KCE REPORT 365

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

# SURVIVAL AND QUALITY OF CARE OFFERED IN BELGIAN HOSPITALS WITH AND WITHOUT RECOGNITION FOR BREAST CANCER





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HEALTH SERVICES RESEARCH

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# COLOPHON


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# TABLE OF CONTENTS

**LIST OF FIGURES** ..... **10**
**LIST OF TABLES** ..... **15**
**LIST OF ABBREVIATIONS** ..... **27**
■ **SCIENTIFIC REPORT** ..... **31**
**1 INTRODUCTION** ..... **31**
1.1 THE BELGIAN SITUATION IN A NUTSHELL ..... 31
1.1.1 The European incentive to establish breast clinics ..... 31
1.1.2 The move to coordinating and satellite breast clinics – a further reduction in the minimal level of activity ..... 32
1.2 RESEARCH QUESTIONS ..... 33
1.3 SECONDARY OBJECTIVES ..... 33
1.4 TARGET AUDIENCE ..... 34
1.5 METHODOLOGY ..... 34
1.6 STRUCTURE OF THE REPORT ..... 35
**2 BACKGROUND** ..... **36**
2.1 BREAST CANCER, THE MOST COMMONLY DIAGNOSED CANCER AMONG WOMEN ..... 36
2.2 BREAST CANCER CARE IN BELGIUM ..... 39
2.2.1 Screening for breast cancer ..... 39
2.2.2 Concentration of breast cancer care, only to some extent ..... 39
2.2.3 Gene expression profiling – agreements solely with coordinating and satellite breast clinics ..... 45
2.2.4 Autologous breast reconstruction – agreements solely with coordinating breast clinics ..... 45
2.3 QUALITY IMPROVEMENT INITIATIVES AT THE EUROPEAN LEVEL ..... 45
2.3.1 EUSOMA's position papers on specialist breast units ..... 45

2.3.2 The European Commission Initiative on Breast Cancer ....47
**3 IDENTIFICATION, SELECTION AND OPERATIONALIZATION OF PROCESS INDICATORS ....49**
3.1 IDENTIFICATION AND SELECTION OF POSSIBLE QUALITY INDICATORS ....49
3.2 OPERATIONALIZATION OF INDICATORS ....50
**4 ANALYSIS OF CANCER REGISTRY AND OTHER AVAILABLE DATA ....51**
4.1 THE STUDY DATABASE - A LINKAGE BETWEEN THE BELGIAN CANCER REGISTRY AND ADMINISTRATIVE DATABASES ....51
4.2 THE STUDY COHORT – WOMEN DIAGNOSED IN 2014 - 2018 WITH DCIS OR IBC ....51
4.3 DEFINING THE TREATMENT SCHEME OF THE PATIENT ....52
4.4 ASSIGNMENT OF EACH PATIENT TO ONE CENTRE ....52
4.4.1 Introduction ....52
4.4.2 Campus or hospital level ....52
4.4.3 Missing campus identification data in the MZG – RHM database ....53
4.4.4 Changes during the study period ....53
4.4.5 Assignment algorithms ....54
4.5 DEFINING THE CAMPUS/HOSPITAL VOLUME ....54
4.6 CASE-MIX ADJUSTMENT ....54
4.7 STATISTICAL ANALYSES ....55
4.7.1 Visualisation of centre variability ....55
4.7.2 Estimation of observed and relative survival ....56
4.7.3 Modelling observed survival ....56
4.7.4 Modelling relative survival ....57
4.7.5 Association between campus recognition status/centre volume with processes of care and observed survival ....57
4.7.6 Association between campus recognition status/centre volume and relative survival ....57

4.7.7 Interpretation of p-values and confidence intervals ....57
4.7.8 Statistical software ....57
4.8 PRE-VALIDATION OF AVAILABLE DATA AND SOME METHODOLOGICAL ISSUES IN TEN HOSPITALS ....58
4.8.1 Objectives and methodology ....58
4.8.2 Results ....59
4.8.3 Impact of the pre-validation on the methodology and/or interpretation of results ....59
4.9 VALIDATION OF THE PROCESS INDICATORS IN ALL BELGIAN HOSPITALS ....60
4.9.1 Objectives and methodology ....60
4.9.2 Results ....61
4.9.3 Impact of the validation study on the methodology and/or interpretation of results ....61
4.10 STRENGTHS AND LIMITATIONS OF THE STUDY DATABASE ....62
4.10.1 Valuable information not available in the consulted databases ....62
4.10.2 Limitations due to invoicing rules ....63
4.10.3 Limitations due to the vague description of nomenclature codes ....64
4.10.4 Limitations due to unclear or limited validity of some data ....64
4.10.5 Treatment performed within the framework of clinical trials ....65
**5 CHARACTERISTICS OF THE STUDY COHORT ....65**
5.1 BASELINE DEMOGRAPHICS AND TUMOUR CHARACTERISTICS ....65
5.1.1 Patient characteristics ....65
5.1.2 Tumour characteristics ....67
5.2 MAIN DIAGNOSTIC AND STAGING PROCEDURES ....67
5.3 MAIN THERAPEUTIC PROCEDURES ....68
5.4 OBSERVED AND RELATIVE SURVIVAL ....69

5.4.1 Patients diagnosed with IBC in 2014 - 2018 ..... 69
5.4.2 Patients diagnosed with non-metastatic IBC in 2014 - 2018, who had surgery ..... 73
**6 ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A CAMPUS AND SURVIVAL ..... 75**
6.1 INTRODUCTION ..... 75
6.2 DISTRIBUTION OF BC CARE IN 2014 - 2018 ..... 75
6.3 UNADJUSTED ASSOCIATION BETWEEN THE RECOGNITION STATUS AND VOLUME OF A CAMPUS, AND OBSERVED SURVIVAL SINCE DIAGNOSIS OF IBC ..... 76
6.4 ADJUSTED ASSOCIATION BETWEEN THE RECOGNITION STATUS AND VOLUME OF A CAMPUS, AND OBSERVED SURVIVAL SINCE DIAGNOSIS ..... 78
6.5 UNADJUSTED ASSOCIATION BETWEEN THE RECOGNITION STATUS AND VOLUME OF A CAMPUS, AND RELATIVE SURVIVAL SINCE DIAGNOSIS ..... 79
6.6 ADJUSTED ASSOCIATION BETWEEN THE RECOGNITION STATUS AND VOLUME OF A CAMPUS, AND RELATIVE SURVIVAL SINCE DIAGNOSIS ..... 79
6.7 ASSOCIATION BETWEEN HOSPITAL VOLUME AND OBSERVED SURVIVAL SINCE DIAGNOSIS IN THE COMPARISON COHORT (2009 - 2013) ..... 80
**7 ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A CAMPUS/HOSPITAL AND PROCESSES & OTHER OUTCOMES OF CARE ..... 81**
7.1 DIAGNOSIS & STAGING ..... 82
7.1.1 Mammography and sonography in patients with IBC ..... 82
7.1.2 Assessment of histology and/or cytology before treatment ..... 84
7.1.3 Assessment of receptor status before any systemic treatment ..... 85
7.1.4 Multidisciplinary team (MDT) meeting ..... 88
7.1.5 TNM stage reporting to the BCR ..... 91
7.2 TIME TO TREATMENT ..... 95
7.3 SURGERY ..... 97

7.3.1 No axillary clearance as first axillary surgery in patients with DCIS ....97
7.3.2 Sentinel lymph-node biopsy (SLNB) only, in patients with invasive pN0 BC....99
7.3.3 Just one breast surgery ....101
7.4 POST-OPERATIVE RADIOTHERAPY IN WOMEN WITH IBC ....106
7.5 SYSTEMIC TREATMENT ....108
7.5.1 Adjuvant chemotherapy and/or endocrine therapy in patients <70 years with M0 IBC ....109
7.5.2 Adjuvant systemic therapy in patients <70 years with M1 IBC ....111
**8 DISCUSSION ....112**
**■ APPENDICES ....117**
**APPENDIX 1. THE EUROPEAN PARLIAMENT RESOLUTION 2002 – CRITERIA FOR CERTIFIED BREAST CENTRES....117**
**APPENDIX 2. ROYAL DECREE OF 26 APRIL 2007, DEFINING THE RECOGNITION CRITERIA FOR BREAST CLINICS ....118**
**APPENDIX 3. CARE PROGRAMME FOR BASIC ONCOLOGICAL CARE AND ONCOLOGY CARE PROGRAMME ....121**
**APPENDIX 4. ROYAL DECREE OF 2013 - ADAPTATIONS COMPARED TO THE ROYAL DECREE OF 2007 121**
**APPENDIX 5. DISTRIBUTION OF COORDINATING AND SATELLITE BREAST CLINICS OVER THE HOSPITAL NETWORKS ....124**
**APPENDIX 6. SELECTION OF QUALITY INDICATORS....127**
**APPENDIX 7. DEFINITION OF BREAST CANCER ....133**
**APPENDIX 8. ANALYSIS OF CANCER REGISTRY AND OTHER AVAILABLE DATA ....133**
APPENDIX 8.1. HEALTH INSURANCE DATA (IMA – AIM DATA) ....133
APPENDIX 8.2. HOSPITAL DISCHARGE DATA - MZG – RHM DATA ....164
APPENDIX 8.3. IDENTIFICATION OF THE STUDY COHORT IN THE BELGIAN CANCER REGISTRY DATABASE ....165
APPENDIX 8.4. ASSIGNMENT OF EACH PATIENT TO ONE CENTRE – ASSIGNMENT ALGORITHMS166
**APPENDIX 9. PRE-VALIDATION STUDY ....170**

APPENDIX 9.1. LIST OF PARTICIPATING HOSPITALS ....170
APPENDIX 9.2. INFORMATION PROVIDED TO THE HOSPITALS FOR EACH ASSIGNED PATIENT AND CHECKS ASKED TO BE DONE ....170
APPENDIX 9.3. RESULTS ....171
**APPENDIX 10. VALIDATION STUDY ....180**
APPENDIX 10.1. VALIDATION OF PROCESS INDICATOR RESULTS ....181
APPENDIX 10.2. VALIDATION OF VOLUME AND CENTRE ALLOCATION ....185
**APPENDIX 11. DESCRIPTION OF THE STUDY COHORT ....186**
APPENDIX 11.1. PATIENT CHARACTERISTICS ....186
APPENDIX 11.2. TUMOUR CHARACTERISTICS ....190
APPENDIX 11.3. MAIN DIAGNOSTIC AND STAGING PROCEDURES ....202
APPENDIX 11.4. MAIN THERAPEUTIC PROCEDURES ....208
APPENDIX 11.5. REFERRAL BETWEEN HOSPITALS ....229
APPENDIX 11.6. OBSERVED AND RELATIVE SURVIVAL ....231
**APPENDIX 12. ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A HOSPITAL CAMPUS AND SURVIVAL ....248**
APPENDIX 12.1. DOCUMENTATION SHEET ....248
APPENDIX 12.2. DISTRIBUTION OF BC CARE IN 2014 - 2018 ....250
APPENDIX 12.3. UNADJUSTED ASSOCIATION BETWEEN RECOGNITION STATUS AND CAMPUS VOLUME, AND 1-, 3- AND 5-YEAR OBSERVED SURVIVAL SINCE DIAGNOSIS ....253
APPENDIX 12.4. ADJUSTED ASSOCIATION BETWEEN RECOGNITION STATUS AND CAMPUS VOLUME, AND 1-, 3- AND 5-YEAR OBSERVED SURVIVAL SINCE DIAGNOSIS ....256
APPENDIX 12.5. UNADJUSTED ASSOCIATION BETWEEN THE RECOGNITION STATUS AND VOLUME OF A CAMPUS, AND RELATIVE SURVIVAL SINCE DIAGNOSIS ....257
APPENDIX 12.6. ASSOCIATION BETWEEN HOSPITAL VOLUME AND OBSERVED SURVIVAL SINCE DIAGNOSIS IN THE COMPARISON COHORT (2009 - 2013) ....261

**APPENDIX 13. MAMMOGRAPHY AND SONOGRAPHY ..... 264**
APPENDIX 13.1. DOCUMENTATION SHEET ..... 264
APPENDIX 13.2. FLOWCHART ..... 267
APPENDIX 13.3. RESULTS ..... 268
**APPENDIX 14. ASSESSMENT OF HISTOLOGY AND/OR CYTOLOGY BEFORE TREATMENT ..... 278**
APPENDIX 14.1. DOCUMENTATION SHEET ..... 278
APPENDIX 14.2. FLOWCHART ..... 280
APPENDIX 14.3. RESULTS ..... 281
**APPENDIX 15. ASSESSMENT OF RECEPTOR STATUS BEFORE ANY SYSTEMIC TREATMENT ..... 286**
APPENDIX 15.1. DOCUMENTATION SHEET ..... 286
APPENDIX 15.2. FLOWCHART ..... 288
APPENDIX 15.3. RESULTS ..... 289
**APPENDIX 16. MULTIDISCIPLINARY TEAM (MDT) MEETING ..... 294**
APPENDIX 16.1. DOCUMENTATION SHEET ..... 294
APPENDIX 16.2. FLOWCHARTS ..... 296
APPENDIX 16.3. RESULTS ..... 298
**APPENDIX 17. TNM STAGE REPORTING TO THE BCR ..... 304**
APPENDIX 17.1. DOCUMENTATION SHEET ..... 304
APPENDIX 17.2. FLOWCHARTS ..... 306
APPENDIX 17.3. RESULTS ..... 308
**APPENDIX 18. TIME TO TREATMENT ..... 320**
APPENDIX 18.1. DOCUMENTATION SHEET ..... 320
APPENDIX 18.2. FLOWCHART ..... 322
APPENDIX 18.3. RESULTS ..... 323

**APPENDIX 19. NO AXILLARY CLEARANCE IN PATIENTS WITH DCIS ..... 333**
APPENDIX 19.1. DOCUMENTATION SHEET ..... 333
APPENDIX 19.2. FLOWCHART ..... 335
APPENDIX 19.3. RESULTS ..... 336
**APPENDIX 20. SENTINEL LYMPH-NODE BIOPSY (SLNB) ONLY IN PATIENTS WITH IBC ..... 341**
APPENDIX 20.1. DOCUMENTATION SHEET ..... 341
APPENDIX 20.2. FLOWCHART ..... 343
APPENDIX 20.3. RESULTS ..... 344
**APPENDIX 21. JUST ONE BREAST SURGERY IN DCIS ..... 350**
APPENDIX 21.1. DOCUMENTATION SHEET ..... 350
APPENDIX 21.2. FLOWCHART ..... 352
APPENDIX 21.3. RESULTS ..... 353
**APPENDIX 22. JUST ONE BREAST SURGERY IN IBC ..... 362**
APPENDIX 22.1. DOCUMENTATION SHEET ..... 362
APPENDIX 22.2. FLOWCHART ..... 364
APPENDIX 22.3. RESULTS ..... 365
**APPENDIX 23. POST-OPERATIVE RADIOTHERAPY IN WOMEN WITH IBC ..... 375**
APPENDIX 23.1. DOCUMENTATION SHEET ..... 375
APPENDIX 23.2. FLOWCHART ..... 377
APPENDIX 23.3. RESULTS ..... 378
**APPENDIX 24. ADJUVANT CHEMOTHERAPY AND/OR ENDOCRINE THERAPY IN PATIENTS <70 YEARS WITH M0 IBC ..... 384**
APPENDIX 24.1. DOCUMENTATION SHEET ..... 384
APPENDIX 24.2. INDICATOR A - ADJUVANT CHEMOTHERAPY IN M0 IBC ..... 386

