	0	2
mammo after 2 years of treatment	1.25	1.00	1	0	2
mammo after 3 years of treatment	1.20	0.98	1	0	2
mammo after 4 years of treatment	1.19	0.98	1	0	2
mammo after 5 years of treatment	1.18	1.00	1	0	2
Year of treatment=2002 (n=3 565)					
mammo after 1 year of treatment	1.90	1.76	2	1	2
mammo after 2 years of treatment	1.85	1.72	2	1	2
mammo after 3 years of treatment	1.82	1.75	2	0	2
mammo after 4 years of treatment	1.73	1.65	2	0	2
Year of treatment=2003 (n=4 571)					
mammo after 1 year of treatment	2.20	2.19	2	0	4
mammo after 2 years of treatment	2.18	2.02	2	1	4
mammo after 3 years of treatment	2.09	2.04	2	0	4
Year of treatment=2004 (n=5 895)					
mammo after 1 year of treatment	2.17	2.08	2	1	4
mammo after 2 years of treatment	2.18	2.08	2	1	4
Year of treatment=2005 (n=6 695)					
mammo after 1 year of treatment	1.73	1.69	2	0	2

Figure 72. Number of mammograms after last treatment



7.13 QUALITY INDICATORS: HISTOPATHOLOGICAL EXAMINATION

7.13.1 BC31: Proportion of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade

7.13.1.1 Rationale

The information contained in pathology reports of breast cancer specimens provides the tumour size and stage information that are of critical importance to orientate physicians in their selection of local regional treatment, adjuvant therapy, evaluation of therapy, estimation of prognosis, and analysis of outcomes[12]. Incomplete cancer resection pathology reports may result in misclassification of women, rework and delays, and suboptimal management.

7.13.1.2 Numerator

Number of breast cancer resection pathology reports that include the tumour size (macro-and microscopically invasive and DCIS), the histologic type of the primary tumour, the pT category (primary tumour), the pN category (regional lymph nodes including numbers), the LVI and the histologic grade, in a given year

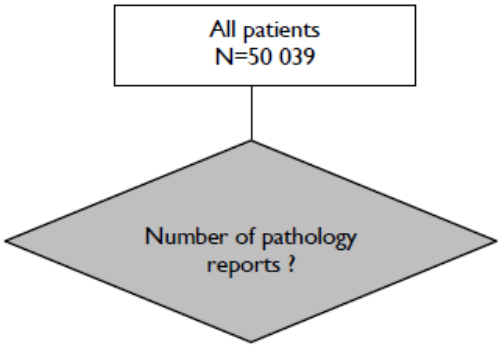
7.13.1.3 Denominator

Number of breast cancer resection pathology reports in a given year

7.13.1.4 Elaboration

Figure 73 provides the algorithm for indicator BC31. From all breast cancer resection pathology reports (denominator), only those that include the tumour size, the histologic type of the primary tumour, the pT category, the pN category, the LVI and the histologic grade were selected (numerator).

Figure 73. Flowchart of indicator BC31



7.13.1.5 Data source(s)

Source database(s)

- BCR for source population

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 codes C50 (BCR)

7.13.1.6 Results

This indicator could not be assessed based on the available data. Only manual revision of every pathology report could give an estimation of the completeness and availability of the required information in the pathology reports. Reabstraction and recoding of pathology reports was not feasible due to the large number of breast cancer patients in this study (N = 50 039).

7.13.2 BC32: Proportion of women with invasive breast cancer undergoing ALND and having 10 or more lymph nodes removed

7.13.2.1 Rationale

Axillary lymph node dissection (ALND) provides important prognostic information that guides staging and planning adjuvant chemotherapy. It plays also an important role in local control of cancer in both node positive and node negative tumours. Node positive status and the number of nodes containing metastases is associated with an increased risk of local recurrence and disease progression[80]. Although there is no minimum number of nodes that should be recovered in an ALND specimen, 16 nodes should be regarded as a target to ensure a high level of confidence that the nodes are negative[80]. Cheng[8] proposed that a minimum of ten lymph nodes should be removed to be confident in the nodes status.

7.13.2.2 Numerator

All women diagnosed with cStage I-III breast cancer in a given year who underwent ALND with 10 or more lymph nodes removed

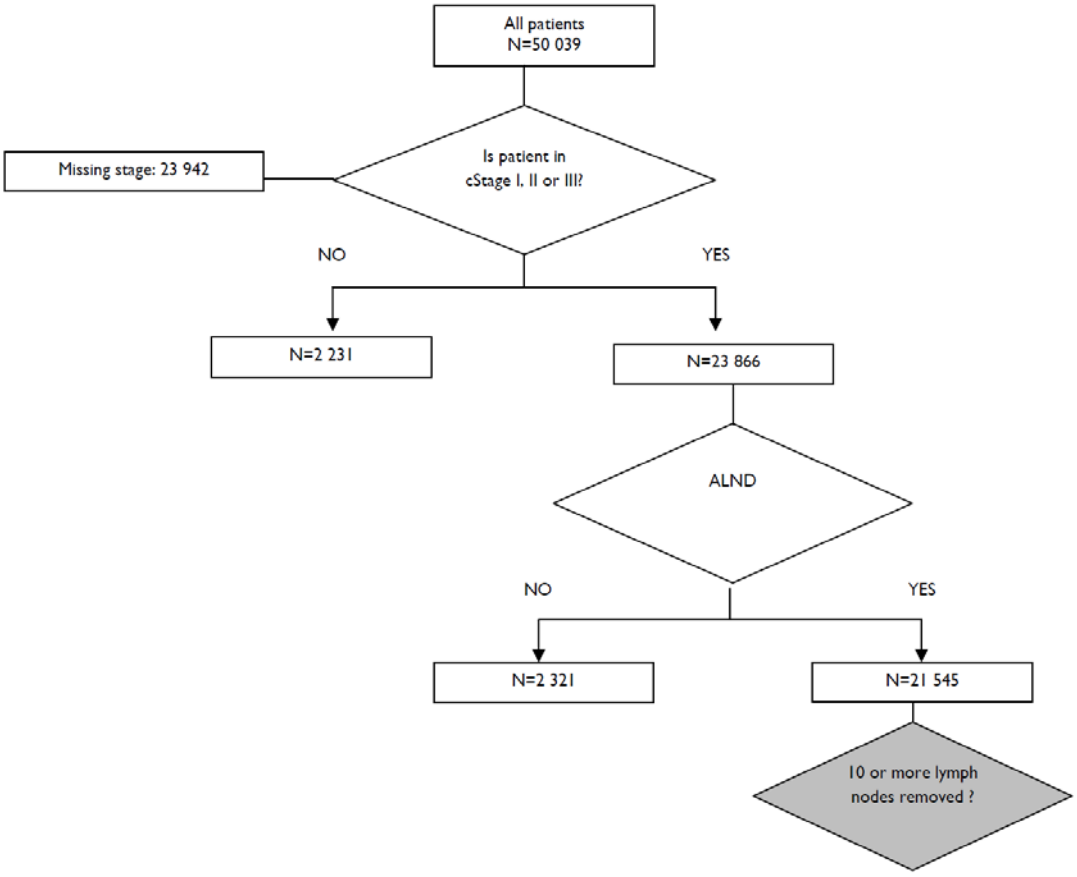
7.13.2.3 Denominator

All women diagnosed with cStage I-III breast cancer in a given year who underwent ALND

7.13.2.4 Elaboration

Figure 74 provides the algorithm for indicator BC32. From all women who were diagnosed with cStage I-III breast cancer (denominator), only those who underwent an ALND with 10 or more lymph nodes removed were selected (numerator).

Figure 74. Flowchart of indicator BC32



7.13.2.5 *Data source(s)*

Source database(s)

- BCR for source population
- IMA

Administrative codes

- *Diagnosis of breast cancer*: ICD-10 code C50 (BCR)
- *Stage*: BCR
- *ALND*: nomenclature codes (IMA) (Table 83) and codes ICD-9-CM) (Table 84)
- Number of lymph nodes removed: no code

7.13.2.6 *Results*

From all women with breast cancer, 47.7% (n=23 866) were diagnosed with a cStage I-III. The proportion of breast cancer patients who underwent an ALND in this specific group could be measured and equalled 90.3% (n=21 545). However, as the number of the lymph nodes that was removed was not reported, this indicator could not be calculated.

7.14 ADMINISTRATIVE CODES

7.14.1 General indicators

Table 71. Nomenclature codes for multidisciplinary team meeting (IMA)

Codes	Description	Omschrijving
350372 – 350383	Rapport écrit d'une concertation oncologique multidisciplinaire avec la participation d'au moins trois médecins de spécialités différentes sous la direction d'un médecin-coordinateur et reprenant la description du diagnostic et du plan de traitement	Schriftelijk verslag van een multidisciplinair oncologisch consult met deelname van minstens drie geneesheren van verschillende specialismen onder leiding van een geneesheer-coördinator, met beschrijving van de diagnose en van het behandelingsplan
350394 – 350405	Participation à la concertation oncologique multidisciplinaire	Deelname aan multidisciplinair oncologisch consult
350416 – 350420	Participation à la concertation oncologique multidisciplinaire par le médecin traitant qui n'est pas membre de l'équipe hospitalière	Deelname aan multidisciplinair oncologisch consult door de behandelende arts die geen deel uitmaakt van de ziekenhuisstaf

7.14.2 Diagnosis and staging

Table 72. Nomenclature codes for mammography (IMA)

Codes	Description	Omschrijving
450096 – 450100 461090 – 461101	Mammographie par sein y compris les clichés axillaires éventuels (quel que soit le nombre de clichés)	Mammografie per borst, inclusief de eventuele okselclichés (ongeacht het aantal clichés)
450192 - 450203	Mammographie des deux seins dans le cadre d'un examen de masse organisé par une autorité	Mammografie van beide borsten, in het kader van een door een overheid georganiseerd bevolkingsonderzoek
450214 - 450225	Deuxième lecture de mammographie de dépistage, des deux seins, dans le cadre d'un examen de masse organisé par une autorité	Tweede lezing van een screeningsmammografie van beide borsten, in het kader van een door een overheid georganiseerd bevolkingsonderzoek

Table 73. Nomenclature codes for mammography (MCD)

Codes	Description	Omschrijving
8737	Mammographie, autre	Overige mammografies

Table 74. Nomenclature codes for a consultation with a specialist (IMA)

Codes	Description	Omschrijving
102012	Consultation, à son cabinet, d'un médecin spécialiste autre que ceux cités aux n°s 102034 (médecine interne), 102174 (neurologie), 102196 (psychiatrie), 102211 (neuro-psychiatrie), 102071 (pédiatrie), 102093 (cardiologie), 102115 (gastro-entérologie), 102130 (pneumologie), 102152 (rhumatologie) et 102734 (dermato-vénérologie)	Raadpleging, in zijn spreekkamer, van een ander geneesheer-specialist dan die, vermeld onder de nrs 102034, 102174, 102196, 102211, 102071, 102093, 102115, 102130, 102152 en 102734

Table 75. Nomenclature codes for two-view mammography or breast sonography (IMA)

Codes	Description	Omschrijving
450096 – 450100 – 461090 – 461101	Mammographie par sein y compris les clichés axillaires éventuels (quel que soit le nombre de clichés)	Mammografie per borst, inclusief de eventuele okselclichés (ongeacht het aantal clichés)
460132 – 460143 469394 - 469405	Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : D'un sein ou des deux seins	Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen : Van één of beiden borsten
459793 - 459804	Echographie d'au moins deux régions anatomiques différentes : contenu du crâne (transfontanellaire), thorax, seins, foie-vésicule biliaire, pancréas-rate, reins-vessie, rétropéritoine, gros vaisseaux abdominaux, bassin masculin ou féminin	Echografie van minstens twee verschillende anatomische regio's : schedelinhoud (transfontanellair), thorax, borsten, lever-galblaas, pancreas-milt, nieren-blaas, retroperitoneum, grote abdominale vaten, mannelijk of vrouwelijk bekken

Table 76. Nomenclature codes for Axillary US with FNAC (IMA)

Codes	Description	Omschrijving
588416 - 588420	Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 588350 - 588361 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement	Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecificeerd in de verstrekkingen 588350 - 588361 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten per afname

Table 77. Nomenclature codes for percutaneous biopsy (IMA)

Codes	Description	Omschrijving
588254 - 588265	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : Biopsies des organes profonds suivants : foie, rein, bassinet, surrénale, prostate, sein, ganglion lymphatique, moelle osseuse, os, glande thyroïde, glande salivaire, plèvre, poumon, testicule, péritoine, rétropéritoine, médiastin, cerveau	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende prelevementen : Biopten van volgende diepe organen : lever, nier, nierbekken, bijnier, prostaat, borst, lymfeklier, beenmerg, bot, schildklier, speekselklier, pleura, long, testikel, peritoneum, retroperitoneum, mediastinum, hersenen

Table 78. Nomenclature codes for HER2 assessment (IMA)