APPENDIX 24.3. INDICATOR B - ADJUVANT ENDOCRINE THERAPY IN M0 IBC .....395
**APPENDIX 25. ADJUVANT SYSTEMIC THERAPY IN PATIENTS <70 YEARS WITH M1 IBC .....404**
APPENDIX 25.1. DOCUMENTATION SHEET.....404
APPENDIX 25.2. FLOWCHART.....406
APPENDIX 25.3. RESULTS .....407
■ **REFERENCES .....411**

# LIST OF FIGURES

Figure 1 – Estimated incidence of IBC in women (all ages) in 2020, by country ....37

Figure 2 – Age-standardised 5-year net survival probability for women diagnosed in 2010-2014 with IBC, by country ....38

Figure 3 – Distribution of the coordinating and satellite breast clinics on 1 September 2022 within the locoregional hospital networks....44

Figure 4 – Forest plot of the adjusted hazard ratio for all-cause death in patients with IBC, by main treatment campus ....72

Figure 5 – Forest plot of the adjusted hazard ratio for all-cause death in patients with non-metastatic IBC who had surgery, by main treatment campus....74

Figure 6 – Observed survival probability, by campus recognition status (left) and average annual campus volume (right)....77

Figure 7 – Proportion of women with IBC with histological or cytological assessment before any treatment, by campus of main treatment ....85

Figure 8 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status was assessed before any systemic treatment (left) and zoom on the highest proportions (right), by campus of main treatment....87

Figure 9 – Scatter plot of the proportion of women with DCIS (left) and IBC (right) for whom a multidisciplinary team meeting was charged within 1 month before until 2 months after incidence date, by hospital of diagnosis ....90

Figure 10 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, by hospital of main treatment....107

Figure 11 – Scatter plot of the proportion patients <70 years with M1 IBC who received systemic therapy, by campus of main treatment ....112

Figure 12 – Decision tree to define incision biopsy, excision biopsy and first surgery....136

Figure 13 – Selection of the study cohort - flowchart ....166

Figure 14 – Correctness and completeness of the patient lists for hospital of diagnosis (incidence years 2013 and 2017), by hospital ....172

Figure 15 – Correctness and completeness of the patient lists for hospital of main treatment (incidence years 2013 and 2017), by hospital ....173

Figure 16 – Correctness of the primary treatment schemes, by hospital ....175
Figure 17 – Correctness of oestrogen receptor status result, by hospital ....178
Figure 18 – Correctness of progesterone receptor status result, by hospital ....178
Figure 19 – Correctness of HER2 receptor status result obtained via immunohistochemical testing, by hospital ....178
Figure 20 – Correctness of HER2 receptor status result obtained via gene amplification through in situ hybridization, by hospital ....178
Figure 21 – Unadjusted observed survival of patients with IBC, by age at diagnosis (A), WHO performance status (B), combined stage (C) and year of diagnosis (D) ....237
Figure 22 – Unadjusted relative survival of patients with IBC, by age at diagnosis (A), number of comorbidities (B), combined stage (C) and treatment modality (D) ....238
Figure 23 – Funnel plot of the 5-year unadjusted observed survival for patients with IBC (left) and zoom on the low precision range (right), by main treatment campus ....239
Figure 24 – Forest plot of the adjusted excess hazard ratio for BC-related excess death in patients with IBC, by main treatment campus ....240
Figure 25 – Unadjusted observed survival of patients with non-metastatic IBC who had surgery, by age at diagnosis (A), WHO performance status (B), combined stage (C) and year of diagnosis (D) ....245
Figure 26 – Unadjusted relative survival of patients with non-metastatic IBC who had surgery, by age at diagnosis (A), number of comorbidities (B), combined stage (C) and treatment modality (D) ....246
Figure 27 – Funnel plot of the 5-year unadjusted observed survival for patients with non-metastatic IBC who had surgery (left) and zoom on the low precision range (right), by main treatment campus ....247
Figure 28 – Observed survival probability at 5 year after diagnosis by campus recognition status and average annual campus volume, bubble plot ....253
Figure 29 – Relative survival, by campus recognition status (left) and average annual campus volume (right) ....257
Figure 30 – Relative survival at 5 year after diagnosis by campus recognition status and average annual campus volume, bubble plot ....258

Figure 31 – Observed survival probability for patients diagnosed in 2009 - 2013 with IBC, by hospital volume .....262

Figure 32 – 10-year observed survival probability for patients diagnosed in 2009 - 2013 with IBC, by hospital volume .....262

Figure 33 – Funnel plot of the proportion of women with IBC with mammography and breast sonography before any treatment, by campus of first treatment .....276

Figure 34 – Bubble plot of the proportion of women with IBC with mammography and breast sonography before any treatment, by campus volume* .....277

Figure 35 – Proportion of women with IBC with histological or cytological assessment before any treatment, by hospital of diagnosis .....285

Figure 36 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status was assessed before any systemic treatment (left) and zoom on the highest proportions (right), by hospital of diagnosis .....293

Figure 37 – Proportion of women with DCIS (left) and IBC (right) for whom a valid cTNM stage is reported to the BCR, by hospital of diagnosis .....311

Figure 38 – Bubble plots of the proportion of women with DCIS (left) and IBC (right) for whom the cTNM stage is reported to the BCR, by hospital volume .....312

Figure 39 – Proportion of women with DCIS (left) and IBC (right) who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by campus of main treatment .....318

Figure 40 – Bubble plots of the proportion of women with DCIS (left) and IBC (right) who were operated for whom the (y)pTNM stage is reported to the BCR, by campus volume .....319

Figure 41 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by campus of first treatment .....330

Figure 42 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by hospital of diagnosis .....331

Figure 43 – Bubble plot of the proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by campus volume .....332

Figure 44 – Scatter plot of the proportion of women with DCIS who did not receive ALND as first axillary surgery, by campus of first surgery .....339

Figure 45 – Bubble plot of the proportion of women with DCIS who did not receive ALND as first axillary surgery, by campus volume* ....340

Figure 46 – Scatter plot of the proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by campus of first surgery ....348

Figure 47 – Bubble plot of the proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by campus volume* ....349

Figure 48 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by campus of first surgery ....359

Figure 49 – Bubble plot of the proportion of women with DCIS who received just one operation (excluding reconstruction), by average annual campus volume ....360

Figure 50 – Proportion of women with DCIS who received just one operation (excluding reconstruction) versus BCS/mastectomy (left) and distribution of campuses over the four quadrants....361

Figure 51 – Proportion of women with IBC who received just one operation (excluding reconstruction), by campus of first surgery ....372

Figure 52 – Bubble plot of the proportion of women with IBC who received just one operation (excluding reconstruction), by campus volume*....373

Figure 53 – Proportion of women with IBC who received just one operation (excluding reconstruction) versus BCS/mastectomy (left) and distribution of campuses over the four quadrants ....374

Figure 54 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, by hospital of main treatment....383

Figure 55 – Scatter plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by campus of main treatment....393

Figure 56 – Bubble plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume* ....394

Figure 57 – Scatter plot of the proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by campus of main treatment....402

Figure 58 – Bubble plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume* .....403

# LIST OF TABLES

Table 1 – Number of campuses in December 2018, by recognition status and average annual volume .....33
Table 2 – Distribution of patients diagnosed with DCIS or IBC in 2018, by recognition status and average annual volume of the campus .....42
Table 3 – Final selection of thirteen quality indicators .....50
Table 4 – Main patient and tumour characteristics at diagnosis .....66
Table 5 – Main treatment schemes in DCIS and IBC .....68
Table 6 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with IBC .....70
Table 7 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with non-metastatic* IBC who had surgery .....73
Table 8 – Number of campuses in 2014 - 2018, by recognition status and average annual volume .....75
Table 9 – Distribution of patients diagnosed with DCIS or IBC in 2014 - 2018, by recognition status and average annual volume of the campus .....76
Table 10 – Observed survival, adjusted HR to die from all causes for patients with IBC, by recognition status and campus volume .....78
Table 11 – Relative survival, unadjusted relative excess risk to die for patients with IBC, by recognition status and campus volume .....79
Table 12 – Relative survival, adjusted excess hazard ratios to die for patients with IBC, by recognition status and campus volume .....80
Table 13 – Association between recognition status for BC and campus volume, and the odds of having mammography and breast sonography before any treatment in women with IBC .....83
Table 14 – Association between hospital volume and a valid cTNM stage reporting to the BCR .....93
Table 15 – Association between recognition status for BC and campus volume, and (y)pTNM stage reporting to the BCR .....94
Table 16 – Association between recognition status for BC and campus volume of the campus of first treatment, and start of first treatment within 6 weeks (42 days) of diagnosis of IBC .....96
Table 17 – Association between recognition status for BC and campus volume, and the odds of not receiving ALND as first axillary surgery in women with DCIS .....99

Table 18 – Association between recognition status for BC and campus volume, and the odds of undergoing SLNB only (excluding pts who received neoadjuvant systemic treatment) in women with IBC and clinically negative axilla ....101
Table 19 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with DCIS ....103
Table 20 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with IBC ....105
Table 21 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant chemotherapy within 4 months after surgery in women <70 years old with M0 IBC ....110
Table 22 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant endocrine therapy within 9 months after surgery in women <70 years old with M0 IBC ....110
Table 23 – Distribution of coordinating and satellite breast clinics over the hospital networks ....124
Table 24 – Long list of quality indicators, their respective source and measurability ....127
Table 25 – Quality indicators not selected by the clinical experts (based on relevance) ....132
Table 26 – ICD-O-3 codes included to define IBC and DCIS ....133
Table 27 – Nomenclature codes for breast biopsy ....138
Table 28 – Nomenclature codes for breast puncture ....139
Table 29 – Nomenclature codes for lymph node puncture ....139
Table 30 – Nomenclature codes for cytological examination ....140
Table 31 – Nomenclature codes for anatomical-pathological examinations ....140
Table 32 – Nomenclature codes for immunohistochemical examination (general) ....142
Table 33 – Nomenclature codes for oestrogen and progesterone testing ....142
Table 34 – Nomenclature codes for HER2 in situ hybridization ....143
Table 35 – Nomenclature codes for BRCA test ....144
Table 36 – Nomenclature codes for mammography ....145
Table 37 – Nomenclature codes for breast ultrasound ....146

Table 38 – Nomenclature codes for breast MRI ..... 147
Table 39 – Nomenclature codes for CT body, scintigraphy, SPECT and SPECT-CT ..... 147
Table 40 – Nomenclature codes for PET(-CT) ..... 150
Table 41 – Nomenclature codes for X-ray of thorax ..... 151
Table 42 – Nomenclature codes for brain imaging (CT scan and MRI) ..... 151
Table 43 – Nomenclature codes for abdominal ultrasound ..... 152
Table 44 – Nomenclature codes for breast conserving surgery (BCS) ..... 153
Table 45 – Nomenclature codes for mastectomy ..... 154
Table 46 – Nomenclature codes for excision biopsy ..... 154
Table 47 – Nomenclature codes for surgery leading to accidental findings ..... 155
Table 48 – Nomenclature codes for lymph node surgery (separate nomenclature codes) ..... 156
Table 49 –Nomenclature codes for radiotherapy ..... 157
Table 50 – ATC codes for chemotherapy ..... 158
Table 51 – ATC codes for targeted therapy ..... 159
Table 52 – ATC codes for endocrine therapy ..... 160
Table 53 – Non specific codes for ultrasound* used for the calculation of quality indicator on mammography and ultrasound before first treatment ..... 161
Table 54 – Code considered as echo-guided biopsy/puncture for the calculation of quality indicator on mammography and ultrasound before first treatment ..... 162
Table 55 – Nomenclature codes for multidisciplinary team meeting (MDT) ..... 163
Table 56 – Assignment algorithm for the hospital of diagnosis, with cumulative % per rule for patients with DCIS and IBC ..... 167
Table 57 – Assignment algorithm for the hospital of main treatment, with cumulative % per rule for patients with DCIS and IBC ..... 167
Table 58 – Assignment algorithm for the campus of main treatment, with cumulative % per rule for patients with DCIS and IBC ..... 168

Table 59 – Assignment algorithm for the hospital of first treatment, with cumulative % per rule for patients with DCIS and IBC ..... 168

Table 60 – Assignment algorithm for the campus of first treatment, with cumulative % per rule for patients with DCIS and IBC ..... 169

Table 61 – Patient characteristics at diagnosis of patients with DCIS, by recognition status of the campus of main treatment ..... 186

Table 62 – Patient characteristics at diagnosis of patients with IBC, by recognition status of the campus of main treatment ..... 188

Table 63 – Histological subtype and sublocalisation (ICD-O-3) in IBC, by recognition status of the campus of main treatment ..... 190

Table 64 – Tumour characteristics in DCIS, by recognition status of the campus of main treatment ..... 192

Table 65 – Tumour characteristics in IBC, by recognition status of the campus of main treatment ..... 193

Table 66 – Tumour characteristics for operated patients with DCIS, not treated with neoadjuvant therapy, by recognition status of the campus of main treatment ..... 196

Table 67 – Tumour characteristics for operated patients with IBC, not treated with neoadjuvant therapy, by recognition status of the campus of main treatment ..... 196

Table 68 – Tumour characteristics for operated patients with IBC, treated with neoadjuvant therapy, by recognition status of the campus of main treatment ..... 198

Table 69 – Consistency between clinical and pathological staging for operated patients diagnosed with IBC, not treated with neoadjuvant therapy ..... 200

Table 70 – Consistency between clinical and pathological staging for patients diagnosed with IBC treated with neoadjuvant therapy ..... 201

Table 71 – Diagnostic and staging procedures performed within 3 months around the incidence date, unless otherwise specified ..... 202

Table 72 – Imaging procedures performed within 3 months around incidence date, excluding all imaging as from start of treatment and additionally for CT those as from 14 days before start date of radiotherapy ..... 204

Table 73 – Imaging procedures[$] for staging in patients diagnosed with IBC, per clinical stage ..... 205

Table 74 – Diagnostic and staging procedures[$] for which the hospital is not known ..... 206

Table 75 – Main treatment schemes in DCIS, by recognition status of the campus of main treatment.....208
Table 76 – Main treatment schemes in IBC, by recognition status of the campus of main treatment .....210
Table 77 – Surgical procedures in DCIS, by recognition status of the campus of main treatment .....212
Table 78 – Surgical procedures in IBC, by recognition status of the campus of main treatment.....214
Table 79 – Radiotherapy in DCIS, by recognition status of the campus of main treatment.....216
Table 80 – Radiotherapy in IBC, by recognition status of the campus of main treatment .....216
Table 81 – Systemic treatment in DCIS, by recognition status of the campus of main treatment .....217
Table 82 – Systemic treatment in IBC, by recognition status of the campus of main treatment .....219
Table 83 – Systemic treatment modalities in patients with invasive, non-metastatic (i.e. combined stage 0, I, II, III) BC.....222
Table 84 – Systemic treatment products in patients with invasive, non-metastatic (i.e. combined stage 0, I, II, III) BC.....223
Table 85 – Characteristics of patients diagnosed with DCIS or IBC who received no oncological treatment .....226
Table 86 – Referral patterns for patients with DCIS and IBC, 2014 - 2018 .....229
Table 87 – Referral patterns for patients with DCIS and IBC, 2009 – 2013.....230
Table 88 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with IBC, by patient and tumour characteristics and treatment modality .....233
Table 89 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with non-metastatic* IBC who had surgery, by patient and tumour characteristics and treatment modality .....241
Table 90 – Number of campuses in 2014 by recognition status and average annual volume.....250
Table 91 – Number of campuses in 2015 by recognition status and average annual volume.....250
Table 92 – Number of campuses in 2016 by recognition status and average annual volume.....251
Table 93 – Number of campuses in 2017 by recognition status and average annual volume.....251
Table 94 – Number of campuses in 2018 by recognition status and average annual volume.....252

Table 95 – 1-, 3-, and 5-year unadjusted observed survival for patients with IBC, by recognition status and campus volume ..... 254

Table 96 – Observed survival, unadjusted HR for patients with IBC, by recognition status and campus volume ..... 255

Table 97 – Observed survival, adjusted HR for patients with IBC, by recognition status and campus volume ..... 256

Table 98 – 1-, 3-, and 5-year unadjusted relative survival for patients with IBC, by recognition status and campus volume ..... 259

Table 99 – Relative survival, unadjusted relative excess risk to die for patients with IBC, by recognition status and campus volume ..... 260

Table 100 – 1-, 3-, 5-, and 10-year unadjusted observed survival for patients diagnosed in 2009 - 2013 with IBC, by hospital volume ..... 261

Table 101 – Observed survival, unadjusted HR for patients diagnosed in 2009 - 2013 with IBC, by hospital volume ..... 262

Table 102 – Observed survival, adjusted HR for patients diagnosed in 2009 - 2013 with IBC, by hospital volume ..... 263

Table 103 – Proportion of women with IBC with mammography and breast sonography before any treatment, by patient and tumour characteristics ..... 268

Table 104 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, by time period ..... 270

Table 105 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, excluding patients <30 year ..... 270

Table 106 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, excluding cT4b/c/d cases ..... 270

Table 107 – Sensitivity analysis: Type of breast imaging in women with IBC before any treatment, by clinical stage ..... 271

Table 108 – Proportion of women with IBC with mammography and breast sonography before any treatment, by recognition status for BC and campus volume ..... 273

Table 109 – Association between recognition status for BC and campus volume, and the odds of having mammography and breast sonography before any treatment in women with IBC, including volume analyses by recognition status....274

Table 110 – Proportion of women with IBC with histological or cytological assessment before any treatment, by patient and tumour characteristics....281

Table 111 – Sensitivity analysis: Proportion of women with IBC with histological or cytological assessment before any treatment, by time period....284

Table 112 – Sensitivity analysis: Proportion of women with IBC with histological or cytological assessment before any treatment, by type of histological or cytological assessment....284

Table 113 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed before any systemic treatment....289

Table 114 – Sensitivity analysis: Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed before any systemic treatment, by time period....291

Table 115 – Sensitivity analysis: Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed within 3 months around incidence date....291

Table 116 – Sensitivity analysis: Proportion of women with IBC in whom HER2 status and/or ER and/or PR status were assessed within 3 months around incidence date (irrespective of treatment)....292

Table 117 – Proportion of women with BC for whom a multidisciplinary team (MDT) meeting was billed within 1 month before until 2 months after incidence date, by patient, tumour and treatment characteristics....298

Table 118 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, by time period....301

Table 119 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, by time period and treatment modalities....302

Table 120 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, excluding patients who died within two months after incidence....303

Table 121 – Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by patient, tumour and treatment characteristics....308

Table 122 – Sensitivity analyses: Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by time period....310

Table 123 – Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by hospital volume ....310

Table 124 – Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by patient, tumour and treatment characteristics ....313

Table 125 – Sensitivity analyses: Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by time period ....315

Table 126 – Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by recognition status for BC and campus volume, including volume analyses by recognition status ....315

Table 127 – Association between recognition status for BC and campus volume, and (y)pTNM stage reporting to the BCR, including volume analyses by recognition status ....316

Table 128 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by patient, tumour and treatment characteristics ....323

Table 129 – Median time (days) between incidence and first treatment for patients with IBC ....326

Table 130 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by time period ....326

Table 131 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by clinical stage ....326

Table 132 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, excluding patients with time to treatment ≤0 days ....327

Table 133 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 (42 days) versus 4 (28 days) weeks of incidence ....327

Table 134 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by recognition status and campus volume ....327

Table 135 – Association between recognition status for BC and campus volume of the campus of first treatment, and start of first treatment within 6 weeks (42 days) of incidence, including volume analyses by recognition status ....328

Table 136 – Proportion of women with DCIS who did not receive ALND as first axillary surgery, by patient characteristics and type of first surgery ....336

Table 137 – Sensitivity analysis: Proportion of women with DCIS who did not receive ALND as first axillary surgery, by time period ....337

Table 138 – Proportion of women with DCIS who did not receive ALND as first axillary surgery, by recognition status for BC and campus volume ....337

Table 139 – Association between recognition status for BC and campus volume, and the odds of not receiving ALND as first axillary surgery in women with DCIS, including volume analyses by recognition status ....338

Table 140 – Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by patient and tumour characteristics ....344

Table 141 – Sensitivity analysis: Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by time period ....345

Table 142 – Sensitivity analysis: Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), including cases with missing cN category ....345

Table 143 – Sensitivity analysis: Proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment) ....345

Table 144 – Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by recognition status for BC and campus volume ....346

Table 145 – Association between recognition status for BC and campus volume, and the odds of undergoing SLNB only (excluding pts who received neoadjuvant systemic treatment) in women with IBC and clinically negative axilla, including volume analyses by recognition status ....347

Table 146 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by patient characteristics and type of first surgery ....353

Table 147 – Proportion of women with DCIS who received breast surgery (excluding surgery leading to accidental findings), by type of first and second surgery (excluding breast reconstruction) ....354

Table 148 – Sensitivity analysis: Proportion of women with DCIS who received just one operation (excluding reconstruction), by time period ....354

Table 149 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by recognition status for BC and campus volume ....354

Table 150 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with DCIS, including volume analyses by recognition status ..... 356

Table 151 – Proportion of women with DCIS who received BCS, by recognition status for BC and campus volume ..... 357

Table 152 – Association between recognition status for BC and campus volume, and the odds of receiving BCS in women with DCIS ..... 358

Table 153 – Proportion of women with IBC who received just one operation (excluding reconstruction), by patient characteristics and type of first surgery ..... 365

Table 154 – Proportion of women with IBC who received breast surgery (excluding surgery leading to accidental findings), by type of first and second surgery (excluding breast reconstruction) ..... 367

Table 155 – Sensitivity analysis: Proportion of women with IBC who received just one operation (excluding reconstruction), by time period ..... 367

Table 156 – Sensitivity analysis: Proportion of women with IBC who received just one operation (excluding reconstruction), by in-/exclusion of cMx ..... 367

Table 157 – Proportion of women with IBC who received just one operation (excluding reconstruction), by recognition status for BC and campus volume ..... 368

Table 158 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with IBC, including volume analyses by recognition status ..... 369

Table 159 – Proportion of women with IBC who received BCS, by recognition status for BC and campus volume ..... 370

Table 160 – Association between recognition status for BC and campus volume, and the odds of receiving BCS in women with IBC ..... 371

Table 161 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by patient, tumour and treatment characteristics ..... 378

Table 162 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by time period ..... 381

Table 163 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine, six, and three months after breast conserving surgery .....381

Table 164 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by type of radiotherapy .....381

Table 165 – Sensitivity analysis: Proportion of women ≥70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, treated with or without adjuvant endocrine therapy .....382

Table 166 – Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by patient, tumour and treatment characteristics .....387

Table 167 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by time period .....390

Table 168 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by in-/exclusion of cMx .....390

Table 169 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by type of adjuvant systemic therapy .....390

Table 170 – Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume .....391

Table 171 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant chemotherapy within 4 months after surgery in women <70 years old with M0 IBC, including volume analyses by recognition status .....392

Table 172 – Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by patient, tumour and treatment characteristics .....396

Table 173 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine within 9 months after surgery, by time period .....399

Table 174 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by in-/exclusion of cMx .....399

Table 175 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by type of adjuvant systemic therapy .....399

Table 176 – Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by recognition status for BC and campus volume....400

Table 177 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant endocrine therapy within 9 months after surgery in women <70 years old with M0 IBC, including volume analyses by recognition status....401

Table 178 – Proportion of women <70 year with metastatic BC who received systemic therapy, by patient and treatment characteristics....407

Table 179 – Sensitivity analysis: Proportion of women <70 year with metastatic BC who received systemic therapy, by time period....409

Table 180 – Sensitivity analysis: Proportion of women with metastatic BC who received systemic therapy, by age category....409

Table 181 – Sensitivity analysis: Proportion of women <70 year with metastatic BC who received systemic therapy, by treatment type....409

# LIST OF ABBREVIATIONS

| ABBREVIATION | DEFINITION |
|---|---|
| ALND | Axillary lymph node dissection |
| ASCO | American Society of Clinical Oncology |
| ASR | Age-standardised incidence rate |
| ATC | Anatomical Therapeutical Chemical |
| BC | Breast cancer |
| BCR | Belgian Cancer Registry |
| BCT | Breast conserving therapy |
| BRCA | Breast cancer gene |
| BSMO | Belgian Society of Medical Oncology |
| CI | Confidence interval |
| cStage | Clinical stage |
| CT | Computerized tomography scan |
| cTNM | Clinical tumour node metastasis staging |
| DCIS | Ductal carcinoma in situ |
| DICA | Dutch Institute for Clinical Auditing |
| DKG | Deutsche Krebsgesellschaft |
| EBCTG | Early Breast Cancer Trialists' Collaborative Group |
| ECCO | European Cancer Organisation |
| ECIBC | European Commission Initiative on Breast Cancer |
| ECIS | European Cancer Information System |
| ECOG PS | Eastern Cooperative Oncology Group Performance Status |
| ER | Oestrogen receptor |
| ERQCC | Essential Requirements for Quality Cancer Care |

| | |
|---|---|
| ESMO | European Society of Medical Oncology |
| EU | European Union |
| EU-27 | 27 member states of the European Union (EU) |
| EUSOMA | European Society of Breast Cancer Specialists |
| FOD VVVL – SPF SPSCAE | Federal Public Service Health, Food Chain Safety and Environment (‘Federale overheidsdienst Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu’/’Service public fédéral Santé publique, Sécurité de la Chaîne Alimentaire et Environnement’) |
| FTE | Full time equivalent |
| GEP | Gene expression profiling |
| HER2 | Human epidermal growth factor receptor 2 |
| HR | Hazard ratio |
| IBC | Invasive breast cancer |
| ICD-9-CM | International Classification of Diseases, 9th Revision, Clinical Modification |
| ICD-10 | International Classification of Diseases, 10th Revision |
| ICD-O-3 | International Classification of Diseases for Oncology, 3rd Edition |
| IDC | Invasive ductal carcinoma |
| IHC | Immunohistochemistry (testing) |
| ILC | Invasive lobular carcinoma |
| IMA – AIM | Intermutualistic Agency (‘Intermutualistisch Agentschap’/‘Agence Intermutualiste’) |
| INCa | National Cancer Institute in France (‘Institut Nationale du Cancer’) |
| INSZ – NISS | Social security number (‘Identificatienummer Sociale Zekerheid’/’Numéro d’identification Securité Sociale) |
| IORT | Intraoperative radiation therapy |
| ISH | In situ hybridization |

| | |
|---|---|
| KCE | Belgian Health Care Knowledge Centre |
| KSZ – BCSS | Crossroads Bank for Social Security (‘Kruispuntbank van de Sociale Zekerheid’ – ‘Banque Carrefour de la Sécurité Sociale’) |
| LCIS | Lobular carcinoma in situ |
| MDT (MOC-COM) | Multidisciplinary team meeting (‘Multidisciplinair Oncologisch Consult’ (MOC)/ ‘Consultation Oncologique Multidisciplinaire’ (COM)) |
| MRI | Magnetic resonance imaging |
| MZG – RHM | Hospital discharge dataset (‘Minimale Ziekenhuis Gegevens’/’Résumé Hospitalier Minimum’) |
| NABON | National Breast Cancer Organisation Netherlands |
| NAT | Neoadjuvant treatment |
| NBCA | NABON Breast Cancer Audit |
| NCDB | National Cancer Database |
| NOS | Not otherwise stated |
| OECD | Organisation for Economic Co-operation and Development |
| OR | Odds ratio |
| OS | Observed survival |
| PAQS | Platform for Continuous Improvement in Quality of Care and Patient Safety (‘Plateforme pour l'Amélioration continue de la Qualité des soins et de la Sécurité des patients’) |
| PET-CT | Positron emission tomography-Computed tomography |
| PR | Progesterone receptor |
| PREM | Patient reported experience measure |
| PROM | Patient reported outcome measure |
| PST | Primary systemic treatment |
| pStage | Pathological stage |

| | |
|---|---|
| pTNM | Patological tumour node metastasis staging |
| Q1 | First quartile |
| Q3 | Third quartile |
| QA | Quality assurance |
| QI | Quality indicator |
| RIZIV – INAMI | National Institute for Health and Disability Insurance (‘Rijksinstituut voor Ziekte- en Invaliditeitsverzekering’/’Institut National d’Assurance Maladie-Invalidité’) |
| RR | Relative risk |
| RT | Radiotherapy |
| SD | Standard deviation |
| SE | Standard error |
| SEER | Surveillance, Epidemiology, and End Results |
| SES | Social economic status |
| SLNB | Sentinel lymph node biopsy |
| TAC/AC-T | Chemotherapeutic combination of an anthracycline agent with cyclophosphamide and taxane |
| TNM | Tumour **n**ode **m**etastasis staging |
| US | Ultrasound scan (sonogram) |
| VIKZ | Flemish Institute for the Quality of Care (‘Vlaams Instituut voor Kwaliteit van Zorg’) |
| WHO | World Health Organisation |
| ypTNM | Pathological **t**umour **n**ode **m**etastasis staging after neoadjuvant treatment |

# SCIENTIFIC REPORT

# 1 INTRODUCTION

## 1.1 The Belgian situation in a nutshell

### *1.1.1 The European incentive to establish breast clinics*

Prompted by the large differences in breast cancer survival among the member states, the European Parliament endorsed in the early 2000s two resolutions on breast cancer (BC).[1, 2] They called on the member states to make the fight against BC a health policy priority, by e.g. the introduction of a nationwide breast screening, the adoption of better information policies on the importance of breast screening, and the 'roll out of a network of certified multidisciplinary breast units which cover the entire population'.[1, 2]

The European Guidelines of 2006 defined a 'critical mass' of at least **150 newly diagnosed cases of primary BC** (at all ages and stages) per breast unit and at least 50 breast surgeries per surgeon.[1, 2] The rationale for recommending a minimum number was 'to ensure a caseload sufficient to maintain expertise for each team member and to ensure cost-effective working of the Breast Unit: the establishment of a clinic staffed by experts is expensive and must have a high through-put of patients.'[2] In addition to other staffing requirements (see also Appendix 1), each breast unit should have at least two specialised breast surgeons who spend at least half of their professional time on breast diseases and perform primary surgery on fifty newly diagnosed cancers per year.