Codes	Description	Omschrijving
588976 – 588980 (créé le 01/07/2009)	Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostiques au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des women oncologiques	Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumour-specifieke medicatie bij oncologische patiënten
588556 – 588560 (créé le 01/08/2007)	Dépistage d'une amplification du gène HER2 au moyen d'une technique de fluorescence avec hybridation in situ dans le cadre du choix thérapeutique pour le carcinome mammaire (Règle diagnostique 1, 13)	Opsporen van HER2 genamplificatie door een fluorescente in situ hybridatie techniek voor therapiekeuze bij mammacarcinoom in de diagnostische investigatiefase (Diagnoseregel 1, 13)

Table 79. Nomenclature codes for ER and PgR status assessment (IMA)

Codes	Description	Omschrijving
435831 – 435842 (créé le 01/03/1995)	Dosage des récepteurs d'oestrogènes et de progestérone dans les tumeurs mammaires, quel que soit le nombre de prélèvements (Maximum 1) (Règle de cumul 66) Classe 32	Doseren van oestrogeen- en progesteronreceptoren in borsttumours, ongeacht het aantal afnamen (Maximum 1) (Cumulregel 66) Klasse 32
588976 – 588980 (créé le 01/08/2007)	Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostiques au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des women oncologiques	Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumour-specifieke medicatie bij oncologische patiënten
588070 – 588081 (créé le 01/03/1995)	Examens immunohistologiques (maximum 4 par prélèvement) pour révéler des antigènes sur des coupes, après incubation d'anticorps, par anti-sérum	Immunohistologische onderzoeken (maximum 4 per afname) voor het aantonen van antigenen in de coupes, na incubatie met antisera, per gebruikt antiserum

Table 80. Nomenclature codes for cytology and histology (IMA)

Codes	Description	Omschrijving
355670 - 355681	Ponction de la glande mammaire pour examen cytologique ou injection	Punctie van de borstklier voor cytologisch onderzoek of inspuiting
588416 - 588420	Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 588350 - 588361 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement	Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecificeerd in de verstrekkingen 588350 - 588361 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten per afname
588011 - 588022	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires, pour les prélèvements ne	Honorarium voor het pathologisch-anatomische onderzoek door inclusie en coupe van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek van operatiestukken, voor die

	correspondant pas aux prestations 588232 - 588243, 588254 - 588265, 588276 - 588280 ou 588291 - 588302	prelevementen die niet overeenkomen met de prestaties 588232 - 588243, 588254 - 588265, 588276 - 588280 of 588291 - 588302
588114 - 588125	Examen anatomo-pathologique avec microscope électronique quelle(s) que soi(en)t la ou les technique(s) utilisée(s), quel que soit le nombre de prélèvements	Pathologisch-anatomisch onderzoek met een elektronenmicroscoop, ongeacht de aangewende techniek of technieken, ongeacht het aantal afnamen
588254 - 588265	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : Biopsies des organes profonds suivants : foie, rein, bassinet, surrénale, prostate, sein, ganglion lymphatique, moelle osseuse, os, glande thyroïde, glande salivaire, plèvre, poumon, testicule, péritoine, rétropéritoine, médiastin, cerveau	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende prelevementen : Biopten van volgende diepe organen : lever, nier, nierbekken, bijnier, prostaat, borst, lymfeklier, beenmerg, bot, schildklier, speekselklier, pleura, long, testikel, peritoneum, retroperitoneum, mediastinum, hersenen
588276 - 588280	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : exérèse de ganglion lympathique, évidement ganglionnaire axillaire unilatéral, évidement ganglionnaire inguinal unilatéral biopsie pulmonaire chirurgicale, thymectomie totale ou partielle, résection de tumeur subaponévrotique, pancréatectomie partielle, hépatectomie partielle, cholécystectomie, splénectomie, tumourectomie mésentérique, tumourectomie rétropéritonéale, résection du globe oculaire, résection d'une glande salivaire (à l'exception des glandes salivaires accessoires), glossectomie partielle ou totale, thyroïdectomie,parathyroïdectomie, pharyngectomie, biopsie par incision du sein, tumourectomie du sein, cystectomie partielle (à l'exception de la résection vésicale endoscopique), adénomectomie prostatique chirurgicale ou endoscopique, épididymectomie, orchidectomie, amputation partielle du pénis, tumourectomie profonde du cou, néphrectomie partielle, annexectomie uni-ou bilatérale, ovariectomie, salpingectomie totale, vulvectomie partielle, conisation ou résection du col de l'utérus, résection de la glande	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende operatiestukken : lymfeklierexerese, eenzijdige lymfeklier okselevidement, eenzijdige lymfeklier liesevidement, heelkundige longbiopsie, totale of partiële thymectomie, resectie van subaponeurotische tumouren, partiële pancreatectomie, partiële hepatectomie, cholecystectomie, splenectomie, mesenteriale tumourectomie, retroperitoneale tumourectomie, oogbol resectie, speekselklierresectie (met uitzondering van de accessoire speekselklieren), partiële of totale glossectomie, thyroidectomie, parathyroidectomie, pharyngectomie, incisionele borstbiopsie, borsttumourectomie, partiële cystectomie (met uitzondering van de endoscopische blaasresectie), heelkundige of endoscopische prostaatadenomectomie, epididymectomie, orchidectomie, partiële penis amputatie, diepe hals tumourectomie, partiële nefrectomie, uniof bilaterale adnexectomie, ovariectomie, totale salpingectomie, partiële vulvectomie, baarmoederhals conisatie of resectie, bijnier resectie, zenuwbiopsie, spierbiopsie, hersen-, ruggemergof hypofysetumour resectie,

	surrénale, biopsie nerveuse, biopsie musculaire, résection d'une tumeur du cerveau, de la moelle épinière ou de l'hypophyse, résection de tumeur osseuse, amygdalectomie (> 18 ans), adénoïdectomie (> 18 ans)	bottumour resectie, tonsillectomie (> 18 jaar), adenoidectomie (> 18 jaar)
588291 - 588302	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : mammectomie partielle avec évidement ganglionnaire, mammectomie totale avec ou sans évidement ganglionnaire, pneumectomie partielle ou totale, résection partielle ou totale de l'oesophage, évidement ganglionnaire inguinal bilatéral, évidement de deux ou plusieurs groupes de ganglions du cou, tumourectomie du plancher buccal avec ou sans mandibulectomie, tumourectomie du palais avec ou sans maxillectomie, maxillectomie totale, gastrectomie partielle ou totale, résection de l'intestin grêle, colectomie partielle ou totale, duodénopancréatectomie, hystérectomie radicale, totale ou subtotale, résection abdominopérinéale, laryngectomie partielle ou totale, cystectomie totale, amputation totale du pénis, néphrectomie totale, prostatectomie totale (avec vésicules séminales), résection cardiaque, bloc coeur poumons complet, hépatectomie totale, pelvectomie totale, vulvectomie totale, foetus de 14 à 24 semaines y compris	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende operatiestukken : partiële mammectomie met okselklier uitruiming, totale mammectomie met of zonder okselklier uitruiming, partiële of totale pneumectomie, partiële of totale slokdarmresectie, bilaterale lies klierevidement, lymfeklierevidement van 2 of meerdere groepen halsklieren, tumourectomie van de mondbodem met of zonder mandibulectomie, tumourectomie van het verhemelte met of zonder maxillectomie, totale maxillectomie, partiële of totale gastrectomie, dunne darm resectie, partiële of totale colectomie, duodenopancreatectomie, radicale, totale of subtotale hysterectomie, abdominoperineale resectie, partiële of totale laryngectomie, totale cystectomie, totale penisamputatie, totale nefrectomie, totale prostatectomie (met zaadblaasjes), hartresectie, hart long blok, totale hepatectomie, totale pelvectomie, totale vulvectomie, foetus van 14 tot en met 24 weken
588070 - 588081	Examens immunohistologiques (maximum 4 par prélèvement) pour révéler des antigènes sur des coupes, après incubation d'anticorps, par anti-sérum	Immunohistologische onderzoeken (maximum 4 per afname) voor het aantonen van antigenen in de coupes, na incubatie met antisera, per gebruikt antiserum
588976 - 588980	Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostiques au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des women oncologiques	Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumour-specifieke medicatie bij oncologische patiënten

7.14.3 Surgery

Table 81. Nomenclature codes for surgical treatments (IMA)

Codes	Description	Omschrijving	Breast conserving surgery/Mastectomy
226951 - 226962	Intervention selon Urban = mastectomie	Ingreep volgens Urban	Mastectomy
226973 - 226984	Intervention selon Halsted ou Pattey = mastectomie	Ingreep volgens Halsted of Pattey met ex tempore pathologisch-anatomisch onderzoek	Mastectomy
226995 - 227006	Intervention selon Halsted ou Pattey	Ingreep volgens Halsted of Pattey	Mastectomy
227010 - 227021	Exérèse d'une tumeur située au-dessus du fascia dans les parties molles mais avec résection totale de l'organe dans lequel se situe la tumeur	Verwijderen van een gezwel uit de weke weefsels boven de spierfascia maar met volledige resectie van het orgaan waarin het gezwel is gelegen	Breast conserving surgery
227032 - 227043	Exérèse d'une tumeur ou d'un kyste de la glande mammaire	Verwijderen van een gezwel of cyste uit de borstklier	Breast conserving surgery
227054 - 227065	Mammectomie partielle ou tumourectomie associée à un curage ganglionnaire axillaire	Gedeeltelijke mammectomie of tumourectomie, geassocieerd met een curage van de okselklieren	Breast conserving surgery
227732 - 227743	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante	Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge	Breast conserving surgery
227754 - 227765	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, non-palpable, avec résection d'une marge de sécurité macroscopiquement suffisante, après procédure de localisation	Volledige, borstsparende, resectie van een bewezen kwaadaardig, niet voelbaar borstletsel met macroscopisch voldoende veiligheidsmarge, na localisatieprocedure	Breast conserving surgery
227776 - 227780	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante et résection du ganglion sentinelle	Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier	Breast conserving surgery
227791 - 227802	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité	Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch	Breast conserving surgery

	macroscopiquement suffisante et résection du ganglion sentinelle avec examen anatomo-pathologique peropératoire du ganglion sentinelle	voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier, met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier	
227813 - 227824	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante et résection du ganglion sentinelle qui en cas d'envahissement tumoural démontré à l'examen anatomo-pathologique peropératoire est suivi d'un évidement ganglionnaire de l'aisselle	Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier, die wanneer tumouraal ingenomen bij peroperatoir anatomo-pathologisch onderzoek gevolgd wordt door een okseluitruiming	Breast conserving surgery
227835 - 227846	Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante, et un évidement ganglionnaire de l'aisselle	Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en een okseluitruiming	Breast conserving surgery
227636 - 227640	Résection complète du sein (mastectomie) pour tumeur maligne	Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumour	Mastectomy
227651 - 227662	Résection complète du sein (mastectomie) pour tumeur maligne et résection du ganglion sentinelle	Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumour en resectie van schildwachtlymfeklier	Mastectomy
227673 - 227684	Résection complète du sein (mastectomie) pour tumeur maligne et résection du ganglion sentinelle avec examen anatomo-pathologique peropératoire du ganglion sentinelle	Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumour en resectie van schildwachtlymfeklier met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier	Mastectomy
227695 - 227706	Résection complète du sein (mastectomie) pour tumeur maligne avec évidement axillaire	Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumour met okseluitruiming	Mastectomy
227710 - 227721	Résection complète du sein (mastectomie) pour tumeur maligne et résection du	Verwijderen van de volledige borstklier (mastectomie) voor	Mastectomy

	ganglion sentinelle qui en cas d'envahissement tumoural démontré à l'examen anatomo-pathologique peropératoire est suivi d'un évidement ganglionnaire de l'aisselle	kwaadaardige tumour en resectie van schildwachtlymfeklier die wanneer tumouraal ingenomen bij peroperatoir anatomo-pathologisch onderzoek gevolgd wordt door een okseluitruiming	

Table 82. Nomenclature codes for surgical treatments (MCD)

Codes	Description	Omschrijving	Breast conserving surgery/Mastectomy
8521	Excision locale de lésion du sein	Locale excisie van een letsel van de mamma	Breast conserving surgery
8522	Résection de quadrant de sein	Resectie van een kwadrant van de mamma	Breast conserving surgery
8523	Mastectomie subtotale	Subtotale-patiele mastectomie	Breast conserving surgery
8525	Excision de mamelon	Excisie van de tepel	Breast conserving surgery
8533	Mammectomie sous-cutanée unilatérale avec greffe simultanée	Unilaterale subcutane mammectomie met gelijktijdig borstimplant	Breast conserving surgery
8534	Mammectomie sous-cutanée unilatérale, autre	Overige subcutane mammectomie	Breast conserving surgery
8535	Mammectomie sous-cutanée bilatérale avec greffe simultanée	Bilaterale subcutane mammectomie met gelijktijdig borstimplant	Breast conserving surgery
8536	Mammectomie sous-cutanée bilatérale, autre	Overige bilaterale subcutane mammectomie	Breast conserving surgery
8541	Mastectomie unilatérale, simple	Eenvoudige unilaterale mastectomie	Mastectomy
8542	Mastectomie bilatérale, simple	Eenvoudige bilaterale mastectomie	Mastectomy
8543	Mastectomie étendue, unilatérale, simple	Eenvoudige uitgebreide unilaterale mastectomie	Mastectomy
8544	Mastectomie étendue, bilatérale, simple	Uitgebreide eenvoudige uitgebreide unilaterale mastectomie	Mastectomy
8545	Mastectomie radicale, unilatérale	Unilaterale radicale mastectomie	Mastectomy
8546	Mastectomie radicale, bilatérale	Bilaterale radicale mastectomie	Mastectomy
8547	Mastectomie radicale, étendue, unilatérale	Unilaterale uitgebreide radicale mastectomie	Mastectomy
8548	Mastectomie radicale, étendue, bilatérale	Bilaterale uitgebreide radicale mastectomie	Mastectomy