Although the resolution's value was not legally binding, initiatives were taken in several member states, also in Belgium. Yet, the proposed minimal annual caseload rouse the emotions. This was no surprise, as at that time only fourteen out of 108 hospitals fulfilled 'the European volume norm', while 44 hospitals treated less than 50 newly diagnosed cases of primary invasive breast cancer (IBC) a year.[3]

On **1 January 2008**, the Royal Decree on the **recognition of breast clinics**[a] became effective.[4] It was based on the standards issued by European Society of Mastology (EUSOMA) and specified the norms that a hospital site had to meet in order to be recognised as a breast clinic (see Appendix 2 for more details). Importantly, the **recognition** was not assigned at the level of a hospital, but **at the level of a hospital site** (from here on called '**campus**').

One of the recognition norms was a **minimal volume of 150 new BC diagnoses**[b] diagnosed annually, to be obtained after a transition period of two years (during which the minimal annual volume was set at 100). Exceptions were made for those centres with no other breast clinic within a radius of fifty km, in which case the cut-off was kept at one hundred (i.e. also after the transition period).[4] In June 2012, the two year transition period to attain the minimal volume of 150 new BC diagnoses, was extended to four years.[5]

In 2008, 41 Belgian hospital campuses received the recognition of breast clinic; this number increased to 53 by December 2013.*(Federal Public Service Health, Food Chain Safety and Environment, personal communication)*

### *1.1.2 The move to coordinating and satellite breast clinics – a further reduction in the minimal level of activity*

The Royal Decree of 15 December 2013 (effective on 3 January 2014) introduced the distinction between '**coordinating breast clinics**'[c] and '**satellite breast clinics**'[d] (for more details see section 2.2.2.2).[6] Through this Royal Decree a further reduction in the minimal level of activity of breast clinics was installed: for the **coordinating breast clinics** the minimal level of activity was set at **125 new BC diagnoses**[b] and for the **satellite breast clinics** at **60**.[6]

The Royal Decree of 19 April **2014** (effective on 2 January 2014) further reduced the minimal annual volume per surgeon from 50 to 30 breast surgeries per year; the principal argument for this further reduction in minimal level of activity being access of care.[7]

Despite the legislator's initial intention to concentrate specialised BC care in dedicated breast clinics, many BC patients are still being treated outside the recognised centres (see section 2.2.2.3). This is legal as the law does not prohibit physicians working in hospital campuses without recognition for BC, from treating patients with BC.

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[a] The breast clinics were also referred to as 'specialised oncological care programme for breast cancer' ('gespecialiseerd oncologisch zorgprogramma voor borstkanker'/'programme de soins oncologiques spécialisé pour le cancer du sein').

[b] 'New breast cancer diagnosis' comprises any case of breast cancer, of any type and at any stage, including in situ cancers, which is diagnosed for the first time and which is treated within the breast clinic. In case the initial diagnosis was made in a centre other than the breast clinic where the first treatment was performed, the case will be included in the volume of the treating breast clinic. The following cases are not included in the hospital volume of the breast clinic: 1) patients referred for radiotherapy to the breast clinic; 2) patients who already received primary treatment in another hospital or in another campus of a hospital; 3) patients who are only referred for adjuvant systemic therapy; 4) patients for whom only the follow-up is organised in the breast clinic after the primary treatment has taken place in another hospital or campus of a hospital; 5) patients who were referred to another hospital or another campus after the first diagnosis had been made in the breast clinic.

[c] Coordinating breast clinic, referred to in Dutch as: 'coördinerend gespecialiseerd oncologisch zorgprogramma voor borstkanker', and in French as 'le programme de soins oncologiques spécialisé coordonné pour le cancer du sein'.

[d] Satellite breast clinic, referred to in Dutch as 'het gespecialiseerd oncologisch zorgprogramma voor borstkanker', and in French as 'le programme de soins oncologiques spécialisé pour le cancer du sein'.

## 1.2 Research questions

Currently, Belgian residents confronted with BC are not only being cared for in coordinating and satellite breast clinics, but also in campuses without recognition for BC, where they may lack the multidisciplinary staffing and guidance at diagnosis, during treatment but also during follow-up (e.g. revalidation phase), which is provided for by law in the recognised campuses. Patient associations further raised the concern that it is not transparent for patients which campus has an official recognition for BC, as some hospitals/campuses without recognition for BC provide misleading information on e.g. their website, or even use the label 'breast clinic' while they do not have a recognition for BC.

These concerns led to the **main research questions** for this report:

1. Is there an association between the **recognition status** of a hospital campus (coordinating breast clinic, satellite breast clinic and campus without recognition for BC) and **observed survival** in women diagnosed with IBC, adjusted for a range of patient and tumour characteristics?
2. Is there an association between the **recognition status** of a hospital campus and **processes of care** and other outcome indicators (e.g. reoperation) in women diagnosed with BC, adjusted (where indicated) for a range of patient and tumour characteristics?

Against all expectations, exploratory analyses at the outset revealed that there was considerable discordance between the recognition status and the average annual volume of a campus: two in five coordinating breast clinics had an average annual volume below 125, while one in ten campuses without recognition for BC had an average annual volume above sixty (Table 1). Therefore, the main research questions were also formulated and analysed in an **alternative way**, i.e. based on the average annual volume, using the volume thresholds defined by the legislator:

3. Is there an association between campus volume and observed survival in women diagnosed with IBC, adjusted for a range of patient and tumour characteristics?
4. Is there an association between campus volume and processes of care in women diagnosed with BC, again adjusted (where indicated) for a range of patient and tumour characteristics?

**Table 1 – Number of campuses in December 2018, by recognition status and average annual volume**

| | Average annual campus volume* (n, %) | | | |
|---|---|---|---|---|
| | ≥125 | [60, 125[ | <60 | Total |
| **Recognition status for BC** | | | | |
| **Coordinating breast clinic** | 32 (61.5) | 17 (32.7) | 3 (5.8) | **52** |
| **Satellite breast clinic** | 0 | 10 (76.9) | 3 (23.1) | **13** |
| **No recognition for BC** | 1 (1.7) | 7 (11.7) | 52 (86.7) | **60** |
| **Total (units of analysis at campus level)** | **33** | **34** | **58** | **125** |

*BC: breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see also section 4.5)*
*Source: BCR-IMA-HDD*

## 1.3 Secondary objectives

Over the past decade, the Belgian Health Care Knowledge Centre (KCE) and the Belgian Cancer Registry (BCR) have engaged in quality improvement initiatives for cancer patients. For that purpose an ideal integrative quality system in oncology was kept in mind: it starts with the development and implementation of clinical practice guidelines, followed by the development of a set of indicators aiming at measuring and improving quality of care. Individual feedback is then provided to all hospitals by the BCR and may lead to corrective actions to improve quality.[8]

This improvement cycle has already been successfully implemented for several cancers at the national level: rectum (in collaboration with PROCARE),[9] breast,[10] testis,[11] oesophagus, stomach,[12] lung,[13] head and neck,[14] and ovarian cancer.[15]

In line with these reports, this study had also some secondary objectives:

- To adapt a selection of EUSOMA quality indicators (QI) to the Belgian context, so that they can be used for subsequent quality assurance initiatives;
- To provide results for these QIs at a national level and at the level of hospitals/campuses, in order to portray the current patterns of care offered to women affected by BC and to provide insight in the variability between the hospitals/campuses; to compare the results obtained in 2014 - 2018 cohort with a comparison cohort, who was diagnosed with BC in 2009 - 2013;
- To identify flaws in data registration and/or data collection which hamper the calculation of certain quality indicators;
- To provide individual feedback to each Belgian hospital/campus (by the BCR), with its own results benchmarked to results obtained by other (blinded) hospitals/campuses.

## 1.4 Target audience

This report is primarily intended for Belgian policymakers competent for public health and health care, both at the federal and at the regional level. In the second place, the results will be of interest to health professionals and hospitals who provide care for patients affected by BC.

We acknowledge that the information needs of some other stakeholders, more precisely patient associations and individual patients, may not be fully addressed. In Appendix 5 we provide a full list of recognised coordinating and satellite breast clinics per hospital network (status September 2022), but we do not provide any results (outcome or process) per campus/hospital. All analyses were performed blinded and all results are reported anonymously. We did so because we wanted to emphasize the honest and constructive evaluation of the results, with a focus on quality improvement rather than competition between hospitals. Hence, this report does not reveal which campus/hospital 'performs better'. As is explained below, patient reported outcomes and experiences are still not routinely collected and could hence not be analysed.

## 1.5 Methodology

To answer the aforesaid research questions, the following research methods were applied:

- A review of policy documents, national and international reports, and the international literature, leading to – among others – the identification of process quality indicators (QIs) needed to answer research question 2 (see section 3);
- The consultation of stakeholders, through:
  - Online surveys, numerous online expert meetings and where indicated email communication in the course of the project with medical professionals (hereinafter called 'the clinical experts'; see the colophon). The clinical experts all have profound expertise and experience in the diagnosis and treatment of patients with BC. They work in academic and non-academic centres, geographically spread over the country, and know the Belgian context (e.g. fees, invoicing rules) very well.
  - Face-to-face online interviews with medical professionals working in coordinating and satellite breast clinics and campuses without recognition for BC (hereinafter called 'the interviews'; see the colophon);
  - Face-to-face and online consultations with three groups of stakeholders, at the start of the project and in the final phase: patient representatives, representatives of healthcare providers involved in breast cancer care and representatives of the federal and federated health authorities (hereinafter called 'the stakeholders'; see the colophon);

- The analysis of cancer registry and other available data of a cohort of women diagnosed with BC in 2014 - 2018 (see section 4), which included two validation phases:
    - The validation in 10 Belgian hospitals of, among others, the hospital assignment algorithms and the identification of diagnostic and therapeutic procedures (hereinafter called 'the pre-validation'; see section 4.8)
    - The validation of the results of the process indicators, the assigned patient volumes and the distribution of these volumes over different campuses in all Belgian hospitals (hereinafter called 'the validation'; see section 4.9)
- A review of this report by three independent scientific experts (hereinafter called 'the validators'; see the colophon).

## 1.6 Structure of the report

In **chapter 2** we provide the reader with some background information on BC and discuss at greater length how BC care is organised in Belgium. We also zoom in on some quality improvement initiatives taken at the European level.

**Chapter 3** gives a concise description of the identification, selection and operationalisation of the process QIs used to answer research question 2;

**Chapter 4** is dedicated to the description of the database, the identification of the study cohort, the assignment of patients to a campus/hospital, the statistical analyses, the pre-validation and validation studies, and the strengths and limitations of the data.

In **chapter 5** we describe the cohort that was selected for this study: the patient and tumour characteristics, the main diagnostic and therapeutic procedures and the 5-year observed and relative survival.

In **chapter 6** we focus on the first research question: Is there an association between the recognition status of a hospital campus and the observed survival in women diagnosed with IBC? And the related sub-question: Is there an association between campus volume and observed survival in women diagnosed with IBC?

**Chapter 7** gives an overview of the selected QIs, the national results as well as the variability between the campuses/hospitals, and offers for each QI an answer to the second research question: Is there an association between the recognition status of a hospital campus and the process of care, adjusted (where indicated) for a range of patient and tumour characteristics? The association between campus volume and processes of care, again adjusted (where indicated) for a range of patient and tumour characteristics, is also assessed.

In **chapter 8** a brief discussion of the most important findings is provided, as well as a discussion of the strengths and limitations of the study.

In **chapter 9** we reflect on how the situation can be improved and formulate policy recommendations to that end.

# 2 BACKGROUND

## 2.1 Breast cancer, the most commonly diagnosed cancer among women

BC is a malignant tumour, which most commonly either develops in the cells of the lobules (the milk-producing glands) or in the ducts that drain the milk from the lobules to the nipple. Less frequently, BC starts in the stromal tissues, the fatty and fibrous connective tissues of the breast.

In the EU-27 countries, BC is the **most frequently occurring cancer**: in 2020, BC accounted for 13.3% of all new cancer diagnoses; in women it accounted for 28.7% of all new cancers.[16] Increasing incidence trends in the EU-27 have been attributed to multiple factors, among others to reproductive factors, increasing obesity and physical inactivity, but also to increased screening intensity.[16] With an **age-standardised incidence** (ASR)[e] of **194.0 per 100 000 population**, Belgium had in 2020 the highest IBC incidence among the EU-27 countries (Figure 1).[17] The EU-27 average was 142.8 per 100 000 population.[17]

Thanks to improvements in the management and treatment of BC, and to tools for detecting BC at early stages, mortality trends for IBC are declining in the EU-27 countries.[16] The largest falls are observed in young women: -22% in women aged 20-49 years between 2002 and 2012.[18] In 2020, the **age-standardised**[e] **mortality rate** for IBC in Belgium was **36.1 per 100 000 population**, somewhat higher than the EU-27 mean (34.1 per 100 000 population).[17]

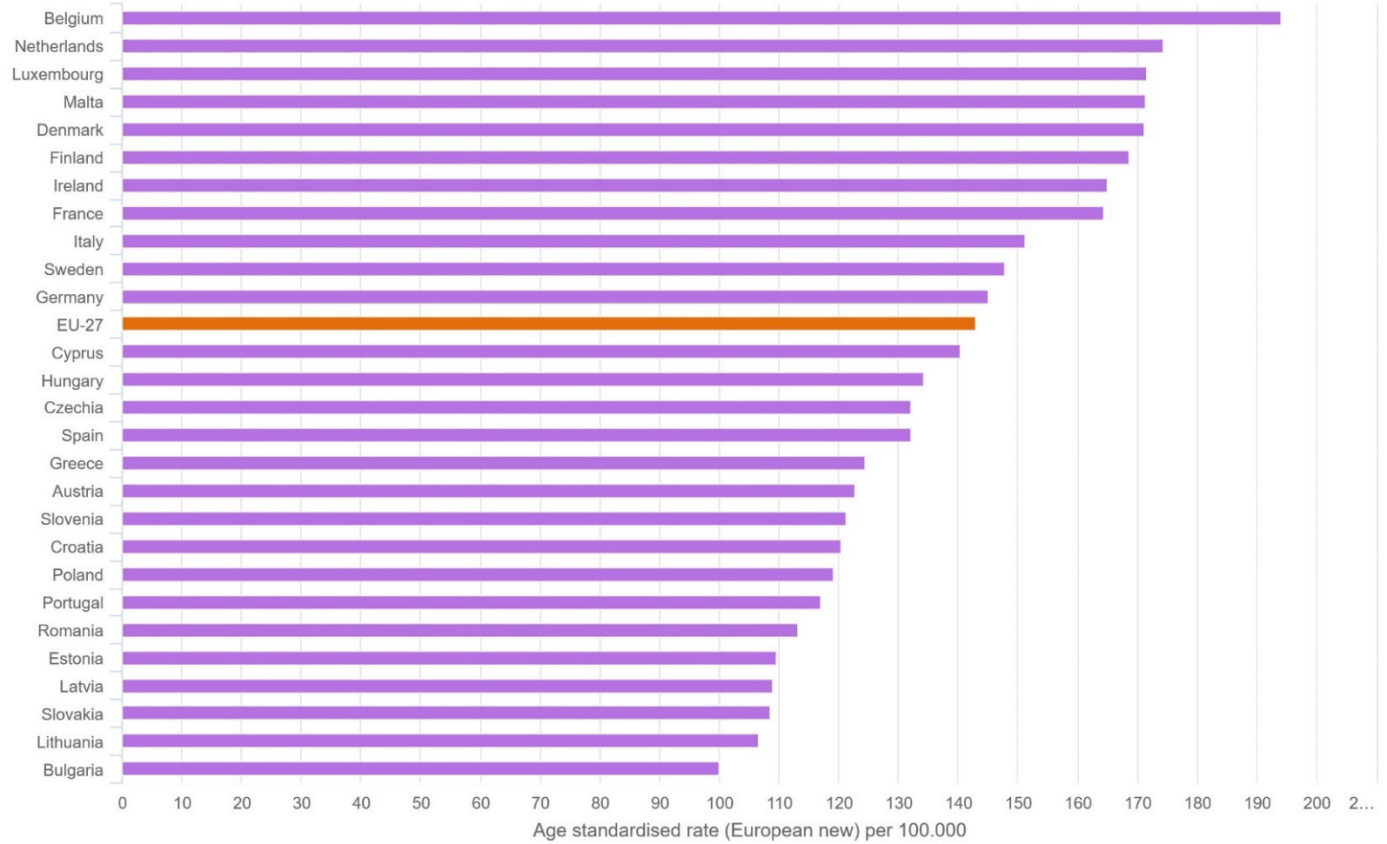
The OECD health data website provides age-standardised 5-year net survival data[f] for women diagnosed with IBC in 2010-2014: for women living in Belgium, the age-standardised 5-year net survival probability was 86.4%, which was in line with other Western European countries, but lower than what was observed in Northern European countries (Figure 2). Differences between countries can – in part – be explained by differences in genetics, socio-economic status, and exposure to risk factors, but also by differences in health policies (e.g. BC screening programmes) and in registration, by varying levels of healthcare expenditure, variability in organisation of care and resulting quality of diagnosis and treatment.[16, 19]

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e The age-standardised incidence rate is a weighted mean of the age-specific rates where the weights are taken from the population distribution of a standard population. The comparison of rates referring to different time periods or different geographical areas should only be done after considering the differences in the age structure of the underlying populations. This is done through age-standardisation: rates are arithmetically adjusted to have the same age structure of a standard population. The age-standardised incidence rate presented here is based on the new European Standard Population. When the old European Standard Population is used, the age-standardised incidence rate for Belgium in 2020 was 152.3 per 100 000 population and the EU-27 average 112.1 per 100 000 population.[17]

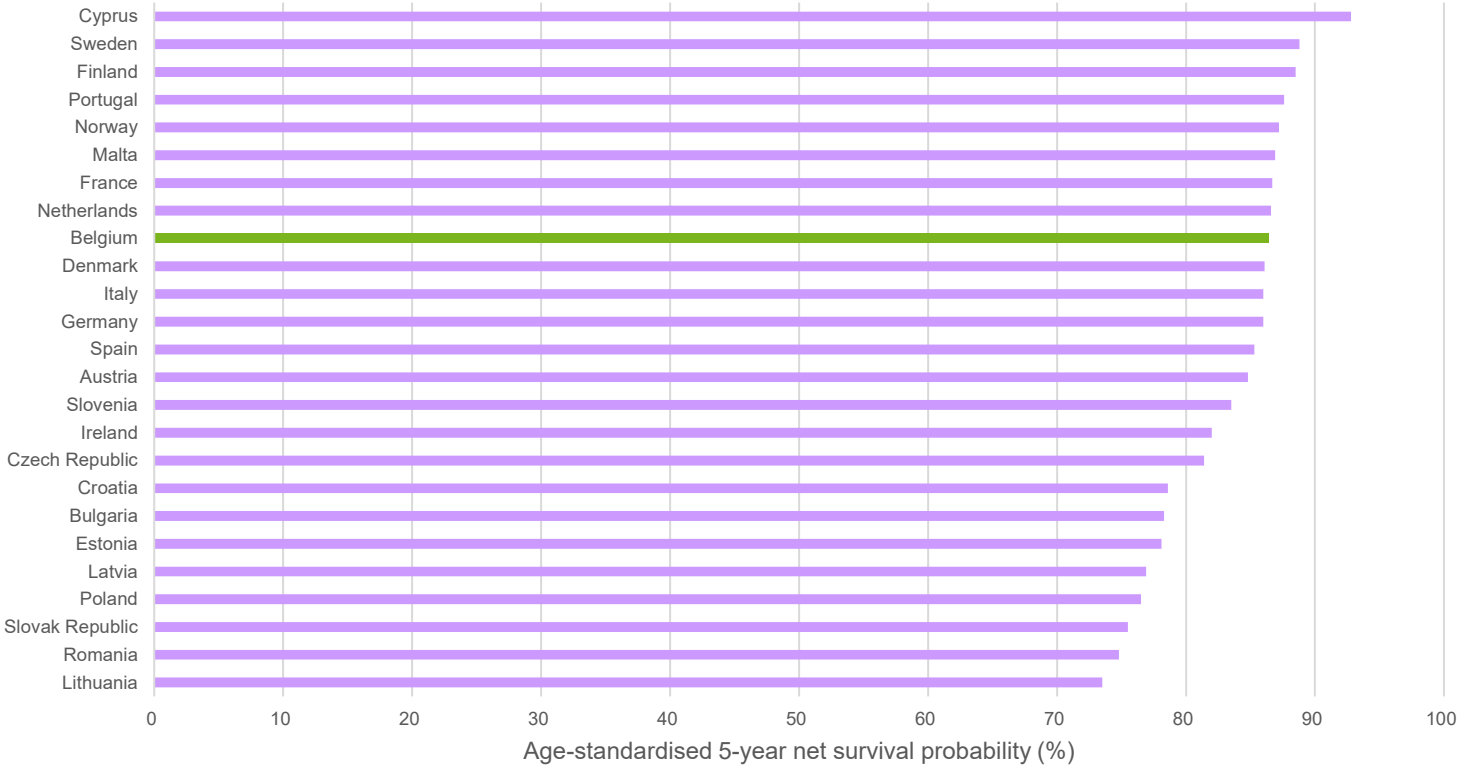
f Five-year net survival is the cumulative probability that cancer patients survive their cancer for at least five years since diagnosis, in absence of death from other causes, and taking into account that competing risks of deaths are higher in the elderly. The period approach was used to allow estimation of five-year survival when five years of follow-up were not available. Cancer survival estimates are age-standardised with the International Cancer Survival Standard (ICSS) weights.

**Figure 1 – Estimated incidence of IBC in women (all ages) in 2020, by country**




*Source: European Cancer Information System (ECIS)*[17]

**Figure 2 – Age-standardised 5-year net survival probability for women diagnosed in 2010-2014 with IBC, by country**




*Source: OECD health statistics*[20]

## 2.2 Breast cancer care in Belgium

### 2.2.1 Screening for breast cancer

Over the last decades, Belgium evolved through six state reforms into a federal state. The competences for a broad range of matters, including health, were transferred in part to the federated entities (the regions). They have become responsible – among others - to define the licensing norms for hospitals, but also for public health, e.g. health promotion and disease prevention, vaccination and the screening programmes for breast, colorectal and cervical cancer.[21]

The BC screening programme started in 2001 in the Flemish region (northern region), and in 2002 in Brussels (capital region) and the Walloon region (southern region). All women aged 50 to 69 are invited to have a screening mammography every other year. The procedure is free of charge for participants.

In 2016, the coverage of the programme was 33.2%, with important differences in participation between the regions: in the Flemish region 50.7%, in Brussels 10.9%, and in the Walloon region 6.8%.[22] When also mammograms were included which were performed beyond the context of the organised screening programme, the coverage was 61.8%, with smaller differences between the regions (the Flemish region: 67.4%, Brussels: 52.9%, and the Walloon region: 53.9%).[22] Yet, this 'overall' coverage is still far below the European target of 90% of the target population being offered breast, cervical and colorectal cancer screening by 2025.[23]

The most recent data available on the IMA – AIM website indicate that the coverage of the screening programme remained stable in the Flemish region and Brussels (50.1% and 10.4%, respectively, in 2019) and decreased slightly in the Walloon region (4.7% in 2019).[24]

### 2.2.2 Concentration of breast cancer care, only to some extent

#### 2.2.2.1 The foundations for the breast clinics

The Royal Decree of 26 April 2007 laid the foundations for the breast clinics in Belgium.[4] It stipulated by and large the criteria listed in Box 1. More details can be found in Appendix 2. In **June 2012**, the two year **transition period** to attain the minimal level of activity of 150 new BC diagnoses was **extended to four years**.[5]

**Box 1 – Recognition criteria for breast clinics (Royal Decree of 26 April 2007) – Main outlines**

- **Care program**: A campus can only be recognised as breast clinic if it also has an oncology care programme (see Appendix 3), in other words: hospitals that have a care programme for basic oncological care cannot be recognised as breast clinic;
- **Minimal volume**: A breast clinic must have a minimal annual activity of at least 150 new BC diagnoses (after a transition period during which 100 new diagnoses a year is sufficient);
- The **medical coordination** of the breast clinic is performed either by a specialist in surgery or gynaecology, a specialist in medical oncology, or a specialist in radiotherapy-oncology; (s)he must work on a full-time basis at the hospital and spends at least eight half-days a week on the treatment of BC;
- A breast clinic must have at least the following **medical specialists**, each with a minimal annual volume and with at least three years' experience:
  - Two specialists in surgery or in gynaecology with a specific expertise in BC surgery (minimal annual volume: 50 surgical interventions);

- Two medical specialists in X-ray imaging with experience in mammography and echography of the breast as well as in the technique of breast sample biopsies (minimal annual volume: 1000 mammographies);
- One medical specialist in pathological anatomy, available at all times and present at the campus during the surgical interventions;
- One medical specialist in radiation oncology;
- One medical specialist in medical oncology who spends at least 8 half-days at the hospital which runs the breast clinic;
- One medical specialist in plastic, reconstructive and aesthetic surgery who has experience in the treatment of patients with BC;

- The nursing care of patients with BC should be coordinated by a **nurse-coordinator**;
- The breast clinic must also have a **psychologist**; the psychosocial support of patients should be guaranteed during all stages of the disease;
- The breast clinic must have **physiotherapists** who are specialised in the prevention of post-operative and post-radio therapeutic lymphoedema and shoulder stiffness;
- A **multidisciplinary consultation** must take place every week for all newly diagnosed patients, and at least before any treatment;
  - At least one physician from each of the medical disciplines participating in the breast clinic (cf. supra), a nurse and a psychologist must attend the MOC-COM and if indicated, a plastic surgeon must also attend;
  - For each multidisciplinary consultation a report is made, which includes a comprehensive description of the primary treatment that will be proposed to the patient and a description of the proposed medical follow-up;
- In addition to the **registration requirements** defined for the oncological care programmes, breast clinics have to register (in coded form):
  - The results of analyses regarding hormonal receptors (ER and PR);
  - The results of analyses regarding HER2 antigens;
- On the site (campus) of the breast clinic, sufficient ambulatory **consultations** must be organised so that:
  - Every new patient with a suspicion or a proven BC who presents at the breast clinic, is seen within five days;
  - In order to ensure that these patients are offered **multidisciplinary advice** during these consultations, a medical specialist in surgery or gynaecology, a medical specialist in radiology, a medical specialist in radiotherapy and a medical specialist in medical oncology must be present at the campus, and if feasible, within the same unit;
  - During these consultations, a clinical examination, the necessary medical imaging examinations and the collection of breast biopsies must be possible;
  - The diagnosis and the treatment plan are communicated with the patient within a maximum of five working days[g] from the first contact; during these consultations a nurse with experience in the management of BC and the psychologist(s) of the breast clinic must be available;

[g] In the RD of 2013, 'five working days' has been replaced by 'as soon as possible'.

- The **surgical infrastructure** must be organised in such a way that:
  - the surgical intervention can - if indicated – take place within a period of fifteen working days from the moment the patient is informed about the surgical intervention;
  - the reconstruction - if indicated – does not cause a delay of the breast surgery;
- The breast clinic must ensure that it can offer **radiotherapy** within three weeks after breast surgery if no systemic treatment is required.

*Source: Royal Decree of 26 April 2007*[4]

#### *2.2.2.2 The introduction of coordinating and satellite breast clinics*

The Royal Decree of 15 December 2013 (effective on 3 January 2014), introduced the coordinating and satellite breast clinics, and defined them as follows:[6]

- The **coordinating specialised oncological care programme for BC** [‘*coordinating breast clinic’*] consists of a package of patient care, comprising the diagnosis, the multidisciplinary consultation, the multidisciplinary treatment, rehabilitation and follow-up of patients with malignant diseases of the breast(s). The coordinating specialised oncological care programme for BC diagnoses annually at least **125 new BCs**;
- The **specialised oncological care programme for BC** [‘*satellite breast clinic’*] which consists of a package of patient care, comprising the diagnosis, the multidisciplinary treatment, rehabilitation and follow-up of patients with malignant diseases of the breast(s). The specialised oncological care programme for BC diagnoses annually at least **60 new BCs** and has a formal collaboration with a coordinating breast clinic.

Compared to what was stipulated in the initial Royal Decree of 2007, the Royal Decree of 15 December 2013, did not only include a reduction of the minimal annual volume, but also some adaptations on e.g. staffing requirements. The **most important adaptations** for the **coordinating breast clinics** are provided in Box 2.[6]

**Box 2 – Main adaptations for the coordinating breast clinics (Royal Decree of 15 December 2013)**

- The reduction of the minimal annual threshold to at least 125 new BC diagnoses[b];
- The appointment of at least a half-time psychologist who has significant experience in the counselling of patients with BC, and in case of a formal collaboration with a satellite breast clinic, the appointment of an additional 0.25 FTE psychologist;
- The opening of a rehabilitation programme, comprising physical, psychological and social rehabilitation;
- The provision of the necessary equipment and infrastructure so that
  - every patient who presents at the coordinating breast clinic is seen within five days during a multidisciplinary consultation, during which both a medical specialist in surgery, a medical specialist in radiotherapy, as well as a medical specialist in oncology are available;
  - the care plan can be initiated within ten working days after the diagnosis has been made;
- The five-yearly submission of a report, including the hospital mortality data, to the Minister responsible for public health.

*Source: Royal Decree of 15 December 2013*[6]

In addition, the Royal Decree of 15 December 2013 also **introduced the satellite breast clinics**;[6] the main outlines are listed in Box 3**.**

**Box 3 – Main outlines for the satellite breast clinics (Royal Decree of 15 December 2013)**

- Must have a minimal annual threshold of at least 60 new BC diagnoses[b];
- Must have a formal collaboration agreement with a coordinating breast clinic, which provides the medical coordination and the chairmanship for the multidisciplinary consultation;
- Must fulfil the same medical staffing and rehabilitation staffing requirements as the coordinating breast clinics;
- Must appoint a half-time breast nurse and a half-time psychologist.