Table 83. Nomenclature codes for ALND (IMA)

Codes	Description	Omschrijving
227592 - 227603	Résection du ganglion sentinelle	Resectie van schildwachtlymfeklier
227614 - 227625	Résection du ganglion sentinelle avec examen per-opératoire anatomo-pathologique du ganglion sentinelle	Resectie van schildwachtlymfeklier met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier
226936 - 226940	Evidement ganglionnaire de l'aisselle dans le cadre du traitement d'une tumeur maligne du sein, démontrée	Okseluitruiming in het kader van de behandeling voor een bewezen kwaadaardig borstgezwel
588276 - 588280	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : exérèse de ganglion lympathique, évidement ganglionnaire axillaire unilatéral, évidement ganglionnaire inguinal unilatéral biopsie pulmonaire chirurgicale, thymectomie totale ou partielle, résection de tumeur subaponévrotique, pancréatectomie partielle, hépatectomie partielle, cholécystectomie, splénectomie, tumourectomie mésentérique, tumourectomie rétropéritonéale, résection du globe oculaire, résection d'une glande salivaire (à l'exception des glandes salivaires accessoires), glossectomie partielle ou totale, thyroïdectomie, parathyroïdectomie, pharyngectomie, biopsie par incision du sein, tumorectomie du sein, cystectomie partielle (à l'exception de la résection vésicale endoscopique), adénomectomie prostatique chirurgicale ou endoscopique, épididymectomie, orchidectomie, amputation partielle du pénis, tumourectomie profonde du cou, néphrectomie partielle, annexectomie uni- ou bilatérale, ovariectomie, salpingectomie totale, vulvectomie partielle, conisation ou résection du col de l'utérus, résection de la glande surrénale, biopsie nerveuse, biopsie musculaire, résection d'une tumeur du cerveau, de la moelle épinière ou de l'hypophyse, résection de tumeur osseuse, amygdalectomie (> 18 ans), adénoïdectomie (> 18 ans)	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende operatiestukken : lymfeklierexerese, eenzijdige lymfeklier okselevidement, eenzijdige lymfeklier liesevidement, heelkundige longbiopsie, totale of partiële thymectomie, resectie van subaponeurotische tumouren, partiële pancreatectomie, partiële hepatectomie, cholecystectomie, splenectomie, mesenteriale tumourectomie, retroperitoneale tumourectomie, oogbol resectie, speekselklierresectie (met uitzondering van de accessoire speekselklieren), partiële of totale glossectomie, thyroidectomie, parathyroidectomie, pharyngectomie, incisionele borstbiopsie, borsttumourectomie, partiële cystectomie (met uitzondering van de endoscopische blaasresectie), heelkundige of endoscopische prostaatadenomectomie, epididymectomie, orchidectomie, partiële penis amputatie, diepe hals tumourectomie, partiële nefrectomie, uniof bilaterale adnexectomie, ovariectomie, totale salpingectomie, partiële vulvectomie, baarmoederhals conisatie of -resectie, bijnier resectie, zenuwbiopsie, spierbiopsie, hersen-, ruggemergof hypofysetumour resectie, bottumour resectie, tonsillectomie (> 18 jaar), adenoidectomie (> 18 jaar)
588291 - 588302	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : mammectomie partielle avec évidement ganglionnaire, mammectomie totale avec ou sans évidement ganglionnaire,	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende operatiestukken : partiële mammectomie met okselklier uitruiming, totale mammectomie met of zonder okselklier uitruiming, partiële of

	pneumectomie partielle ou totale, résection partielle ou totale de l'oesophage, évidement ganglionnaire inguinal bilatéral, évidement de deux ou plusieurs groupes de ganglions du cou, tumourectomie du plancher buccal avec ou sans mandibulectomie, tumourectomie du palais avec ou sans maxillectomie, maxillectomie totale, gastrectomie partielle ou totale, résection de l'intestin grêle, colectomie partielle ou totale, duodénopancréatectomie, hystérectomie radicale, totale ou subtotale, résection abdominopérinéale, laryngectomie partielle ou totale, cystectomie totale, amputation totale du pénis, néphrectomie totale, prostatectomie totale (avec vésicules séminales), résection cardiaque, bloc coeur poumons complet, hépatectomie totale, pelvectomie totale, vulvectomie totale, foetus de 14 à 24 semaines y compris	totale pneumectomie, partiële of totale slokdarmresectie, bilaterale lies klierevidement, lymfeklierevidement van 2 of meerdere groepen halsklieren, tumourectomie van de mondbodem met of zonder mandibulectomie, tumourectomie van het verhemelte met of zonder maxillectomie, totale maxillectomie, partiële of totale gastrectomie, dunne darm resectie, partiële of totale colectomie, duodenopancreatectomie,radicale, totale of subtotale hysterectomie, abdominoperineale resectie, partiële of totale laryngectomie, totale cystectomie, totale penisamputatie, totale nefrectomie, totale prostatectomie (met zaadblaasjes), hartresectie, hart long blok, totale hepatectomie, totale pelvectomie, totale vulvectomie, foetus van 14 tot en met 24 weken

Table 84. Nomenclature codes for ALND (MCD)

Codes	Description	Omschrijving
4023	Excision de ganglion lymphatique axillaire	Excisie van axillaire lymfklier
4051	Excision radicale de ganglion lymphatique axillaire	Radikale excisie van axillaire lymfklieren

7.14.4 (Neo)adjuvant treatment

Table 85. CNK codes for chemotherapy used for breast cancer

ATC5	Name	Pack_name	CNK_NUM	Non-anthracyclines (NA) / Anthracyclines (A)
L01AA01	Cyclophosphamide	endoxan flac 5x 500mg poeder	39123	NA
L01AA01	Cyclophosphamide	endoxan vial 10 x 200 mg	39131	NA
L01AA01	Cyclophosphamide	endoxan vial 10 x 100 mg	39149	NA
L01AA01	Cyclophosphamide	endoxan tab. 50x 50mg	110882	NA
L01AA01	Cyclophosphamide	endoxan flac 1g poeder	246942	NA
L01AA01	Cyclophosphamide	ENDOXAN 500 mg vial inj. 1 x 500 mg	706234	NA
L01AA01	Cyclophosphamide	ENDOXAN drag. 1 x 50 mg	706242	NA
L01AA01	Cyclophosphamide	ENDOXAN fl. inj. 1 x 100 mg	706259	NA
L01AA01	Cyclophosphamide	ENDOXAN 200 mg fl. inj. 1 x 200 mg	706267	NA
L01AA01	Cyclophosphamide	ENDOXAN 1 g vial inj. 1 x 1 g	736769	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	197996	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	198002	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	198010	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	198028	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	246942	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	703777	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	703785	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	703793	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	703801	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	703819	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	736769	NA
L01AA01	Cyclophosphamide	CYCLOPHOSPHAMIDE	817411	NA
L01BA01	Methotrexate	emthexate vial 1 x 250 mg/10 ml	33308	NA
L01BA01	Methotrexate	emthexate flac inf. 5 g/50ml	33415	NA
L01BA01	Methotrexate	emthexate flac 50mg/2ml	34041	NA

L01BA01	Methotrexate	emthexate flac inf. 500mg/20ml	34108	NA
L01BA01	Methotrexate	emthexate flac inf. 1 g/40ml	34223	NA
L01BA01	Methotrexate	ledertrexate flac 5mg/2ml	53314	NA
L01BA01	Methotrexate	ledertrexate sodium fl amp 1x 50mg	53405	NA
L01BA01	Methotrexate	ledertrexate flac 12x 5mg poeder	53439	NA
L01BA01	Methotrexate	emthexate fl lyoph 10 x 5 mg	324103	NA
L01BA01	Methotrexate	emthexate vial 25 x 2 ml 50 mg	324111	NA
L01BA01	Methotrexate	emthexate vial 10 x 20 ml 500 mg	324129	NA
L01BA01	Methotrexate	emthexate vial 10 x 40 ml 1 g	324137	NA
L01BA01	Methotrexate	emthexate vial 10 x 50 ml 5 g	324145	NA
L01BA01	Methotrexate	ledertrexate sp forte fl 200mg/ 8ml	640177	NA
L01BA01	Methotrexate	ledertrexate sp forte fl 50mg/ 2ml	640185	NA
L01BA01	Methotrexate	ledertrexate sp forte fl1000mg/40ml	640193	NA
L01BA01	Methotrexate	ledertrexate sp forte fl 500mg/20ml	640201	NA
L01BA01	Methotrexate	EMTHEXATE fl. inj. lyoph. 1 x 5 mg	706143	NA
L01BA01	Methotrexate	EMTHEXATE fl. inj. lyoph. à 50 mg	706150	NA
L01BA01	Methotrexate	EMTHEXATE fl. inj. lyoph. à 500 mg	706168	NA
L01BA01	Methotrexate	EMTHEXATE fl. inj. lyoph. à 1 g	706176	NA
L01BA01	Methotrexate	LEDERTREXATE 2,5 mg compr. 1 x 2,5 mg	710566	NA
L01BA01	Methotrexate	LEDERTREXATE 5 mg/2 ml amp. inj. 1 x 5 mg/2 ml	710574	NA
L01BA01	Methotrexate	LEDERTREXATE 5 mg fl. inj. 1 x 5 mg	710582	NA
L01BA01	Methotrexate	LEDERTREXATE SODIUM fl. inj. 1 x 50 mg	710590	NA
L01BA01	Methotrexate	LEDERTREXATE 500 fl. pr. sol. inj. 1 x 500 mg	710608	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 50 mg/2 ml	729053	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 250 mg/10 ml	729061	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 500 mg/20 ml	729079	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 1 g/40 ml	729087	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 5 g/50 ml	729095	NA
L01BA01	Methotrexate	LEDERTREXATE FORTE 50 mg/2 ml fl. inj. 1 x 50 mg/2 ml	731828	NA
L01BA01	Methotrexate	LEDERTREXATE SP FORTE fl. inj. 1 x 200 mg/8 ml	731836	NA
L01BA01	Methotrexate	LEDERTREXATE FORTE 500 mg/20 ml fl. inj. 1 x 500 mg/20 ml	731844	NA
L01BA01	Methotrexate	LEDERTREXATE FORTE 1000 mg/40 ml fl. inj. 1 x 1 g/40 ml	731851	NA
L01BA01	Methotrexate	EMTHEXATE vial 1 x 5 mg/2 ml	742676	NA
L01BA01	Methotrexate	EMTHEXATE 2,5 mg compr. 1 x 2,5 mg	744102	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 50 Ready To Use fl. inj. 2 ml 25 mg/ml	744698	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 200 Ready To Use fl. inj. 8 ml 25 mg/ml	744755	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 2.000 Ready To Use fl. inj. 80 ml 25 mg/ml	744763	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 500 Ready To Use fl. inj. 20 ml 25 mg/ml	744771	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 1.000 Ready To Use fl. inj. 40 ml 25 mg/ml	744789	NA
L01BA01	Methotrexate	METHOBLASTINE FORTE 5.000 Ready To Use fl. inj. 200 ml 25 mg/ml	744797	NA
L01BA01	Methotrexate	LEDERTREXATE CONCENTRATE fl. inj. 1 x 100 mg/ml	746081	NA
L01BA01	Methotrexate	LEDERTREXATE CONCENTRATE 1000 mg/10 ml fl. inj. 1 x 1 g/10 ml	746099	NA
L01BA01	Methotrexate	LEDERTREXATE CONCENTRATE 5000 mg/50 ml fl. inj. 1 x 5 g/50 ml	746107	NA
L01BA01	Methotrexate	METHOTREXATUM vial inj. 1 x 50 mg/2 ml	746909	NA
L01BA01	Methotrexate	METHOTREXATUM vial inj. 1 x 500 mg/20 ml	746917	NA
L01BA01	Methotrexate	METHOTREXATUM vial inj. 1 x 1000 mg/10 ml	762369	NA
L01BA01	Methotrexate	METHOTREXATE MAYNE 5 g/50 ml ONCO-VIAL fl. inj. 1 x 5 g/50 ml	771584	NA
L01BA01	Methotrexate	METHOTREXATE MAYNE 1g/40 ml ONCO-VIAL fl. inj. 1 x 1 g/40 ml	773366	NA
L01BA01	Methotrexate	MERCK-METHOTREXATE 5 mg/2 ml 1 flacon	789156	NA

		injectable x 2,5 mg/ml Méthotrexate		
L01BA01	Methotrexate	MERCK-METHOTREXATE 500 mg/20 ml 1 flacon injectable x 25 mg/ml Méthotrexate	789743	NA
L01BA01	Methotrexate	MERCK-METHOTREXATE 5 g/50 ml 1 flacon injectable x 100 mg/ml Méthotrexate	789750	NA
L01BA01	Methotrexate	MERCK-METHOTREXATE 50 mg/2 ml 1 flacon injectable x 25 mg/ml Méthotrexate	789768	NA
L01BA01	Methotrexate	emthexate fl lyoph 1 x 50 mg	806703	NA
L01BA01	Methotrexate	emthexate fl lyoph 1 x 500 mg	806778	NA
L01BA01	Methotrexate	emthexate fl lyoph 1 x 1 g	806786	NA
L01BA01	Methotrexate	emthexate fl lyoph 1 x 5 mg	812867	NA
L01BA01	Methotrexate	ledertrexate sodium fl amp 1x500mg	885152	NA
L01BA01	Methotrexate	emthexate flac 5mg/2ml	1156199	NA
L01BA01	Methotrexate	emthexate fl inj lyoph 1x5mg	1156207	NA
L01BA01	Methotrexate	methoblastine frt rtu 2ml 25mg/ml	1238179	NA
L01BA01	Methotrexate	methoblastine frt rtu 8ml 25mg/ml	1238187	NA
L01BA01	Methotrexate	methoblastine frt rtu 20ml 25mg/ml	1238195	NA
L01BA01	Methotrexate	methoblastine frt rtu 40ml 25mg/ml	1238203	NA
L01BA01	Methotrexate	methoblastine frt rtu 80ml 25mg/ml	1238229	NA
L01BA01	Methotrexate	methoblastine frt rtu 200ml 25mg/ml	1238237	NA
L01BA01	Methotrexate	methotrexate vial inj 1x 50mg/ 2ml	1287762	NA
L01BA01	Methotrexate	methotrexate vial inj 1x500mg/20ml	1287770	NA
L01BA01	Methotrexate	ledertrexate flac concentrate 1 g/10ml	1319623	NA
L01BA01	Methotrexate	ledertrexate flac concentrate 5 g/50ml	1319631	NA
L01BA01	Methotrexate	methotrexate vial inj 1x1000mg/10ml	1447739	NA
L01BA01	Methotrexate	methotrexate 5g/50ml 1 vial 50 m	1591445	NA
L01BA01	Methotrexate	methotrexate 1g/40ml 1 vial	1751650	NA
L01BA01	Methotrexate	methotrexate mylan 5mg/ 2ml sol inj. flacon 1	2462521	NA
L01BA01	Methotrexate	methotrexate mylan 50mg/ 2ml sol inj. flacon 1	2462539	NA
L01BA01	Methotrexate	methotrexate mylan 5000mg/50ml sol inj. flacon 1	2462547	NA
L01BA01	Methotrexate	methotrexate mylan 500mg/20ml sol inj. flacon 1	2462554	NA
L01BA01	Methotrexate	emthexate flac 10x 5mg/2ml	2536159	NA
L01BC02	Fluorouracil	efudix zalf 20g 50mg/ g	38521	NA
L01BC02	Fluorouracil	fluoro-uracil amp 5 x 250 mg/10 ml	42184	NA
L01BC02	Fluorouracil	fluoro-uracil amp 10x250mg/10ml ud	42200	NA
L01BC02	Fluorouracil	fluorouracil vial inj 1x 500mg/20ml	497511	NA
L01BC02	Fluorouracil	fluorouracil vial inj 5x 250mg/10ml	497529	NA
L01BC02	Fluorouracil	fluroblastine flac 500mg/10ml	615229	NA
L01BC02	Fluorouracil	EFUDIX ungt. 1 x 50 mg/g	706044	NA
L01BC02	Fluorouracil	FLUORO-URACIL amp. inj. 1 x 250 mg/5 ml	707521	NA
L01BC02	Fluorouracil	FLUROBLASTINE 500 mg fl. I.V./perf. 1 x 500 mg/10 ml	731273	NA
L01BC02	Fluorouracil	FLUOROURACIL "DELAGRANGE" vial inj. 1 x 250 mg/10 ml	736835	NA
L01BC02	Fluorouracil	FLUOROURACIL "DELAGRANGE" vial inj. 1 x 500 mg/20 ml	736843	NA
L01BC02	Fluorouracil	FLUOROURACIL DAVID BULL vial inj. 1 x 100 ml 25 mg/ml	742080	NA
L01BC02	Fluorouracil	FLUOROURACIL DAVID BULL vial inj. 1 x 10 ml 25 mg/ml	742098	NA
L01BC02	Fluorouracil	FLUOROURACIL DAVID BULL vial inj. 1 x 20 ml 25 mg/ml	742106	NA
L01BC02	Fluorouracil	FLURACEDYL fl. inj. 1 x 20 ml 50 mg/ml	742775	NA
L01BC02	Fluorouracil	FLURACEDYL fl. inj. 1 x 5 ml 50 mg/ml	742783	NA
L01BC02	Fluorouracil	FLURACEDYL fl. inj. 1 x 10 ml 50 mg/ml	742791	NA
L01BC02	Fluorouracil	FLUROBLASTINE fl. I.V./perf. 1 x 250 mg/5 ml	746883	NA
L01BC02	Fluorouracil	FLUROBLASTINE 1000 mg fl. I.V./perf. 1 x 1 g/20 ml	746891	NA
L01BC02	Fluorouracil	FLURACEDYL 5000 mg/100 ml fl. inj. 1 x 100 ml 50 mg/ml	762476	NA
L01BC02	Fluorouracil	FLUOROURACIL MAYNE 2500 mg/50 ml ONCO-VIAL vial inj. 1 x 50 ml 50 mg/	772814	NA
L01BC02	Fluorouracil	fluorouracil vial 5x 10ml 25mg/ml	1149970	NA

L01BC02	Fluorouracil	fluorouracil vial 5x 20ml 25mg/ml	1149988	NA
L01BC02	Fluorouracil	fluorouracil vial 1x100ml 25mg/ml	1149996	NA
L01BC02	Fluorouracil	fluracedyl fl inj 250mg/ 5ml	1173764	NA
L01BC02	Fluorouracil	fluracedyl fl inj 500mg/10ml	1173772	NA
L01BC02	Fluorouracil	fluracedyl flac inf. 1 g/20ml	1173780	NA
L01BC02	Fluorouracil	fluroblastine fl iv per 1x250mg/5ml	1360411	NA
L01BC02	Fluorouracil	fluroblastine flac 1 g/20ml	1360429	NA
L01BC02	Fluorouracil	fluracedyl flac inf. 5 g/100ml	1458710	NA
L01BC02	Fluorouracil	fluorouracil faulding onco-vial 250	1745223	NA
L01BC05	Gemcitabine	GEMZAR fl. lyoph. I.V. 1 x 200 mg	747436	NA
L01BC05	Gemcitabine	GEMZAR fl. lyoph. 1 x 1 g	747444	NA
L01BC05	Gemcitabine	GEMCITABINE SANDOZ 200 mg	792507	NA
L01BC05	Gemcitabine	GEMCITABINE SANDOZ 1 g	792515	NA
L01BC05	Gemcitabine	gemzar flac inf. 1g poeder	1281054	NA
L01BC05	Gemcitabine	gemzar flac inf. 200mg poeder	1281062	NA
L01BC05	Gemcitabine	gemcitabine mylan 38mg/ml pulv 1000mg sol inj	2661056	NA
L01BC05	Gemcitabine	gemcitabine mylan 38mg/ml pulv 200mg sol inj	2661064	NA
L01BC06	Capecitabine	XELODA compr. 1 x 150 mg	768093	NA
L01BC06	Capecitabine	XELODA compr. 1 x 500 mg	768101	NA
L01BC06	Capecitabine	xeloda tab. 60x 150mg	1415314	NA
L01BC06	Capecitabine	xeloda tab. 120x 500mg	1415322	NA
L01CA04	Vinorelbine	NAVELBINE sol. i.v. 1 x 50 mg/5 ml	760470	NA
L01CA04	Vinorelbine	NAVELBINE sol. i.v. 1 x 10 mg/ml	760488	NA
L01CA04	Vinorelbine	VINORELBIN ACTAVIS 10 mg/ml	793885	NA
L01CA04	Vinorelbine	VINORELBIN ACTAVIS 10 mg/ml	793893	NA
L01CA04	Vinorelbine	VINORELBINE "EBEWE PHARMA" 10 mg/ml	793901	NA
L01CA04	Vinorelbine	VINORELBINE "EBEWE PHARMA" 10 mg/ml	793919	NA
L01CA04	Vinorelbine	navelbine flac inf. 10x 10mg/1ml	1466895	NA
L01CA04	Vinorelbine	navelbine flac inf. 10x 50mg/5ml	1466903	NA
L01CA04	Vinorelbine	navelbine caps. 20mg	2444768	NA
L01CA04	Vinorelbine	navelbine caps. 30mg	2444776	NA
L01CA04	Vinorelbine	vinorelbin actavis flac inf. 10x 10mg/1ml	2585271	NA
L01CA04	Vinorelbine	vinorelbin actavis flac inf. 10x 50mg/5ml	2585297	NA
L01CA04	Vinorelbine	vinorelbine ebewe flac inf. 5x 10mg/1ml	2648897	NA
L01CA04	Vinorelbine	vinorelbine ebewe flac inf. 5x 50mg/5ml	2648905	NA
L01CD01	Paclitaxel	TAXOL 6 mg/ml fl. I.V./perf. 1 x 30 mg/5 ml	743286	NA
L01CD01	Paclitaxel	TAXOL 6 mg/ml fl. I.V./perf. 1 x 100 mg/17 ml	748558	NA
L01CD01	Paclitaxel	TAXOL 6 mg/ml fl. I.V./perf. 1 x 300 mg/51 ml	776146	NA
L01CD01	Paclitaxel	PAXENE 30 mg fl.	778654	NA
L01CD01	Paclitaxel	PAXENE 100 mg fl.	778662	NA
L01CD01	Paclitaxel	PAXENE 300 mg fl.	778670	NA
L01CD01	Paclitaxel	PAXENE 150 mg fl.	778688	NA
L01CD01	Paclitaxel	PACLITAXIN 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	782987	NA
L01CD01	Paclitaxel	PACLITAXIN 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	783001	NA
L01CD01	Paclitaxel	PACLITAXIN 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	783902	NA
L01CD01	Paclitaxel	PACLITAXEL MAYNE PHARMA 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	784850	NA
L01CD01	Paclitaxel	PACLITAXEL MAYNE PHARMA 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	784868	NA
L01CD01	Paclitaxel	PACLITAXEL MAYNE PHARMA 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	784876	NA
L01CD01	Paclitaxel	PACLITAXEL MAYNE PHARMA 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	784884	NA
L01CD01	Paclitaxel	PACLITAXEL EG 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	785972	NA
L01CD01	Paclitaxel	PACLITAXEL EG 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	785980	NA
L01CD01	Paclitaxel	PACLITAXEL EG 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	785998	NA
L01CD01	Paclitaxel	PACLITAXEL EG 6 mg/ml 1 flacon injectable x 6	786186	NA