For more details on the recognition requirements defined for the coordinating and satellite breast clinics, the reader is referred to Appendix 4.

#### *2.2.2.3 Coordinating and satellite breast clinics, but also breast cancer care outside these recognised centres*

Currently, patients affected by BC are treated in Belgium in coordinating and satellite breast clinics, but also outside these recognised centres. As was said before, the law does not prohibit campuses without recognition for BC from offering BC care, and there are no financial penalties for patients or providers. In 2018, for instance, almost one in five patients diagnosed with BC (ductal carcinoma in situ (DCIS) or invasive breast cancer (IBC)) was treated in a campus without recognition for BC (Table 2). Hence, the quality of care and the multidisciplinary approach, which are provided through the criteria stipulated for the coordinating and satellite breast clinics, may not be offered to patients with BC who are treated in campuses without recognition for BC. Also, only 57.4% of all patients affected by BC in 2018 were treated in coordinating breast clinics that fulfilled the volume criterion.

**Table 2 – Distribution of patients diagnosed with DCIS or IBC in 2018, by recognition status and average annual volume of the campus**

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC** | | | | |
| **Coordinating breast clinic** | 5 518 (78.6) | 1 482 (21.1) | 18 (0.3) | **7 018** (73.0) |
| **Satellite breast clinic** | 0 | 655 (83.9) | 126 (16.1) | **781** (8.1) |
| **No recognition for BC** | 150 (8.3) | 411 (22.6) | 1 254 (69.1) | **1 815** (18.9) |
| **Total** | **5 668 (59.0)** | **2 548 (26.5)** | **1 398 (14.5)** | **9 614** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see also section 4.5)*
*Source: BCR-IMA-HDD*

#### *2.2.2.4 Recognition at the campus level, not at the level of the hospital*

It is important to emphasize that the **recognition of coordinating and satellite breast clinics** is awarded **at the level of a hospital campus** (site/facility), not at the level of the hospital. You may thus have hospitals in Belgium with a campus recognised as coordinating breast clinic, another campus with a recognition as satellite breast clinic and a third campus without recognition for BC care. Therefore, the bulk of analyses were performed at the level of the campus (see section 4.4.2).
However, from the discussion with the clinical experts and from the feedback provided during the interviews and on the occasion of the validation study

(see section 4.9), we learnt that in daily practice several forms of collaboration between campuses and between hospitals have been installed over the years, ranging from the minimal requirements as defined in the Royal Decree (see Appendix 4), to whole medical and para-medical teams traveling between two campuses (e.g. one with recognition, the second without) and 'offering in both the same care'.
Nevertheless, since it was impossible to categorise or quantify the various forms of collaboration, it was impracticable to take them into account in the analyses. Hence, we had to adhere to the **official recognition status of each campus** in the analyses.

#### 2.2.2.5 *Financing by federal health authorities, but recognition by regional health authorities*

In addition to the financing of the oncological care programs for paramedical staff (e.g. data managers, oncological nurse, psychologist) based on the number of MDTs), the coordinating and satellite breast clinics receive annually a dedicated budget of € 85 855.44 euro (index 1 January 2011; indexed amount in June 2022: € 106 749.64) from the federal public authorities[h].[25] This amount is the same for the coordinating and satellite breast clinics, and is not dependent on the annual volume of patients.*(Federal Public Service Health, Food Chain Safety and Environment, personal communication)*

As a result of the sixth State Reform, the regions have become competent for the care policy at the level of care facilities (with the exception of those authorisations that are explicitly reserved for the federal government), preventive healthcare and the recognition of healthcare professions.[26] For BC care, this implies that the regions are responsible for the recognition, the quality and audit of the coordinating and satellite breast clinics.

In view of the responsibility of quality assessment and assurance in health care facilities, the Flemish Institute for Quality of Care ('Vlaams Instituut voor Kwaliteit van Zorg', VIKZ) was founded in 2017. VIKZ aims to improve quality and safety of care by measuring and publicly reporting results on evidence-based quality indicators. Via Zorgkwaliteit.be VIKZ offers healthcare facilities a platform for valid and user-friendly information and comparison of the quality of care in Flanders.[27] For BC, VIKZ provides the onymous results for various quality indicators of all Flemish hospitals which treated patients diagnosed with BC in 2012-2014. Updated results will be published following this report.
A similar agency exists in Brussels and the Walloon region, i.e. 'Plateforme pour l'Amélioration continue de la Qualité des soins et de la Sécurité des patients' (PAQS); it has not taken initiatives of the same kind yet for BC care.

#### 2.2.2.6 *Geographical distribution of coordinating and satellite breast clinics*

On 1 September 2022, there were 51 coordinating and 20 satellite breast clinics in Belgium. They are not evenly spread over the territory (see Figure 3). The distribution is to some extent related to the incidence of BC: in Brussels, for instance, where BC incidence is very high, there is a high concentration of coordinating breast clinics. On the other hand, in the province of Luxemburg (south of Belgium), where the incidence of BC is very low, there are no coordinating or satellite breast clinics.

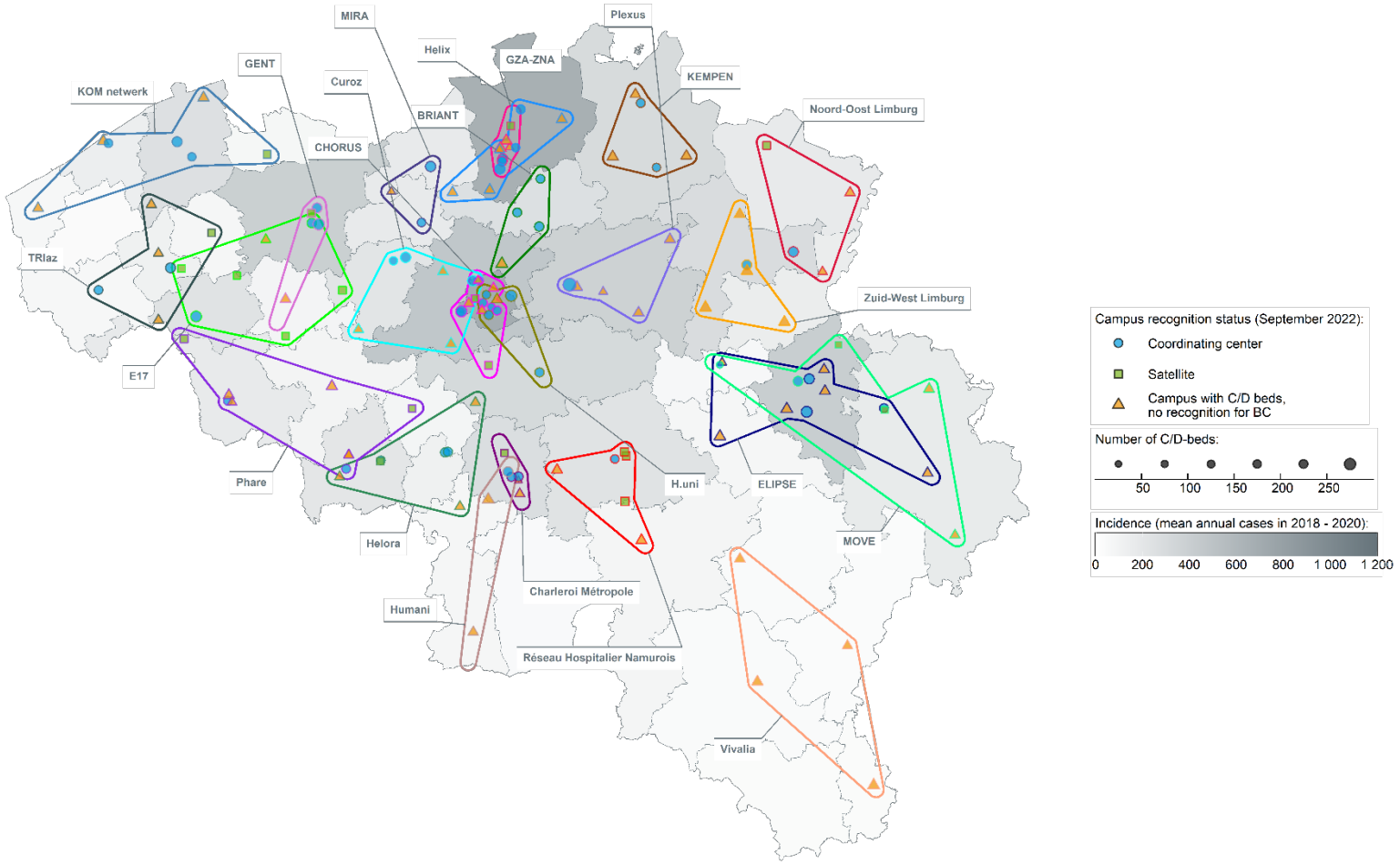
The distribution of coordinating and satellite breast clinics within the locoregional hospital networks[i] indicates that all networks have at least one coordinating breast clinic. There is one exception: Vivalia, in Luxembourg, has no coordinating nor satellite breast clinic within its network.
A comprehensive list of coordinating and satellite breast clinics per hospital network is provided in Table 23 in Appendix 5.

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h The financing of the coordinating and satellite breast clinics is based on part B4 (article 74 nonies) of the Royal Decree of 25 April 2002, determining the budget of financial means of hospitals. This dedicated amount is supplementary to the funding allocated to the oncology care programme for additional staff based on the number of MDTs (art. 64§1 and 2 of the same Royal Decree).

i The locoregional hospital networks offer particularly a framework in which hospitals can collaborate.[28]

**Figure 3 – Distribution of the coordinating and satellite breast clinics on 1 September 2022 within the locoregional hospital networks**




*Note: The graph depicts hospital networks as of 1 January 2022; campus size is based on C/D beds, i.e. licensed acute beds for surgical care (index C) and internal medicine (index D).*
*Source: BCR, federated entities and Federal Public Service Health, Food Chain Safety and Environment*

### 2.2.3 Gene expression profiling – agreements solely with coordinating and satellite breast clinics

Gene expression profiling (GEP; e.g. Oncotype DX, MammaPrint) analyses a number of different genes within cancer cells to predict the risk of cancer progression and/or recurrence. The results of gene expression profiling tests help doctors determine who may benefit from additional (adjuvant) treatment after surgery. However, in a Health Technology Assessment on GEP tests performed by KCE, it was concluded that there was insufficient evidence to recommend the overall roll-out of this test. In addition, it was not clear on which parameters clinicians based their decision (recommendation) whether or not to treat patients at high clinical risk with preventive chemotherapy.[29, 30]

To prevent the uncontrolled proliferation of its use, to limit the budget impact and to be able to gather extra data on clinicians' (and patients') treatment decisions/strategy, a pilot project with limited access to reimbursed GEP-tests was set up in 2019. Only patients with early stage (tumour size < 5 cm, HER2 negative and ER and/or PR positive, and maximum three positive lymph nodes) treated in hospitals that entered into an agreement with the National Institute for Health and Disability Insurance (RIZIV-INAMI; i.e. 'conventie'/'convention') qualify for this reimbursed test. Only coordinating and satellite breast clinics can enter the GEP agreement.[31]

### 2.2.4 Autologous breast reconstruction – agreements solely with coordinating breast clinics

In order to clamp down on the (sometimes considerable) 'aesthetic supplements' that were charged by plastic surgeons from patients undergoing autologous breast reconstruction after mastectomy, agreements with RIZIV-INAMI were installed in 2016.[32] Patients treated in hospitals that entered into an agreement with RIZIV-INAMI, can obtain better reimbursement for the autologous breast reconstruction and face smaller co-payments. The agreement further provides greater transparency of the chargeable costs and the introduction of a number of quality requirements. Aesthetic supplements for autologous breast reconstruction are no longer allowed in hospitals that entered the agreement. Only coordinating breast clinics can engage in the agreement.[32]

## 2.3 Quality improvement initiatives at the European level

### 2.3.1 EUSOMA's position papers on specialist breast units

In 2000 the European Society of Breast Cancer Specialists (EUSOMA) published the position paper 'The requirements of a specialist breast unit'.[33] With this document, EUSOMA was the first to set out standards for establishing high-quality BC units across Europe.

The most recent update of the requirements was published in 2020, and was endorsed by the European Cancer Organisation (ECCO, as part of Essential Requirements for Quality Cancer Care (ERQCC) programme), and by the European Society of Medical Oncology (ESMO).[34] The authors call for special attention to **multidisciplinarity** and **patient-centred pathways** from diagnosis, to treatment, and to survivorship.

In the 2020 EUSOMA paper a dedicated section is included with challenges in BC care; several of these challenges do also apply to the Belgian situation and should thus be addressed when BC care is taken to the next level (Box 4).

**Box 4 – EUSOMA 2020 position paper – Non-exhaustive list of challenges in BC care**

- **Primary care physicians** must be involved in many steps of the cancer journey, starting with screening and early diagnosis; it is essential to promote **close collaboration** between these specialists and breast centres for a fast referral;
- Most pathology departments are general and may lack pathologists experienced in the **increasingly complex area of breast pathology** and may also lack **sufficient volume** of cases to develop and maintain expertise;

- The **availability of intraoperative pathology assessment** is crucial to substantially decrease the rate of re-interventions;
- Dedicated **breast nurses** are essential members of the core **MDT**; it is important that the breast care nurse present knows the **patient's wishes** and expectations to ensure they can be shared at the MDT;
- **Fertility preservation** is crucial and should be part of the breast centre's services;
- Women with higher **socioeconomic status** in Europe have a higher BC incidence but lower mortality than women in lower status groups;
- A cornerstone of research should be to investigate the **impact of intervention** on endpoints that are **patient oriented**; there is a pressing need for the development and incorporation of patient reported outcomes/measures (PROs/PROMs), and research on quality of life and survivorship;
- A particular shortcoming in BC is that few cancer registries collect **data on recurrences**, including distant, which means that there are only estimates of the number of patients living with incurable disease. This makes it hard for healthcare services and wider society to allocate resources for one of the largest populations of advanced cancer patients.

*Source: Biganzoli et al., 2020*[34]

The EUSOMA paper provides also a full list of requirements that breast centres should fulfil. Again, we focus on those that may be inspiring for the Belgian context (Box 5).