		mg/ml Paclitaxel		
L01CD01	Paclitaxel	PACLITAXEL MERCK 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	786772	NA
L01CD01	Paclitaxel	PACLITAXEL MERCK 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	786780	NA
L01CD01	Paclitaxel	PACLITAXEL MERCK 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	786798	NA
L01CD01	Paclitaxel	PACLITAXEL 'EBEWE PHARMA' 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	788620	NA
L01CD01	Paclitaxel	PACLITAXEL 'EBEWE PHARMA' 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	788638	NA
L01CD01	Paclitaxel	PACLITAXEL 'EBEWE PHARMA' 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	788646	NA
L01CD01	Paclitaxel	PACLITAXEL 'EBEWE PHARMA' 6 mg/ml 1 flacon injectable x 6 mg/ml Paclitaxel	789099	NA
L01CD01	Paclitaxel	PACLITAXIN 150 mg/25 ml	792176	NA
L01CD01	Paclitaxel	PACLITAXEL	795062	NA
L01CD01	Paclitaxel	PACLITAXEL	795070	NA
L01CD01	Paclitaxel	PACLITAXEL	795096	NA
L01CD01	Paclitaxel	taxol flac inf. 30mg/5ml	1115369	NA
L01CD01	Paclitaxel	taxol flac inf. 100mg/17ml	1352509	NA
L01CD01	Paclitaxel	taxol flac inf. 300mg/51ml	2103935	NA
L01CD01	Paclitaxel	paxene 30mg/ 5,0ml	2160430	NA
L01CD01	Paclitaxel	paxene 150mg/25,0ml	2160448	NA
L01CD01	Paclitaxel	paxene 100mg/16,7ml	2160455	NA
L01CD01	Paclitaxel	paxene 300mg/ 50ml	2160463	NA
L01CD01	Paclitaxel	paclitaxin flac inf. 30mg/5ml	2275808	NA
L01CD01	Paclitaxel	paclitaxin flac inf. 100mg/16,7ml	2275816	NA
L01CD01	Paclitaxel	paclitaxin flac inf. 300mg/50ml	2275824	NA
L01CD01	Paclitaxel	paclitaxel hospira flac inf. 30mg/5ml	2374247	NA
L01CD01	Paclitaxel	paclitaxel hospira flac inf. 100mg/16,7ml	2374254	NA
L01CD01	Paclitaxel	paclitaxel hospira flac inf. 150mg/25ml	2374262	NA
L01CD01	Paclitaxel	paclitaxel hospira flac inf. 300mg/50ml	2374270	NA
L01CD01	Paclitaxel	paclitaxel eg flac inf. 30mg/5ml	2404531	NA
L01CD01	Paclitaxel	paclitaxel eg flac inf. 100mg/16,7ml	2404549	NA
L01CD01	Paclitaxel	paclitaxel eg flac inf. 150mg/25ml	2404556	NA
L01CD01	Paclitaxel	paclitaxel eg flac inf. 300mg/50ml	2404564	NA
L01CD01	Paclitaxel	paclitaxel mylan flac inf. 30mg/5ml	2430304	NA
L01CD01	Paclitaxel	paclitaxel mylan flac inf. 300mg/50ml	2430312	NA
L01CD01	Paclitaxel	paclitaxel mylan flac inf. 100mg/16,7ml	2430320	NA
L01CD01	Paclitaxel	paclitaxel ebewe flac inf. 30mg/5ml	2491033	NA
L01CD01	Paclitaxel	paclitaxel ebewe flac inf. 100mg/16,7ml	2491041	NA
L01CD01	Paclitaxel	paclitaxel ebewe flac inf. 300mg/50ml	2491058	NA
L01CD01	Paclitaxel	paclitaxel ebewe flac inf. 150mg/25ml	2540995	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2602787	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2602795	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2602803	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2650711	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2650729	NA
L01CD01	Paclitaxel	PACLITAXEL FRESENIUS KABI - 6 mg/ml	2650737	NA
L01CD02	Docetaxel	TAXOTERE fl. I.V. 1 x 20 mg/0,5 ml	746032	NA
L01CD02	Docetaxel	TAXOTERE fl. I.V. 1 x 80 mg/2 ml + solv.	746370	NA
L01CD02	Docetaxel	taxotere flac inf. 20mg/0,5ml	1232354	NA
L01CD02	Docetaxel	taxotere flac inf. 80mg/2ml	1232362	NA
L01XA01	Cisplatin	platosin vial iv 1 x 10 mg/20 ml	17368	NA
L01XA01	Cisplatin	platosin vial iv 1 x 50 mg/100 ml	17434	NA
L01XA01	Cisplatin	platinol fl iv lyoph 1 x 10 mg	66035	NA
L01XA01	Cisplatin	platinol fl inj iv 1 x 10 mg/20 ml	66217	NA
L01XA01	Cisplatin	platosin vial 10 x 20 ml 10 mg	324152	NA
L01XA01	Cisplatin	platosin vial 5 x 100 ml 50 mg	324160	NA
L01XA01	Cisplatin	PLATINOL Lyophilized 10 mg fl. I.V. lyoph. 1 x 10 mg	715094	NA

L01XA01	Cisplatin	PLATINOL Ready to Use 10 mg/20 ml fl. I.V. 1 x 10 mg/20 ml	715102	NA
L01XA01	Cisplatin	PLATINOL READY TO USE fl. I.V. 1 x 50 mg/100 ml	715110	NA
L01XA01	Cisplatin	PLATISTINE 10 mg fl. I.V. lyoph. 1 x 10 mg	715128	NA
L01XA01	Cisplatin	PLATISTINE 50 mg fl. I.V. lyoph. 1 x 50 mg	715136	NA
L01XA01	Cisplatin	PLATINOL Lyophilized 50 mg fl. I.V. lyoph. 1 x 50 mg	725945	NA
L01XA01	Cisplatin	PLATOSIN vial I.V. 1 x 10 mg/20 ml	729327	NA
L01XA01	Cisplatin	PLATOSIN vial I.V. 1 x 50 mg/100 ml	729335	NA
L01XA01	Cisplatin	PLATOSIN fl. inj. 1 x 10 mg/20 ml	742833	NA
L01XA01	Cisplatin	PLATOSIN fl. inj. 1 x 50 mg/100 ml	742841	NA
L01XA01	Cisplatin	PLATOSIN fl. I.V. pulv. 1 x 10 mg	743476	NA
L01XA01	Cisplatin	CISPLATINE EFEKA fl. I.V. sol. 1 x 10 mg	743484	NA
L01XA01	Cisplatin	PLATOSIN fl. I.V. pulv. 1 x 50 mg	743492	NA
L01XA01	Cisplatin	CISPLATINE EFEKA fl. I.V. sol. 1 x 50 mg	743500	NA
L01XA01	Cisplatin	CISPLATINUM DELTA WEST vial inj. 1 x 10 mg/10 ml	746818	NA
L01XA01	Cisplatin	CISPLATINUM DELTA WEST vial inj. 1 x 50 mg/50 ml	746826	NA
L01XA01	Cisplatin	CISPLATINUM DELTA WEST vial inj. 1 x 100 mg/100 ml	746834	NA
L01XA01	Cisplatin	PLATOSIN fl. inj. 1 x 10 mg/10 ml	748368	NA
L01XA01	Cisplatin	PLATOSIN fl. inj. 1 x 50 mg/50 ml	748376	NA
L01XA01	Cisplatin	PLATOSIN fl. inj. 1 x 100 mg/100 ml	748509	NA
L01XA01	Cisplatin	PLATINOL Ready to Use 50 mg/50 ml fl. I.V. 1 x 50 mg/50 ml	766600	NA
L01XA01	Cisplatin	PLATINOL Ready to Use 100 mg/100 ml fl. I.V. 1 x 100 mg/100 ml	768192	NA
L01XA01	Cisplatin	CISPLATINE MAYNE 50 mg/50 ml Onco-Tain fl. inj. 1 x 50 mg/50 ml	770198	NA
L01XA01	Cisplatin	CISPLATINE MAYNE 100 mg/100 ml Onco-Tain fl. inj. 1 x 100 mg/100 ml	770206	NA
L01XA01	Cisplatin	platinol fl inj iv 1 x 50 mg/100 ml	865246	NA
L01XA01	Cisplatin	platistine fl lyoph iv 1 x 10 mg	891341	NA
L01XA01	Cisplatin	platistine fl lyoph iv 1 x 50 mg	891358	NA
L01XA01	Cisplatin	platinol fl iv lyoph 1 x 50 mg	895623	NA
L01XA01	Cisplatin	cisplatine fl iv pulv 10mg	1182815	NA
L01XA01	Cisplatin	cisplatine fl pulv iv 1x50mg	1182823	NA
L01XA01	Cisplatin	cisplatine fl iv sol 10mg	1182831	NA
L01XA01	Cisplatin	cisplatine fl iv sol 50mg	1182849	NA
L01XA01	Cisplatin	platosin fl lyoph 1x10mg/ 20ml	1200633	NA
L01XA01	Cisplatin	platosin fl lyoph 1x50mg/100ml	1200641	NA
L01XA01	Cisplatin	cisplatinum vial 1x 10mg/ 10ml	1287739	NA
L01XA01	Cisplatin	cisplatinum vial 1x 50mg/ 50ml	1287747	NA
L01XA01	Cisplatin	cisplatinum vial 1x 100mg/100ml	1287754	NA
L01XA01	Cisplatin	platosin flac inf. 10mg/10ml	1402635	NA
L01XA01	Cisplatin	platosin flac inf. 50mg/50ml	1402643	NA
L01XA01	Cisplatin	platosin flac inf. 100mg/100ml	1402650	NA
L01XA01	Cisplatin	cisplatine hospira flac inf. 100mg/100ml	1466424	NA
L01XA01	Cisplatin	cisplatine hospira flac inf. 50mg/50ml	1466432	NA
L01XA01	Cisplatin	platinol 1 fiole 50mg/ 50ml	1586270	NA
L01XA01	Cisplatin	platinol 1 fiole 100mg/100ml	1586288	NA
L01XA01	Cisplatin	platosin 50 mg pulv	1670603	NA
L01XA01	Cisplatin	platosin 10 mg pulv	1670611	NA
L01XA02	Carboplatin	paraplatin fiole 1 x 150 mg	56283	NA
L01XA02	Carboplatin	PARAPLATIN fl. I.V. lyoph. 1 x 150 mg	730242	NA
L01XA02	Carboplatin	CARBOPLATINE 150 DAVID BULL fl. I.V./perf. lyoph. 1 x 15 ml 10 mg/ml	742114	NA
L01XA02	Carboplatin	CARBOPLATINE 450 DAVID BULL fl. I.V./perf. lyoph. 1 x 45 ml 10 mg/ml	742122	NA
L01XA02	Carboplatin	PARAPLATIN sol. I.V. 1 x 5 ml 10 mg/ml	743005	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 50 mg/5 ml ONCO-TAIN sol. I.V. 1 x 5 ml 10 mg/ml	743195	NA

L01XA02	Carboplatin	PARAPLATIN sol. I.V. 1 x 45 ml 10 mg/ml	743203	NA
L01XA02	Carboplatin	PARAPLATIN sol. I.V. 1 x 15 ml 10 mg/ml	743211	NA
L01XA02	Carboplatin	CARBOSIN 150 mg vial I.V. 1 x 15 ml 10 mg/ml	744581	NA
L01XA02	Carboplatin	CARBOSIN 500 mg vial I.V. 1 x 50 ml 10 mg/ml	744599	NA
L01XA02	Carboplatin	CARBOSIN 50 mg vial I.V. 1 x 5 ml 10 mg/ml	744607	NA
L01XA02	Carboplatin	CARBOPLATINUM PHARMACIA 150 mg vial 1 x 15 ml 10 mg/ml	746040	NA
L01XA02	Carboplatin	CARBOPLATINUM PHARMACIA 450 mg vial 1 x 45 ml 10 mg/ml	746057	NA
L01XA02	Carboplatin	CARBOPLATINUM PHARMACIA 50 mg vial 1 x 5 ml 10 mg/ml	746065	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 150 mg/15 ml Onco-Vial fl. I.V./perf. 1 x 15 ml 10 mg/ml	761445	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 450 mg/45 ml Onco-Vail fl. I.V./perf. 1 x 45 ml 10 mg/ml	761452	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 150 mg/15 ml Onco-Tain fl.	779488	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 450 mg/45 ml Onco-Tain fl.	779496	NA
L01XA02	Carboplatin	CARBOSIN 450 mg 1 flacon injectable x 10 mg/ml Carboplatine	783639	NA
L01XA02	Carboplatin	CARBOSIN 600 mg 1 flacon injectable x 10 mg/ml Carboplatine	783647	NA
L01XA02	Carboplatin	CARBOPLATINE MAYNE 600 mg/60 ml Onco-Tain 1 flacon injectable x 10 mg/ml Carboplatine	787499	NA
L01XA02	Carboplatin	CARBOPLATINE MYLAN 50 mg/5 ml	792473	NA
L01XA02	Carboplatin	CARBOPLATINE MYLAN 150 mg/15 ml	792481	NA
L01XA02	Carboplatin	CARBOPLATINE MYLAN 450 mg/45 ml	792499	NA
L01XA02	Carboplatin	CARBOPLATINE MYLAN 600 mg/60 ml	792911	NA
L01XA02	Carboplatin	carboplatine fl iv 15ml 10mg/ml	1149871	NA
L01XA02	Carboplatin	carboplatine vial 1x45ml 450mg/45ml	1149889	NA
L01XA02	Carboplatin	paraplatin sol iv 1x 5ml 10mg/ml	1174184	NA
L01XA02	Carboplatin	paraplatin sol iv 1x15ml 10mg/ml	1174192	NA
L01XA02	Carboplatin	paraplatin sol iv 1x45ml 10mg/ml	1174200	NA
L01XA02	Carboplatin	carboplatin fl iv/perf 10mg/1ml 5ml	1182476	NA
L01XA02	Carboplatin	carbosin flac inf. 150mg/15ml	1226083	NA
L01XA02	Carboplatin	carbosin flac inf. 50mg/5ml	1226091	NA
L01XA02	Carboplatin	carbosin 500mg vial iv 50ml 10mg/ml	1226109	NA
L01XA02	Carboplatin	carboplatinum flac inf. 50mg	1287671	NA
L01XA02	Carboplatin	carboplatinum flac inf. 150mg	1287697	NA
L01XA02	Carboplatin	carboplatinum flac inf. 450mg	1287705	NA
L01XA02	Carboplatin	carboplatine iv perf 1x15ml 10mg/ml	1484823	NA
L01XA02	Carboplatin	carboplatine iv perf 1x45ml 10mg/ml	1484831	NA
L01XA02	Carboplatin	carboplatine hospira flac onco-tain 150mg/15ml	2210888	NA
L01XA02	Carboplatin	carboplatine hospira flac onco-tain 450mg/45ml	2210896	NA
L01XA02	Carboplatin	carbosin flac inf. 600mg/60ml	2322576	NA
L01XA02	Carboplatin	carbosin flac inf. 450mg/45ml	2322584	NA
L01XA02	Carboplatin	carboplatine hospira flac onco-tain 600mg/60ml	2459071	NA
L01XA02	Carboplatin	carboplatine fl inj 1 x 5ml 10mg/ml	2601888	NA
L01XA02	Carboplatin	carboplatine fl inj 1 x 15ml 10mg/ml	2601896	NA
L01XA02	Carboplatin	carboplatine fl inj 1 x 45ml 10mg/ml	2601904	NA
L01XA02	Carboplatin	carboplatine 600 mg/60 ml fl inj 1 x 60ml 10mg/ml	2612836	NA
L01DB01	Doxorubicin	adriblastina flac 5x 10mg poeder	16261	A
L01DB01	Doxorubicin	adriblastina flac 50mg/25ml	251454	A
L01DB01	Doxorubicin	adriblastina flac 10mg/5ml	288399	A
L01DB01	Doxorubicin	doxorubin fl lyoph. 10 x 10 mg	312256	A
L01DB01	Doxorubicin	doxorubin fl lyoph. 10 x 50 mg	312264	A
L01DB01	Doxorubicin	ADRIBLASTINA 10 mg fl. inj. 1 x 10 mg + solv.	700187	A
L01DB01	Doxorubicin	ADRIBLASTINA READY TO USE 50 mg fl. inj. 1 x 50 mg/25 ml	736785	A
L01DB01	Doxorubicin	ADRIBLASTINA READY TO USE 10 mg fl. inj. 1 x 10 mg/5 ml	737510	A

L01DB01	Doxorubicin	DOXORUBIN fl. I.V. lyoph. 1 x 10 mg	739243	A
L01DB01	Doxorubicin	DOXORUBIN fl. I.V. lyoph. 1 x 50 mg	739250	A
L01DB01	Doxorubicin	DOXORUBIN fl. I.V. sol. 1 x 10 mg/5 ml	743567	A
L01DB01	Doxorubicin	DOXORUBIN fl. I.V. sol. 1 x 50 mg/25 ml	743575	A
L01DB01	Doxorubicin	DOXORUBIN fl. I.V. sol. 1 x 200 mg/20 ml	743708	A
L01DB01	Doxorubicin	ADRIBLASTINA READY TO USE 200 mg fl. inj. 1 x 200 mg/100 ml	744409	A
L01DB01	Doxorubicin	CAELYX 2 mg/ml vial 1 x 10 ml 2 mg/ml	760546	A
L01DB01	Doxorubicin	DOXORUBICINE MAYNE 10 mg Onco-Tain fl. I.V. 1 x 10 mg	770172	A
L01DB01	Doxorubicin	DOXORUBICINE MAYNE 50 mg Onco-Tain fl. I.V. 1 x 50 mg	770180	A
L01DB01	Doxorubicin	CAELYX 2 mg/ml fl. inj. 1 x 25 ml 2 mg/ml	773614	A
L01DB01	Doxorubicin	MYOCET 1 flacon injectable x 50 mg Doxorubicine, chlorhydrate	782334	A
L01DB01	Doxorubicin	DOXORUBICINE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Doxorubicine, chlorhydrate	787713	A
L01DB01	Doxorubicin	DOXORUBICINE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Doxorubicine, chlorhydrate	787721	A
L01DB01	Doxorubicin	DOXORUBICINE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Doxorubicine, chlorhydrate	787739	A
L01DB01	Doxorubicin	DOXORUBICINE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Doxorubicine, chlorhydrate	787747	A
L01DB01	Doxorubicin	doxorubin flac inf. 10mg/5ml	1182856	A
L01DB01	Doxorubicin	doxorubin flac inf. 50mg/25ml	1182864	A
L01DB01	Doxorubicin	doxorubin flac inf. 200mg/100ml	1182872	A
L01DB01	Doxorubicin	doxorubin fl lyoph. 1 x 10mg	1182880	A
L01DB01	Doxorubicin	doxorubin fl lyoph. 1 x 50mg	1182898	A
L01DB01	Doxorubicin	adriblastina flac 200mg/100ml	1204379	A
L01DB01	Doxorubicin	caelyx flac inf. 20mg/10ml	1462522	A
L01DB01	Doxorubicin	doxorubicine 50 mg pulv lyoph	1466382	A
L01DB01	Doxorubicin	doxorubicine 10 mg pulv lyoph	1466622	A
L01DB01	Doxorubicin	caelyx flac inf. 50mg/25ml	1796192	A
L01DB01	Doxorubicin	myocet flac inf. 2x 50mg	2308153	A
L01DB01	Doxorubicin	doxorubicine ebewe flac 100mg/50ml	2454759	A
L01DB01	Doxorubicin	doxorubicine ebewe flac 10mg/5ml	2454767	A
L01DB01	Doxorubicin	doxorubicine ebewe flac 50mg/25ml	2454775	A
L01DB01	Doxorubicin	doxorubicine ebewe flac 200mg/100ml	2481190	A
L01DB03	Epirubicin	farmorubicine flac 10mg poeder	14365	A
L01DB03	Epirubicin	farmorubicine flac 50mg poeder	70243	A
L01DB03	Epirubicin	FARMORUBICINE 10 mg fl. pulv. inj. 1 x 10 mg	727735	A
L01DB03	Epirubicin	FARMORUBICINE 50 mg fl. pulv. inj. 1 x 50 mg	727743	A
L01DB03	Epirubicin	FARMORUBICINE 10 mg Ready To Use fl. I.V. 1 x 10 mg/5 ml	747535	A
L01DB03	Epirubicin	FARMORUBICINE 50 mg Ready To Use fl. I.V. 1 x 50 mg/25 ml	747543	A
L01DB03	Epirubicin	FARMORUBICINE 10 mg Cytovial vial 1 x 10 mg/5 ml	749747	A
L01DB03	Epirubicin	FARMORUBICINE 50 mg Cytovial vial 1 x 50 mg/25 ml	749754	A
L01DB03	Epirubicin	FARMORUBICINE 200 mg Cyto Vial 1 flacon injectable x 2 mg/ml Epirubicine, chlorhydrate	780882	A
L01DB03	Epirubicin	EPIRUBICIN MAYNE 2 mg/ml 1 flacon injectable x 2 mg/ml Epirubicine, chlorhydrate	788786	A
L01DB03	Epirubicin	EPIRUBICIN MAYNE 2 mg/ml 1 flacon injectable x 2 mg/ml Epirubicine, chlorhydrate	788794	A
L01DB03	Epirubicin	EPIRUBICIN MAYNE 2 mg/ml 1 flacon injectable x 2 mg/ml Epirubicine, chlorhydrate	788802	A
L01DB03	Epirubicin	EPIRUBICINE "EBEWE PHARMA" 2 mg/ml	790600	A
L01DB03	Epirubicin	EPIRUBICINE "EBEWE PHARMA" 2 mg/ml	790618	A
L01DB03	Epirubicin	EPIRUBICINE "EBEWE PHARMA" 2 mg/ml	790626	A

L01DB03	Epirubicin	EPIRUBICINE "EBEWE PHARMA" 2 mg/ml	790964	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN 10 mg/5 ml	791095	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN 50 mg/25 ml	791103	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN 200 mg/100 ml	791111	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN 20 mg/10 ml	791129	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 2 mg/ml	791632	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 2 mg/ml	791640	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 2 mg/ml	791657	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 10 mg	791665	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 50 mg	791673	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 2 mg/ml	792580	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS 2 mg/ml	792598	A
L01DB03	Epirubicin	EPIRUBICINE TEVA 2 mg/ml	794560	A
L01DB03	Epirubicin	EPIRUBICINE TEVA 2 mg/ml	794578	A
L01DB03	Epirubicin	EPIRUBICINE TEVA 2 mg/ml	794586	A
L01DB03	Epirubicin	EPIRUBICINE TEVA 2 mg/ml	794594	A
L01DB03	Epirubicin	EPIRUBICINE TEVA 2 mg/ml	794602	A
L01DB03	Epirubicin	farmorubicine sol inj 10mg	1388016	A
L01DB03	Epirubicin	farmorubicine sol inj 50mg	1388024	A
L01DB03	Epirubicin	farmorubicine flac cytovial 10mg/5ml	1405224	A
L01DB03	Epirubicin	farmorubicine flac cytovial 50mg/25ml	1405232	A
L01DB03	Epirubicin	farmorubicine flac cytovial 200mg/100ml	2222941	A
L01DB03	Epirubicin	epirubicin hospira flac onco tain 10mg/5ml	2481091	A
L01DB03	Epirubicin	epirubicin hospira flac onco tain 50mg/25ml	2481109	A
L01DB03	Epirubicin	epirubicin hospira 2 mg/ml fl inj 100 ml sol inj	2481125	A
L01DB03	Epirubicin	epirubicine ebewe pharma flac 10mg/5ml	2566891	A
L01DB03	Epirubicin	epirubicine ebewe pharma flac 50mg/25ml	2566909	A
L01DB03	Epirubicin	epirubicine ebewe pharma flac 200mg/100ml	2566917	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN - 10 mg/5 ml	2575470	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN - 20 mg/10 ml	2575488	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN - 50 mg/25 ml	2575496	A
L01DB03	Epirubicin	EPIRUBICINE MYLAN - 200 mg/100 ml	2575504	A
L01DB03	Epirubicin	epirubicin ebewe 2 mg/ml 50 ml	2583581	A
L01DB03	Epirubicin	Epirubicine	2585404	A
L01DB03	Epirubicin	EPIRUBICIN ACTAVIS - 50 mg	2585412	A
L01DB03	Epirubicin	Epirubicine	2585420	A
L01DB03	Epirubicin	epirubicin actavis 2mg/ml sol inj 20mg/ 10ml	2585438	A
L01DB03	Epirubicin	Epirubicine	2585446	A
L01DB03	Epirubicin	epirubicin actavis 2mg/ml sol inj 100mg/ 50ml	2585453	A
L01DB03	Epirubicin	Epirubicine	2585461	A
L01DB07	Mitoxantrone	novantrone fl inj 5 ml 10 mg	609479	A
L01DB07	Mitoxantrone	NOVANTRONE 20 fl. inj. 1 x 20 mg/10 ml	728378	A
L01DB07	Mitoxantrone	NOVANTRONE 25 fl. inj. 1 x 25 mg/12,5 ml	728386	A
L01DB07	Mitoxantrone	XANTROSIN 2 mg/ml fl.	779298	A
L01DB07	Mitoxantrone	XANTROSIN 2 mg/ml fl.	779306	A
L01DB07	Mitoxantrone	MITOXANTRONE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Mitoxantrone	787804	A
L01DB07	Mitoxantrone	MITOXANTRONE "EBEWE" 2 mg/ml 1 flacon injectable x 2 mg/ml Mitoxantrone	787812	A
L01DB07	Mitoxantrone	novantrone fl inj 1 x 25 mg/12,5 ml	802918	A
L01DB07	Mitoxantrone	novantrone fl inj 1 x 20 mg/10 ml	802926	A
L01DB07	Mitoxantrone	xantrosin flac inf. 20mg/10ml	2198539	A
L01DB07	Mitoxantrone	xantrosin flac inf. 25mg/12,5ml	2198547	A
L01DB07	Mitoxantrone	mitoxantrone ebewe flac inf. 20mg/10ml	2454734	A
L01DB07	Mitoxantrone	mitoxantrone ebewe flac inf. 10mg/5ml	2454742	A

Table 86. CNK codes for hormonal therapy (endocrine therapy) used for breast cancer (anti-oestrogènes)