**Box 5 – EUSOMA 2020 position paper – Main outlines of requirements for breast centres**

- A breast centre must be of sufficient size to manage at least **150 newly diagnosed cases of early BC** (all ages, based on surgery) coming under its care each year. The breast centre must **also** treat at least **50 cases of metastatic BC** a year, independently from the line of treatment. The minimum number is necessary to ensure a caseload[j] sufficient to maintain expertise for each team member and to ensure cost-effective working of the breast centre;
- The breast centre should participate in **external benchmarking** activities (comparison of results with those of other centres);
- The centre must have a **formal internal review meeting** at least once a year to discuss all performance aspects;
- **Staffing requirements** [*that are more demanding than the Belgian recognition criteria for coordinating breast clinics*]:
  - At least **two breast radiographers**, each performing at least 1000 mammograms a year;
  - At least **two dedicated breast pathologists**, who must spend at least 50% of their working time on breast disease;
  - At least **two breast medical oncologists** dedicated to BC, who must spend 50% of their working time on BC;
  - At least **two radiation oncologists** dedicated to BC, who must spend at least 50% of their working time on BC;
  - At least **one medical physicist and two radiation therapists/dosimetrists** should have BC as a main interest;

[j] The EUSOMA 2020 position paper defines also the **minimum caseload for core MDT members**: Breast radiologist: 1000 mammographic exams (5000 for breast radiologists participating in a centralised screening programme), 200 breast ultrasounds and 50 magnetic resonance imaging (MRI) studies and 50 breast guided interventions per year; Breast radiographer: 1000 mammograms per year; Breast pathologist: 50 preoperative samples and 50 primary breast cancer resections per year, and should report on 25 metastatic breast surgical specimens (biopsy performed for suspicious metastasis) per year; Breast surgeon: 50 primary breast surgeries per year; Breast medical oncologist: 50 early and 25 metastatic BC patients treated per year; Breast radiation oncologist: 50 early breast cancer patients treated per year; Breast nurse: 50 early and 25 metastatic breast cancer patients cared for per year.[34]

- At least **two physiotherapists** with expertise in lymphatic drainage for the treatment of lymphoedema and its related sequelae, and to ensure good shoulder mobility; Physiotherapists with expertise in rehabilitation of metastatic patients with sequelae of bone or brain metastases and their treatments must be available for breast centre patients;
- At least **two breast care nurses** dedicating all their working time to BC;

- A **psychiatrist** must also be available to patients;
- The breast centre must have access to **geriatricians with oncology experience**.

*Source: Biganzoli et al., 2020*[34]

### 2.3.2 The European Commission Initiative on Breast Cancer

Despite the two European Parliament resolutions of 2003 and 2006 (see also 1.1.1),[1, 2] and despite numerous resolutions and declarations issued since then, which repeated – among others – the call to ensure that all women and men affected by BC in Europe are treated in **multidisciplinary specialist breast units** and to develop a **certification protocol for specialist breast units** in accordance with EU Guidelines by 2011,[35] a survey held in 2016 revealed that the implementation remained a challenge[k].[37] In most countries the 2016 deadline for all patients to access breast centres was not met.[38]

Few respondents of a survey for EU member states reported having breast units mandated by law, and about half have recommendations for breast units. Not many have national or local accreditation, and only a minority of respondents noted that mandatory requirements for multidisciplinary teams, training and professional development are in place.[37] The **minimal case-load of 150 newly diagnosed cases of primary BC**, was also implemented to various extends. In countries like Finland, Norway, Sweden and France, the minimal annual case-load was not mandatory, but according to the respondents, most primary BC cases were treated in a centre which volume was higher than 150 new cases per year.[37]

Meanwhile, the European Commission Initiative on Breast Cancer (ECIBC[l]), was initiated; its overall goal is to improve health and to reduce health inequalities in Europe by ensuring, improving and harmonising the quality of BC services across European countries on a sustainable basis.[19] ECIBC has developed evidence-based recommendations on BC screening and diagnosis (under the European Commission's Joint Research Centre coordination),[39] which are easy to access online through a user-friendly interface and easily understandable by the public at large thanks to a clear and comprehensible wording.[40] On the ECIBC website, one can also find a collection of national and international guidelines on BC care, referred to as the 'Guidelines Platform'.

In spring 2021, ECIBC published the Manual for Breast Cancer Services. This European quality assurance (QA) scheme 'is a collection of 86 quality and safety requirements, based on evidence, that can be followed by any BC service wishing to improve the quality of care offered to women'[m]. It covers the full extent of BC management, from screening to follow-up and end-of-life care.[45] Several requirements have been translated into quality indicators, some of which are also elaborated in this report (which is then mentioned in a footnote). In Box 6 some requirements are listed that are not fulfilled/endorsed yet in Belgium.

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k The EU does not define health policies, nor the organisation and provision of health services and medical care in the member states; the EU's role is to support national policies.[36] It is up to national governments to organise healthcare and ensure that it is provided.

l https://healthcare-quality.jrc.ec.europa.eu/

m To support the implementation of the QA scheme, a self-assessment tool is available,[41] and a quality indicators calculator is under development. The latter will help BC centres to calculate QIs in a standardised way in order to measure compliance with the QA scheme.[42] The QA scheme is in a testing phase;[43] it will be finalised based on the outcomes obtained during feasibility checks in real settings and a pilot run of the certification process.[44]

**Box 6 – ECIBC's Manual for Breast Cancer Services – Non-exhaustive list of quality and safety requirements**

1. The Breast Cancer Services must have a clinical director and the following **professionals**: radiologists, radiographers, oncoplastic breast surgeons (or both a breast surgeon and a plastic surgeon), pathologists, medical oncologists, radiation oncologists, breast care nurses, data managers, psycho-oncologists, clinical geneticists, clinical psychologists, nuclear medicine specialists, medical technical assistants, physiotherapists, nutrition specialists and lymphoedema specialists. Professionals can be in the same hospital or associated through a written agreement/contract;
2. The abovementioned healthcare professionals working in the Breast Cancer Services are **trained in communication skills and shared decision making** periodically (at least every 5 years), to be demonstrated by attendance certificates;
3. The Breast Cancer Services must have a policy for **routine measurement of patient-reported outcomes** to monitor the well-being of women with BC throughout the care pathway;
4. The Breast Cancer Services must have a written policy on informing patients about the **possibility of fertility preservation**;
5. The Breast Cancer Services must have **at least two breast care nurses** available throughout the entire patient pathway to ensure continuity of care;
6. Each pathologist working in a BC centre must personally perform at least **100 routine assessments of breast specimens per year**;
7. Each surgeon performing BC surgery must personally carry out the **primary surgery on a minimum of 50 newly diagnosed BCs per year**.

*Source: Janusch Roi et al., 2021*[45]

In 2021, Europe's Beating Cancer Plan was also published; it outlines the Commission's will to establish, by 2025, an EU Network linking recognised National Comprehensive Cancer Centres in every Member State.[23] The Cancer Plan aims to ensure that 90% of eligible patients have access to such centres by 2030.

# 3 IDENTIFICATION, SELECTION AND OPERATIONALIZATION OF PROCESS INDICATORS

## 3.1 Identification and selection of possible quality indicators

Possible quality indicators (QIs), needed to answer the second research question, were identified from previous work on quality of care in BC performed in Belgium and Europe:

- The KCE report on QIs in BC (2010), developed in close collaboration with the Belgian Cancer Registry (BCR), presenting results for 13 process indicators and the association between volume and outcomes (incidence years: 2001-2006);[10]
- The BCR evaluation of the quality of care offered to patients diagnosed with BC in 2012-2014 (2017), refining some QIs from the KCE report;
- The EUSOMA position paper (2017), describing the updated set of benchmark QIs that could be adopted by breast centres to allow standardised auditing and quality assurance and to establish an agreed minimum standard of care. For the present study, only the 'mandatory requirements' were considered;[46]
- The QIs developed by the Belgian Society of Medical Oncology (BSMO) and BCR, dedicated to systemic treatment of BC (incidence years: 2010-2014) with a strong emphasis on elderly patients, metastatic patients and molecular subtyping;[47-51]

The resulting long list can be consulted in Appendix 6 (Table 24). After removal of doubles and slight reformulation of some QIs (e.g. due to availability of some data in a structured format), the **measurability** of these QIs was assessed. To that end, the availability of data for every single element of the QIs was evaluated, which resulted in an interim list of 25 measurable QIs.

The clinical experts assessed the **clinical relevance** of this interim list in an online survey, which was completed by seventeen clinical experts. It resulted in the removal of some QIs (Table 25) and the adaptation of other QIs. The EUSOMA indicator on breast reconstruction[n] was not selected, as there was consensus among the clinical experts that without additional information on the clinical decision making process, this indicator would not inform us about the quality of care provided. Moreover, they argued that the QI may also become (inadvertently) an incentive for some clinicians to force their patients for having immediate reconstruction, in order to obtain high QI results for their campus/hospital.

During the further development of the quality indicators, the pre-validation (see section 4.8), validation (see section 4.9) and discussion with the experts, some more QIs had to be adapted or removed, often due to availability of (reliable and/or sufficiently specific) data. These issues are further discussed in section 4.10. The final list of process QIs, used to answer research question 2, is presented in Table 3.

In line with previous QI reports on BC,[10] we zoom in in this report on IBC, but, where relevant for the Belgian context, according to the clinical experts, QIs were also calculated for patients diagnosed with DCIS.

[n] EUSOMA indicator on breast reconstruction: 'Proportion of patients receiving immediate reconstruction at the same time of mastectomy'.

**Table 3 – Final selection of thirteen quality indicators**

| Category | Quality Indicator |
|---|---|
| **Diagnosis and staging** | Proportion of women with IBC who received mammography and breast sonography before any oncological treatment – Target: 95% (EUSOMA) |
| | Proportion of women with IBC with histological or cytological assessment before any oncological treatment - Target: 90% (EUSOMA) |
| | Proportion of women with IBC in whom human epidermal growth factor receptor 2 (HER2) status and/or oestrogen receptor (ER) and/or progesterone receptor (PR) status were assessed before any systemic treatment - Target: 98% (EUSOMA) |
| | Proportion of women with BC discussed at the multidisciplinary team meeting - Target: NA |
| | Proportion of women with BC for whom a valid cTNM stage is reported to the Belgian Cancer Registry (BCR) - Target: 98% (EUSOMA)<br>Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR - Target: 98% (EUSOMA) |
| **Timeliness of treatment** | Proportion of women with IBC for whom the time interval between the incidence date and the date of first treatment was ≤ 6 weeks - Target: 90% (EUSOMA) |
| **Surgery** | Proportion of women with DCIS who do not undergo axillary lymph node dissection (ALND) as first axillary surgery - Target: NA |
| | Proportion of patients with IBC and clinically negative axilla who undergo sentinel lymph-node biopsy (SLNB) only (excluding patients who received neoadjuvant systemic treatment) - Target: NA |
| | Proportion of women with DCIS who received just one operation (excluding reconstruction) - Target: 90% (EUSOMA) |
| | Proportion of patients with IBC (M0) who received a single (breast) operation for the primary tumour (excluding reconstruction) - Target: 90% (EUSOMA) |
| **Radiotherapy** | Proportion of women <70 years old with IBC (M0) who started radiotherapy within nine months after breast conserving surgery - Target: 95% (EUSOMA) |
| **Systemic treatment** | Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy and/or endocrine therapy – Target: NA |
| | Proportion of women <70 years old with metastatic BC who received systemic therapy - Target: NA |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; EUSOMA: European Society of Breast Cancer Specialists; NA: not applicable (see respective section in chapter 7 for more details); Source for all indicators (except those on systemic treatment): EUSOMA[46]; the indicators on systemic treatment were developed with the clinical experts.*

## 3.2 Operationalization of indicators

For all QIs a technical fiche was developed with an algorithm specifying the in- and exclusion criteria, the need for subgroup analyses, risk adjustment and sensitivity analyses. For each variable, relevant codes of the fee schedule (hereinafter called 'nomenclature codes') were searched in the IMA – AIM database (see Appendix 8.1). The technical fiches were discussed with the clinical experts before the start of the analyses.

# 4 ANALYSIS OF CANCER REGISTRY AND OTHER AVAILABLE DATA

## 4.1 The study database - a linkage between the Belgian Cancer Registry and administrative databases

The principal data source for this study was the **Belgian Cancer Registry** database, which was linked, with:

1. **Health insurance data,** obtained via the **Intermutualistic Agency (IMA – AIM)**, providing information on **diagnostic and therapeutic procedures** as well as **pharmaceuticals** which are reimbursed by the national health insurance; hereinafter they are called 'IMA – AIM data(base)'.

   Inherently, only invoiced procedures were taken into account in the analyses; it was therefore considered redundant to add the adjective "billed" to each procedure/pharmaceutical in the text. Procedures performed within the context of clinical trials are not (routinely) invoiced and hence not included in the IMA – AIM data. The impact of clinical trials on the correctness of the defined treatment scheme was assessed during the pre-validation phase (see section 4.8); this limitation is also discussed under section 4.10.

   The linkage with the IMA – AIM data, as well as identification and selection of diagnostic and therapeutic procedures within well-defined time frames, are fully elaborated in Appendix 8.1.

2. **Hospital discharge data (MZG – RHM)**, informing the **campus** where procedures had taken place; hereinafter these data are called MZG – RHM data. More information on MZG – RHM data can be found in Appendix 1.1. Overall, 96.7% of patients diagnosed during the period 2014 - 2018, with an official residence in Belgium at the time of diagnosis and having an INSZ, were linked with MZG – RHM data.

3. **Vital status data**, obtained via the Crossroads Bank for Social Security ('Kruispuntbank van de Sociale Zekerheid' – 'Banque Carrefour de la Sécurité Sociale', KSZ-BCSS). Using the active follow-up method, patients were followed up until **1 March 2022**, allowing a follow-up of at least five years for the majority of patients.

The linkage of the above databases is based on the patients' unique social security number (INSZ – NISS), and has been approved by the Sector Committee of Social Security and of Health (Health Section) of the Belgian Privacy Commission (Sectoraal comité van de Sociale Zekerheid en van de Gezondheid, afdeling gezondheid/Comité sectoriel de la Sécurité Sociale et de la Santé, section santé).[52]

In order to obtain the campus identification data, a dedicated request had to be submitted; approval was obtained in December 2021.[53] The linked database is hereinafter called 'BCR-IMA(-HDD)'.

## 4.2 The study cohort – women diagnosed in 2014 - 2018 with DCIS or IBC

For the study period 2014 - 2018, a total of 63 756 breast tumours, corresponding to 61 149 unique patients, were identified in the Belgian Cancer Registry (BCR) database, which is a nationwide database. This selection concerned 6 219 in situ breast tumours (9.8%; ICD-10: D05) and 57 537 invasive breast tumours (90.2%; ICD-10: C50).

Patients diagnosed in 2004[o]-2018 with multiple invasive tumours (breast or non-breast) and/or with multiple breast tumours (invasive or in situ) were excluded from the analyses, in order to maximally ensure that recorded procedures were indeed performed to diagnose or treat the breast tumour under study and not another malignancy. In consultation with the clinical experts, in situ tumours with an ICD-O-3 morphology other than ductal

[o] The BCR database is considered complete at the national level from the year 2004 onwards.

carcinoma in situ (DCIS) and invasive breast tumours with an ICD-O-3 morphology corresponding with sarcoma or Paget's disease, were also excluded since treatment can be different for these tumour types. Similarly, male patients were also excluded because the incidence numbers are too small to assess quality of care currently dispersed over about hundred Belgian hospitals (and even more campuses).

After additional exclusion of those patients for whom there were no IMA – AIM data available, or who died or were lost to follow-up at the date of diagnosis, a final cohort of **3 973 patients diagnosed with DCIS**[p] and **46 035 patients diagnosed with IBC** was included.

More details on the selection of the study cohort can be found in Appendix 8.3. The main characteristics of the study cohort are presented in chapter 5.