ATC5	Name	Pack_name	CNK_NUM
L02BA01	TAMOXIFEN	nolvadex comp 100x10mg	61432
L02BA01	TAMOXIFEN	nolvadex comp 30x10mg	61564
L02BA01	TAMOXIFEN	nolvadex forte comp 30x40mg	65573
L02BA01	TAMOXIFEN	TAMOXIFEN	290585
L02BA01	TAMOXIFEN	TAMOXIFEN	290593
L02BA01	TAMOXIFEN	TAMOXIFEN	290601
L02BA01	TAMOXIFEN	TAMOXIFEN	383257
L02BA01	TAMOXIFEN	TAMOXIFEN	383281
L02BA01	TAMOXIFEN	TAMOXIFEN	383299
L02BA01	TAMOXIFEN	TAMOXIFEN	383315
L02BA01	TAMOXIFEN	TAMOXIFEN	383323
L02BA01	TAMOXIFEN	TAMOXIFEN	383331
L02BA01	TAMOXIFEN	TAMOXIFEN	485565
L02BA01	TAMOXIFEN	TAMOXIFEN	485573
L02BA01	TAMOXIFEN	TAMOXIFEN	485599
L02BA01	TAMOXIFEN	TAMOXIFEN	674184
L02BA01	TAMOXIFEN	TAMOXIFEN	674192
L02BA01	TAMOXIFEN	TAMOXIFEN	679076
L02BA01	TAMOXIFEN	TAMOXIFEN	679084
L02BA01	TAMOXIFEN	TAMOXIFEN	679092
L02BA01	TAMOXIFEN	NOLVADEX 10 compr. 1 x 10 mg	713032
L02BA01	TAMOXIFEN	NOLVADEX - D 20 compr. 1 x 20 mg	713040
L02BA01	TAMOXIFEN	NOLVADEX FORTE compr. 1 x 40 mg	728840
L02BA01	TAMOXIFEN	TAMOXIFENE compr. 1 x 10 mg	732552
L02BA01	TAMOXIFEN	TAMOPLEX compr. 1 x 10 mg	733410
L02BA01	TAMOXIFEN	TAMIZAM 10 compr. 1 x 10 mg	733998
L02BA01	TAMOXIFEN	TAMOXIFEN	735522
L02BA01	TAMOXIFEN	TAMOXIFEN	735530
L02BA01	TAMOXIFEN	TAMOXIFEN	739565
L02BA01	TAMOXIFEN	TAMOXIFEN	739581
L02BA01	TAMOXIFEN	TAMOXIFEN	739607
L02BA01	TAMOXIFEN	TAMOXIFEN	745075
L02BA01	TAMOXIFEN	TAMOXIFEN	745083
L02BA01	TAMOXIFEN	TAMOXIFEN	748400
L02BA01	TAMOXIFEN	TAMOXIFEN	748418
L02BA01	TAMOXIFEN	TAMOXIFEN	748483
L02BA01	TAMOXIFEN	TAMOXIFEN	760447
L02BA01	TAMOXIFEN	TAMOXIFEN	760454
L02BA01	TAMOXIFEN	TAMOXIFEN	764142
L02BA01	TAMOXIFEN	TAMOXIFEN	764159
L02BA01	TAMOXIFEN	TAMOXIFEN	766113
L02BA01	TAMOXIFEN	TAMOXIFEN	774851
L02BA01	TAMOXIFEN	TAMOXIFEN	777573
L02BA01	TAMOXIFEN	TAMOXIFEN	777912
L02BA01	TAMOXIFEN	TAMOXIFEN	790634
L02BA01	TAMOXIFEN	TAMOXIFEN	792754
L02BA01	TAMOXIFEN	TAMOXIFEN	824680
L02BA01	TAMOXIFEN	TAMOXIFEN	1197771
L02BA01	TAMOXIFEN	TAMOXIFEN	1197789
L02BA01	TAMOXIFEN	TAMOXIFEN	1197797
L02BA01	TAMOXIFEN	TAMOXIFEN	1277573
L02BA01	TAMOXIFEN	TAMOXIFEN	1281310
L02BA01	TAMOXIFEN	TAMOXIFEN	1281328
L02BA01	TAMOXIFEN	TAMOXIFEN	1281336
L02BA01	TAMOXIFEN	TAMOXIFEN	1390236

L02BA01	TAMOXIFEN	TAMOXIFEN	1402577
L02BA01	TAMOXIFEN	TAMOXIFEN	1402585
L02BA01	TAMOXIFEN	TAMOXIFEN	1402593
L02BA01	TAMOXIFEN	TAMOXIFEN	1402601
L02BA01	TAMOXIFEN	TAMOXIFEN	1402882
L02BA01	TAMOXIFEN	TAMOXIFEN	1463843
L02BA01	TAMOXIFEN	TAMOXIFEN	1463850
L02BA01	TAMOXIFEN	TAMOXIFEN	1463868
L02BA01	TAMOXIFEN	TAMOXIFEN	1467042
L02BA01	TAMOXIFEN	TAMOXIFEN	1537240
L02BA01	TAMOXIFEN	TAMOXIFEN	1560010
L02BA01	TAMOXIFEN	TAMOXIFEN	1656172
L02BA01	TAMOXIFEN	TAMOXIFEN	2116929
L02BA01	TAMOXIFEN	TAMOXIFEN	2162451
L02BA01	TAMOXIFEN	TAMOXIFEN	2162469
L02BA01	TAMOXIFEN	TAMOXIFEN	2566925
L02BA01	TAMOXIFEN	TAMOXIFEN	2612174
L02BA02	TOREMIFENE	FARESTON compr. 1 x 60 mg	749572
L02BA02	TOREMIFENE	fareston tab. 100x 60mg	1356658
L02BA03	FULVESTRANT	FASLODEX 250 mg/5 ml 1 seringue préremplie x 50 mg/ml Fulvestrant	788232
L02BA03	FULVESTRANT	faslodex spuitamp. i.m. 250mg/5ml	2160653

Table 87. CNK codes for hormonal therapy (endocrine therapy) used for breast cancer (LHRHa)

ATC5	Name	Pack_name	CNK_NUM
L02AE02	LEUPRORELIN	lucrin depot 1 fl im 3,75 mg + solv	282905
L02AE01	BUSERELIN	suprefact neusspray 100d 0,1mg/dosis	432971
L02AE03	GOSERELIN	zoladex spuitamp. s.c. 3,6mg	603159
L02AE04	TRIPTORELIN	decapeptyl spuitamp. sr 3,75mg/2ml	676882
L02AE01	BUSERELIN	SUPREFACT NASAL fl. 1 x 100 dos. 0,1 mg/dos.	727990
L02AE01	BUSERELIN	SUPREFACT PRO INJECT. fl. inj. 1 x 5,5 ml 1 mg/ml	728006
L02AE03	GOSERELIN	ZOLADEX s. inj. s.c. 1 x 3,6 mg	730739
L02AE04	TRIPTORELIN	DECAPEPTYL SUSTAINED RELEASE 3,75 mg s. I.M. 1 x 3,75 mg + solv.	733881
L02AE02	LEUPRORELIN	LUCRIN DEPOT fl. I.M. 1 x 3,75 mg + solv.	737650
L02AE02	LEUPRORELIN	PRAMETIL fl. I.M. 1 x 3,75 mg + solv.	739912
L02AE03	GOSERELIN	ZOLADEX LONG ACTING s. S.C. 1 x 10,8 mg	748129
L02AE04	TRIPTORELIN	DECAPEPTYL SUSTAINED RELEASE 11,25 mg fl. lyoph. i.m. 1 x 11,25 mg + solv.	749887
L02AE02	LEUPRORELIN	LUCRIN TRI-DEPOT 11,25 mg fl. pulv. 1 x 11,25 mg + solv.	760868
L02AE01	BUSERELIN	SUPREFACT DEPOT 3 MOIS-IMPLANT ser. 1 x 9,9 mg	768747
L02AE03	GOSERELIN	ZOLADEX (Aktuapharma) s. inj. s.c. 1 x 3,6 mg	776450
L02AE02	LEUPRORELIN	LUCRIN DEPOT 3,75 mg (Aktuapharma) fl.	778936
L02AE02	LEUPRORELIN	LUCRIN DEPOT 3,75 mg 1 seringue préremplie x 3,75 mg/ml Leuproréline, acétate de	781229
L02AE02	LEUPRORELIN	LUCRIN TRI-DEPOT 11,25 mg 1 seringue préremplie x 11,25 mg/ml Leuproréline, acétate de	781237
L02AE02	LEUPRORELIN	DEPO-ELIGARD 7,5 mg 1 seringue préremplie (+seringue préremplie) x 7,5 mg Leuproréline, acétate de	784074
L02AE02	LEUPRORELIN	DEPO-ELIGARD 22,5 mg 1 seringue préremplie (+ seringue préremplie) x 22,5 mg Leuproréline, acétate de	784082
L02AE04	TRIPTORELIN	DECAPEPTYL 0,1 mg 1 flacon injectable (+ ampoule) x 0,1 mg/ml Triptoréline, lyophilisé	788125
L02AE02	LEUPRORELIN	DEPO-ELIGARD 45 mg	790311
L02AE04	TRIPTORELIN	SALVACYL 11,25 mg	793729
L02AE01	BUSERELIN	suprefact neusspray 400d 0,1mg/dosis	895946
L02AE01	BUSERELIN	suprefact pro inj fl 2x 5,5mg/5,5ml	895953
L02AE02	LEUPRORELIN	prametil fl im 1 x 3,75mg + solv	1004340
L02AE01	BUSERELIN	suprefact depot 3 mois-3 maanden	1079193
L02AE03	GOSERELIN	zoladex spuitamp. la 10,8mg	1278480
L02AE04	TRIPTORELIN	decapeptyl flac s.c. 7x 0,1mg	1375120
L02AE02	LEUPRORELIN	lucrin tri depot fl 11,25 mg	1413863

L02AE02	LEUPRORELIN	gyno lucrin depot fl im 1x3,75mg	1423912
L02AE04	TRIPTORELIN	decapeptyl spuitamp. sr 11,25mg/2ml	1428143
L02AE03	GOSERELIN	zoladex spuitamp. s.c. 3,6mgaktuapharma	2125300
L02AE02	LEUPRORELIN	lucrin depot fl im 3,75 mg + solv	2195832
L02AE02	LEUPRORELIN	lucrin depot spuitamp. 3,75mg	2216125
L02AE02	LEUPRORELIN	lucrin tri-depot spuitamp. 11,25mg	2216133
L02AE02	LEUPRORELIN	depo-eligard spuitamp. s.c. 22,5mg	2224657
L02AE02	LEUPRORELIN	depo-eligard spuitamp. s.c. 7,5mg	2224665
L02AE02	LEUPRORELIN	depo-eligard spuitamp. s.c. 45mg	2544880
L02AE04	TRIPTORELIN	salvacyl flac i.m. 11,25mg	2581882

Table 88. CNK codes for hormonal therapy (endocrine therapy) used for breast cancer (aromatase inhibitors)

ATC5	Name	Pack_name	CNK_NUM
L02BG03	ANASTROZOLE	ARIMIDEX compr. 1 x 1 mg	749937
L02BG04	LETROZOLE	FEMARA compr. 1 x 2,5 mg	749945
L02BG06	EXEMESTANE	AROMASIN 25 mg compr. 1 x 25 mg	765107
L02BG03	ANASTROZOLE	arimidex tab. 28x 1mg	1217488
L02BG04	LETROZOLE	femara tab. 30x 2,5mg	1295393
L02BG06	EXEMESTANE	aromasin tab. 30x 25mg	1537364
L02BG06	EXEMESTANE	aromasin tab. 100x 25mg	1537380
L02BG03	ANASTROZOLE	arimidex tab. 84x 1mg	1749167
L02BG04	LETROZOLE	femara tab. 100x 2,5mg	2463669

Table 89. CNK codes for Trastuzumab

ABC5	Name	Pack_name	CNK_NUM
L01XC03	Trastuzumab	HERCEPTIN 150 mg pulv. pr. sol. perf. 1 x 150 mg	769000
L01XC03	Trastuzumab	herceptin flac inf. 150mg poeder	1501923

Table 90. Nomenclature codes for cardiac assessment (IMA)

Codes	Description	Omschrijving
460456-460460	Bilan échographique transthoracique complet du cœur, comprenant l'acquisition d'images bidimensionnelles dans au moins trois plans de coupe différents, et de signaux Doppler en mode couleur et en mode spectral au niveau d'au moins trois orifices valvulaires. L'enregistrement et l'archivage de l'examen sur bande magnétique ou support digital et le protocole détaillé sont exigés	Volledig transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen en in spectraal mode ter hoogte van minstens drie klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist evenals een gedetailleerd protocol
460574 - 460585	Bilan échographique transoesophagien complet du cœur, comprenant l'acquisition d'images bidimensionnelle dans au moins 3 plans de coupe différents, et de signaux Doppler en mode couleur au niveau d'au moins 3 orifices valvulaires. L'enregistrement et l'archivage de l'examen sur bande magnétique ou support digital et le protocole détaillé sont exigés	Volledig transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden in minstens drie verschillende snedevlakken, en kleuren-Doppler signalen ter hoogte van minstens 3 klepopeningen. De opname en archivering van het onderzoek op magneetband of digitale drager is vereist, evenals een gedetailleerd protocol
461230-461241	Examen échographique transthoracique limité du cœur, comprenant l'acquisition d'images bidimensionnelles et de signaux Doppler en mode spectral. L'enregistrement et l'archivage de l'examen et une description succincte répondant au problème clinique sont	Beperkt transthoracaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord

	exigés	geeft op het klinisch probleem
461252-461263	Examen échographique transoesophagien limité du coeur, comprenant l'acquisition d'images bidimensionnelles et de signaux Doppler en mode couleur. L'enregistrement et l'archivage de l'examen et une description succincte répondant au problème clinique sont exigés	Beperkt transoesofagaal echografisch bilan van het hart, waarbij bidimensionele beelden bekomen worden, en kleuren-Doppler signalen in spectraal mode. De opname en archivering van het onderzoek is vereist, evenals een beknopte beschrijving die een antwoord geeft op het klinisch probleem
476195-476206	Cathétérismes cardiaques en vue d'angiocardiographies et/ou angiopneumographies y compris la dénudation, les contrôles radioscopiques télévisés, les contrôles électrocardiographiques éventuels (nom cumulable avec la consultation)	Hartcatheterismen met het oog op angiocardiografieën en/of angiopneumografieën, inclusief de eventuele denudatie, radioscopische controles met televisie, elektrocardiografische controles (mogen niet worden gecumuleerd met de raadpleging)

Table 91. Nomenclature codes for radiotherapy (IMA)

Codes	Description	Omschrijving
444113 - 444124	Honoraires forfaitaires pour une série d'irradiations externes simples de 1 à 10 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 1	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van 1 tot 10 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 1
444135 - 444146	Honoraires forfaitaires pour une série d'irradiations externes simples de 11 à 35 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 2	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van minstens 11 tot 35 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 2
444150 - 444161	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 3	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 3
440016 - 440020 440053 - 440064 Created on 01.04.1985 Suppressed on 01.06.2001	Traitement par irradiation externe : une ou plusieurs localisations dans un même volume cible par haute énergie ou gammathérapie (accélérateur linéaire, télécobalt, neutrons, protons) : Dans un service disposant de télécobalt et d'un accélérateur et d'un simulateur et d'un système de dosimétrie avec ordinateur (min. 20 séances)	In een dienst die beschikt over telekobalt én een accelerator én een simulator én een dosimetriesysteem met computer (minimum 20 zittingen)
444172-444183	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 4	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 4
444312-444323	Honoraires forfaitaires pour curiethérapie combinée à une série d'irradiations externes chez un patient qui répond aux critères ou pathologie repris en catégorie 6	Forfaitair honorarium voor curietherapie gecombineerd met uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 6

Catégorie 1

Patients traités par irradiation externe pour les affections malignes ou bénignes suivantes:"

"A.R. 19.4.2001" (en vigueur 1.6.2001 (*)) + "A.R. 3.7.2003" (en vigueur 28.7.2003)

"Tumeurs malignes :

- métastases (osseuses, cérébrales, cutanées, hépatiques, tissus mous)
- irradiations à visée curative où sont administrées moins de 11 fractions.

Affections bénignes :

- …

Catégorie 2

Patients traités par irradiation externe à visée curative ou en vue d'un contrôle tumoural définitif au niveau d'un volume cible en raison d'affections malignes ou d'une des affections bénignes suivantes :

Affections bénignes :

- - …

Catégorie 3

"A.R. 3.7.2003" (en vigueur 28.7.2003)

- "Traitements tridimensionnels chez des patients de catégorie 2 en raison de tumeurs cérébrales, de tumeurs tête-cou (sauf larynx T1N0 et T2N0), tumeurs pulmonaires, du pancréas, pelviennes, de l'oesophage, de l'estomac, des tissus mous."

"A.R. 19.4.2001" (en vigueur 1.6.2001 (*))

- "Champs en mantelets (maladie de Hodgkin) ou champs complexes infradiaphragmatiques (maladie de Hodgkin, cancers des testicules ou ovaires ou lymphomes).
- Champs complexes pour médulloblastomes ou épendymomes et autres tumeurs pédiatriques."

Categorie 4

- Totale lichaamsbestraling in het kader van een beenmerg-transplantatie
- Peroperatieve elektronenbestraling of foto-nenbestraling via lineaire versneller uitgerust met specifieke applicatoren.
- De dosimetrische karakteristieken van de applicatoren moeten individueel voor elke beschikbare elektronenergie in 3 dimensies zijn opgemeten.
- Totale huid elektronentherapie (minimaal 15 fracties)
- De dosimetrische karakteristieken van de gebruikte velden en hun aansluitingen moeten opgemeten zijn.
- Stereotactische radiotherapie voor AVM behandeling, meningiomen, hypofysetumouren en acusticus neurinomen, of bij maligne hersentumouren kleiner dan 3 cm.
    - Radiotherapie met gemoduleerde intensiteit (IMRT) bij patiënten van categorie 3 volgens eén der volgende technieken :
    - tomotherapie, statische gesegmenteerde bundels (min 15 segmenten), dynamische multileafcollimatie (sliding window, close-in, dynamische wig is geen IMRT), patiëntindividueel vervaardigde compensatoren of IMAT.
    - Minstens 15 fracties dienen volgens IMRT toegediend te worden.
    - Voor de technieken met statische bundelincidenties, dienen de berekende fluentieprofielen van elke bundel bij het patiëntdossier te worden gevoegd.

Categorie 6

- Patiënten behandeld met een combinatie van curietherapie en externe bestraling voor borsttumouren en intraluminele toepassingen op slokdarm, bronchus of galwegen.
- Beide behandelingstypes zijn cumuleerbaar tijdens éénzelfde behandelingsperiode.

Table 92. Nomenclature codes for radiotherapy (MCD)

Codes	Description	Omschrijving
V580	scéance de radiothérapie	
9221	Radiothérapie superficielle	Superficiele-oppervlakkige radiotherapie R.T.
9222	Radiothérapie profonde	Orthovoltage R.T.

Table 93. CNK codes for Biphosphonates (IMA)

ATC5	Name	Pack_name	CNK_NUM
M05BA02	Clodronic acid	BONEFOS amp. sol. perf. 1 x 300 mg/5 ml	742569
M05BA02	Clodronic acid	BONEFOS caps. 1 x 400 mg	743278
M05BA02	Clodronic acid	OSTAC amp. inj. 1 x 300 mg/10 ml	744060
M05BA02	Clodronic acid	OSTAC caps. 1 x 400 mg	744078
M05BA02	Clodronic acid	BONEFOS compr. 1 x 400 mg	748467
M05BA02	Clodronic acid	BONEFOS compr. 1 x 800 mg	748517
M05BA02	Clodronic acid	bonefos caps 100x400mg	1115096
M05BA02	Clodronic acid	bonefos caps 30x400mg	1115104
M05BA02	Clodronic acid	bonefos amp. inf. 300mg/5ml	1115112
M05BA02	Clodronic acid	ostac caps 60 x 400mg	1187897
M05BA02	Clodronic acid	ostac caps 120 x 400mg	1187905
M05BA02	Clodronic acid	ostac pro infus 300mg/10ml amp 5	1187913
M05BA02	Clodronic acid	bonefos comp 30 x 400 mg	1327550
M05BA02	Clodronic acid	bonefos comp 100 x 400 mg	1327568
M05BA02	Clodronic acid	bonefos tab. 50x 800mg	1327576
M05BA02	Clodronic acid	bonefos comp 10 x 800 mg	1327584
M05BA03	Pamidronic acid	aredia amp. inf. 2x 15mg/5ml	495465
M05BA03	Pamidronic acid	AREDIA amp. I.V. 1 x 15 mg/5 ml	736132
M05BA03	Pamidronic acid	PAMIDRONAAT MAYNE 15 mg/5 ml fl. I.V. 1 x 15 mg/25 ml	773093
M05BA03	Pamidronic acid	PAMIDRONAAT MAYNE 30 mg/10 ml fl. I.V. 1 x 30 mg/10 ml	773101
M05BA03	Pamidronic acid	PAMIDRONAAT MAYNE 60 mg/10 ml fl. I.V. 1 x 60 mg/10 ml	773119
M05BA03	Pamidronic acid	PAMIDRONAAT MAYNE 90 mg/10 ml fl. I.V. 1 x 90 mg/10 ml	773127
M05BA03	Pamidronic acid	PAMIDRO-CELL 15 mg/5 ml fl.	779546
M05BA03	Pamidronic acid	PAMIDRO-CELL 30 mg/10 ml fl.	779553
M05BA03	Pamidronic acid	PAMIDRO-CELL 60 mg/20 ml fl.	779561
M05BA03	Pamidronic acid	PAMIDRO-CELL 90 mg/30 ml fl.	779579
M05BA03	Pamidronic acid	PAMIDRONATE MERCK 15 mg/ml amp. 1	780171
M05BA03	Pamidronic acid	PAMIDRONATE MERCK 15 mg/ml amp. 1	780189
M05BA03	Pamidronic acid	PAMIDRONATE MERCK 15 mg/ml amp. 1	780197
M05BA03	Pamidronic acid	PAMIDRONATE MERCK 15 mg/ml amp. 1	780213
M05BA03	Pamidronic acid	PAMIPRO 15 mg/5 ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	781427
M05BA03	Pamidronic acid	PAMIPRO 30 mg/10 ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	781435
M05BA03	Pamidronic acid	PAMIPRO 60 mg/20 ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	781443
M05BA03	Pamidronic acid	PAMIPRO 90 mg/30 ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	781450
M05BA03	Pamidronic acid	PAMIDRIN 3 mg/ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	783399
M05BA03	Pamidronic acid	PAMIDRIN 3 mg/ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	783407
M05BA03	Pamidronic acid	PAMIDRIN 3 mg/ml 1 flacon injectable x 3 mg/ml Pamidronate, disodique	783415
M05BA03	Pamidronic acid	PAMIDRIN 3 mg/ml 1 flacon injectable x 3 mg/ml Pamidronate,	783423

		disodique	
M05BA03	Pamidronic acid	pamidronaat hospira amp. inf. 90mg/10ml	1731231
M05BA03	Pamidronic acid	pamidronaat hospira amp. inf. 30mg/10ml	1731264
M05BA03	Pamidronic acid	pamidronaat hospira amp. inf. 5x 15mg/5ml	1731298
M05BA03	Pamidronic acid	pamidronaat 60 mg vial 1 x 60 mg	2040384
M05BA03	Pamidronic acid	pamidronate eg flac inf. 90mg/30ml	2186666
M05BA03	Pamidronic acid	pamidronate eg flac inf. 30mg/10ml	2186674
M05BA03	Pamidronic acid	pamidronate eg flac inf. 60mg/20ml	2186682
M05BA03	Pamidronic acid	pamidronate eg flac inf. 15mg/5ml	2186690
M05BA03	Pamidronic acid	pamidronate mylan amp. inf. 15mg/1ml	2216059
M05BA03	Pamidronic acid	pamidronate mylan amp. inf. 30mg/2ml	2216067
M05BA03	Pamidronic acid	pamidronate mylan amp. inf. 60mg/4ml	2216075
M05BA03	Pamidronic acid	pamidronate mylan amp. inf. 90mg/6ml	2216083
M05BA03	Pamidronic acid	pamipro 15 mg/ 5 ml fl iv 1 x 15 mg	2292662
M05BA03	Pamidronic acid	pamipro 30 mg/10 ml fl iv 1 x 30 mg	2292688
M05BA03	Pamidronic acid	pamipro 60 mg/20 ml fl iv 1 x 60 mg	2292704
M05BA03	Pamidronic acid	pamipro 90 mg/30 ml fl iv 1 x 90 mg	2292720
M05BA03	Pamidronic acid	pamidrin flac inf. 15mg/5ml	2322592
M05BA03	Pamidronic acid	pamidrin flac inf. 30mg/10ml	2322600
M05BA03	Pamidronic acid	pamidrin 3 mg/ml fl 20 ml	2322618
M05BA03	Pamidronic acid	pamidrin flac inf. 90mg/30ml	2322626
M05BA06	Ibandronic acid	BONDRONAT 2 mg/2 ml amp.	779124
M05BA06	Ibandronic acid	BONDRONAT 6 mg/6 ml amp.	779132
M05BA06	Ibandronic acid	BONDRONAT 50 mg comp	779140
M05BA06	Ibandronic acid	BONVIVA 1 comprimé pelliculé x 150 mg Acide Ibandronique	782953
M05BA06	Ibandronic acid	BONVIVA 3 mg/3 ml 1 seringue préremplie x 1 mg/ml Acide Ibandronique	785501
M05BA06	Ibandronic acid	bondronat flac inf. 6mg/6ml	2090678
M05BA06	Ibandronic acid	bondronat tab. 84x 50mg	2090686
M05BA06	Ibandronic acid	bondronat flac inf. 2mg/2ml	2180677
M05BA06	Ibandronic acid	bonviva tab. 3x 150mg	2243822
M05BA06	Ibandronic acid	bonviva spuitamp. 3mg/3ml	2321685
M05BA08	Zoledronic acid	ZOMETA fl. I.V. 1 x 4 mg	770487
M05BA08	Zoledronic acid	ACLASTA 5 mg 1 flacon injectable x 0,05 mg/ml Acide zolédronique, monohydrate	781773
M05BA08	Zoledronic acid	zometa flac inf. 4mg	1692458
M05BA08	Zoledronic acid	aclasta flac inf. 5mg/100ml	2213114

7.14.5 Follow-up

Table 94. Nomenclature codes for mammography in the context of follow-up (IMA)

Codes	Description	Omschrijving
450096 – 450100 – 461090 – 461101	Mammographie par sein y compris les clichés axillaires éventuels (quel que soit le nombre de clichés)	Mammografie per borst, inclusief de eventuele okselclichés (ongeacht het aantal clichés)

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