## 4.3 Defining the treatment scheme of the patient

Based on the IMA – AIM data, a treatment scheme was defined for all patients. First, surgery for the primary tumour was defined, followed by the definition of pre-operative and adjuvant treatments. When no surgery with curative intent could be identified, radiotherapy (RT) and systemic therapy were defined. Based on these treatment modalities, treatment schemes were defined and grouped into seven categories:

- Surgery (BCS, mastectomy) followed by adjuvant RT
- Surgery (BCS, mastectomy) followed by adjuvant systemic treatment
- Surgery (BCS, mastectomy) followed by adjuvant RT and systemic treatment
- Neoadjuvant treatment followed by surgery with/without adjuvant treatment
- Surgery (BCS, mastectomy) only
- Primary systemic therapy and/or RT (no surgery)
- No oncological treatment (identified in the database)

## 4.4 Assignment of each patient to one centre

### 4.4.1 Introduction

For the benchmarking between the different hospitals, the volume-outcome analyses, as well as the individual feedback to the hospitals, each patient must be assigned to one centre. This is straightforward for patients who were diagnosed and treated in just one centre, but much more complex if patients were taken care of in more than one centre. Depending on the quality indicator under assessment, patients had to be assigned to either the centre of diagnosis, the centre of main treatment, the centre of first treatment or the centre of first surgery. For this purpose several assigning algorithms were constructed; they are presented in Appendix 8.4. The main algorithms were validated during the pre-validation study in ten Belgian hospitals (see section 4.8).

### 4.4.2 Campus or hospital level

In the present study additional complexity was added by performing the (majority of) analyses at the campus level, in view of the recognition status which is assigned at the campus level (not at the hospital level). As was explained in section 4.1, the IMA – AIM data only inform in which hospital a procedure was performed, not in which campus. The identification of the campus can only be deduced from the hospital discharge data.

For **surgery and chemotherapy**, patients are admitted in a campus/hospital (inpatient or day care), and hence for these procedures the benchmarking could be performed at the **campus level**.

[p] Registration of DCIS at BCR is based on the information provided by the oncological care programs and laboratories for anatomical pathology to BCR. They use the International Classification of Diseases for Oncology third edition (ICD-O-3), to code the behaviour as '/0: benign', '/1: uncertain', '/2: carcinoma in situ' or '/3: malignant'. Registration of DCIS in the BCR database is thus not based on (y)pTis information.

Because in the majority of cases, the diagnostic and staging procedures are performed when a patient is not admitted in a campus/hospital, no hospital discharge data are available for these procedures. As a result, for diagnostic and staging procedures only the hospital could be identified, not the campus. When benchmarking was performed based on the **centre of diagnosis**, this was always done at the **hospital level**.

Nor was it possible for **radiotherapy** (RT) to identify the exact campus where it was performed. In 2014 - 2018, RT was provided in twenty-five 'main radiation oncology departments' and in nine 'associated radiotherapy units' (which are affiliated with one of the main centres). However, based on the RIZIV – INAMI licensing codes the distinction between a main and an associated unit cannot be made. Hence, all patients who had RT were assigned to one of the main RT centres, while in reality they may have been treated in one of the associated centres.

### *4.4.3 Missing campus identification data in the MZG – RHM database*

If campus identification data were missing in the MZG – RHM database, but the hospital could be identified, the following rules were applied:

a. if the hospital had only one campus, the patient was assigned to that campus;

b. if the hospital had multiple campuses with only one campus offering BC care (based on MZG – RHM data), the patient was assigned to that campus;

c. if the hospital had multiple campuses with multiple campuses offering BC care (based on MZG – RHM data), the patient could not be assigned to a campus and hence assigned to the 'missing campus' category for the respective hospital.

Overall, 149 patients with DCIS and 3 021 patients with IBC could not be assigned to a campus (of main treatment), and were thus excluded from the analyses at the level of the campus. Obviously, we do not know how they are distributed over the various recognition and volume categories, hence we have no idea of the impact on the results.

Patients for whom the campus could not be identified were somewhat older (DCIS: 62.1 years vs. 58.5 years, IBC: 77.1 years vs. 61.5 years), had more frequently a WHO performance status >0 (DCIS: 51.0% vs. 28.5%, IBC: 76.5% vs. 43.6%) and comorbidities (DCIS: 48.3% vs. 38.2%, IBC: 70.9% vs. 45.5%) compared to women for whom the campus was known (0). Clinical stage (DCIS: 49.0% vs. 32.8%, IBC: 23.0% vs. 10.4%) and grade information (DCIS: 54.4% vs. 32.5%, IBC: 21.6% vs. 6.3%) was also more frequently missing in the subgroup of patients with unknown campus.

### *4.4.4 Changes during the study period*

In the study period 2014 - 2018, several changes in the hospital landscape took place. In case of fusions of hospitals, the status at the end of 2018 was taken into account.

Also the **recognition status of some campuses changed over the 2014 - 2018 study period**. For instance, campus K without recognition for BC may have become a satellite breast clinic in March 2015[q]. Hence, patients treated in campus K from January 2014 up to February 2015 were considered as patients treated in a campus without recognition for BC. But, patients treated in campus K from March 2015 up to December 2018, were considered patients treated in a satellite breast clinic.

In the plots, campuses that had the same recognition status as well as the same number of beds (i.e. no fusion or closure of campus) throughout the whole study period are represented as **filled symbols**. Those campuses that changed recognition status and/or underwent a change in number of

[q] For each campus an activity period has been defined. An activity period starts the first of the month following the change in status/volume, or if the change was done at the 1st day of the months, the activity period starts the first of that month.

beds during the 2014 - 2018 study period, can be identified as **open symbols** on the plots.

Campus K, for instance, is represented as an open symbol for a campus without recognition for BC for the period January 2014-february 2015, and as an open symbol for a satellite breast clinic for the period March 2015-December 2018. As a consequence, campus K is represented twice in the plots; campus K is thus also counted as two **units of analyses** at the campus level. The recognition status and the calculation of the average annual volume were defined for each unit of analysis. This inherently entails that this recognition status/average volume is applicable over the full period of activity of that unit of analysis.

### *4.4.5 Assignment algorithms*

The various assignment algorithms and the number of patients with DCIS and IBC assigned at each step are provided in Appendix 8.4. Which assignment algorithm is used for which indicator can be found in the documentation sheet of the respective indicators.

## 4.5 Defining the campus/hospital volume

The **(average annual) campus/hospital volume** refers to the **main treatment volume** of a campus/hospital; this comprises all patients with DCIS and IBC treated in a campus/hospital, also patients who were excluded from the study cohort (e.g. Paget's disease, Phyllodes tumours, other sarcomas (other than Phyllodes tumours), LCIS, or multiple invasive tumours (breast and non-breast) or multiple breast tumours (invasive or in situ), as well as men with BC; see section 4.2). In this way, volume **reflects the actual experience** a campus/hospital has with all types of BC. Individual specialist volume data (e.g. surgeon volume) were not available in the database.

The **volume categories** (i.e. ≥125, [60, 125[, and <60) are based on the volume thresholds defined for the recognition of coordinating and satellite breast clinics in the legislation (see section 2.2.2). For the ease of reading, they are hereinafter referred to as **high-, medium- and low-volume campuses** (hospitals), respectively. In addition, for observed survival sensitivity analyses were performed comparing campuses with an average annual caseload smaller than 150 and campuses with an average annual caseload of 150 and more.

## 4.6 Case-mix adjustment

When measuring quality of care and benchmarking hospitals, case-mix adjustment is an essential part of the analyses. Without adjustment for case-mix variables, the comparison of treatment outcomes between providers may be misleading.[54]

The case-mix variables that were available for case-mix adjustment, are these:

- **Age at diagnosis**, categorized as <50 years, 50-59 years, 60-69 years, 70-79 years, 80+ years;
- **Combined TNM stages[r] at the time of diagnosis**;
- **Grading**, which can help predict how the cancer will behave, including how fast it's likely to grow and spread, which may impact the recommended treatment. The Nottingham histological score specifies three categoris (G1: well differentiated, G2: moderately differentiated, and G3: poorly differentiated), based on three parameters: architecture, nuclear polymorphism and mitotic activity;[57]

[r] In order to overcome to some extent missing stage data, a combined stage was calculated, where known pathological stage prevailed over known clinical stage, except when there was clinical proof of distant metastasis (cM1). When only the clinical stage was known, this stage determined the combined stage. Obviously, when neither the pathological stage nor the clinical stage were known, the combined stage was unknown too. The TNM classification was performed according to the 7th (incidence years 2014-2016) and 8th edition (incidence years 2017-2018) of the TNM Classification of Malignant Tumours, International Union Against Cancer.[55, 56]

- The fitness for treatment was assessed through the Eastern Cooperative Oncology Group Performance Status (ECOG PS), which has been adopted by the World Health Organization (WHO);[58] in this report it was limited to scores 0 to 4[s], and hereinafter referred to as '**WHO performance status**';
- **Patients' comorbidities** were restricted to information on cardiovascular and respiratory diseases, and diabetes; the same methodology was applied as developed in KCE report 266;[13]
- The **number of days spent in a hospital** in the year prior to incidence, was categorized as no days, 1-5 days, 6-15 days and more than 15 days, and is hereinafter referred to as 'previous inpatient bed days'.

Because the cohort under study was restricted to women with BC, sex was not included as case-mix variable.

In section 4.10 other (case-mix) variables, that would have had an added value in this study, but for which no reliable data were available (and which were thus not included in the analyses), are discussed.

For the assessment of the association between campus recognition status/volume and processes of care (see section 7), it was discussed upfront with the clinical experts whether the analyses should be adjusted for case-mix variables. If so, unadjusted and adjusted odds ratios are reported, as well as the case-mix variables for which adjustment was performed. Comparison cohort of women diagnosed with DCIS or IBC in 2009 - 2013

Wherever possible in this report, results obtained for the study cohort (at the national level) were compared with a comparison cohort of 3 830 women who were diagnosed with DCIS in 2009 - 2013 and 43 507 women diagnosed with IBC in 2009 - 2013. The selection criteria for this comparison cohort were the same as for the study cohort (see section 4.2).

## 4.7 Statistical analyses

### *4.7.1 Visualisation of centre variability*

#### *4.7.1.1 Funnel plots*

For most quality indicators, the observed indicator result per hospital/campus is visualised in funnel plots. A funnel plot is a scatter plot of the estimate of an indicator on the vertical axis versus its precision on the horizontal axis. This precision equals the inverse of the standard error of the estimate (1/SE) or the square of it (1/SE2).

Moreover, when a reference or population value can be assigned and a distribution assumed, prediction limits can be added to the funnel plot. These control limits are the upper and lower values of the expected (100-α)% prediction interval by centre size given the reference value and the distribution (α often equals 5 or 1). It is further assumed that all units have the same underlying population value. These prediction limits allow the comparison of the variability of the observed estimates with the expected variability.

The precision on the proportion of a binary indicator is proportional to the unit size. The funnel plot for a binary proportion therefore obtains an elegant representation: the estimates are plotted versus the number of observations of the campuses/hospitals, i.e. the number of patients that a campus/hospital contributes to the denominator of the QI. The binomial distribution is used for the construction of the 95% and 99% funnel limits for the binary indicators.

For the observed and relative survival results, the precision does not exist for an observed survival of 0 or 100%. Hospitals/campuses with an observed survival of 0 or 100% were not displayed on the funnel plots because the

[s] WHO performance status score 0: asymptomatic, fully active, score 1: symptomatic but completely ambulatory, score 2: symptomatic, up and about more than 50% of waking hours, score 3: symptomatic, confined to bed or chair more than 50% of waking hours and score 4: completely disabled, totally confined to bed or chair.

precision is infinity (as the standard error is 0). The prediction limits on the survival funnel plots were constructed assuming an asymptotic normal distribution using a log-log transformation.

All funnel plots were constructed around the target set for the respective process indicator.

#### 4.7.1.2 *Forest plots*

The centre comparison in the funnel plots does not take differences in indicator results between hospitals/campuses due to differences in patient case-mix into account. Therefore, odds ratios (OR) or hazard ratios (HR) adjusted for case-mix are visualised in forest plots.

A forest plot is a scatter plot showing an estimate (e.g. an outcome variable, a regression parameter) with its confidence interval on the vertical axis versus unit ranking on the horizontal axis. The OR and HR estimates are relative to the 'average hospital'. A horizontal reference line is added to the forest plots which represents the 'average patient', obtained by a weighted average of the hospital OR/HR with the number of patients per hospital divided by the total number of patients as weight.

If the reference line cuts the confidence interval, the estimate for that hospital/campus is not statistically significantly different from the reference (at the confidence level applied, mostly 95%). If the confidence interval does not contain the reference value, the estimate for that centre is statistically significantly different from the reference (at the significance level applied).

### 4.7.2 *Estimation of observed and relative survival*

Observed survival (OS) proportions were estimated using the Kaplan-Meier method.[59] Relative survival was calculated as the ratio of the observed survival and the expected survival for a similar group of persons from the general Belgian population (stratified on gender, age, calendar year and region). The Ederer II method was applied to estimate the expected survival using the Belgian national lifetables.[60]

The date of diagnosis was taken as time origin.

### 4.7.3 *Modelling observed survival*

The survival over the 0-5-year time interval was modelled with Cox proportional hazards models. Patients surviving beyond five years were censored at 5.05 years. Non-proportional hazards between the levels of categorical covariates were evaluated in a univariate way. Detected non-proportional hazards were resolved with a 'piece-wise proportional hazards model' (i.e., proportionality assumption holds within consecutive time intervals). This implies that the follow-up time is split into subintervals, in each interval proportional hazards are assumed. In each subinterval, a HR was estimated that is assumed to be constant over that interval. A split at one year, for example, results in two time intervals, [0,1] and [1,5], both with their specific estimated HR. Then all covariates were combined in the Cox model, including their non-proportional hazard terms. Non-proportional hazards terms that were no longer significant, were dropped. Patients with a follow-up that is shorter than five years, contribute to the model until their moment of censoring.

Second order interactions between the main terms were evaluated in a backwards elimination model building procedure. The model assumptions were evaluated on the basis of Schoenfeld and generalised Cox-Snell residuals.

The baseline patient case-mix variables taken into account were: age at diagnosis, WHO performance score, cardiovascular and respiratory diseases, diabetes, the number of inpatient bed days during the year prior to incidence date, tumour stage and tumour differentiation grade).

Survival differences between campuses were evaluated by estimating their HR adjusted for patient case-mix and displayed in a forest plot relative to the average hospital. Therefore, hospital was added as a fixed effect in the Cox regression model.

### 4.7.4 Modelling relative survival

A generalized linear model with a Poisson error structure based on collapsed data using exact survival times was used to model the excess hazard.[61] Second order interactions between the main terms were evaluated in a backwards elimination model building procedure. Due to the limited number of excess deaths the case mix adjustment had to be restricted to age and combined stage at diagnosis.

Relative survival differences between campuses were evaluated by estimating their EHR (excess hazard ratio) adjusted for patient case-mix and displayed in a forest plot relative to the average campus.

### 4.7.5 Association between campus recognition status/centre volume with processes of care and observed survival

The association between campus recognition status or average annual centre volume on the one hand and process indicators or observed survival on the other hand was evaluated with regression models. Logistic models were applied for the binary process indicators and Cox proportional hazards models in case of the observed survival.

The association with campus recognition status and centre volume was evaluated separately, i.e. distinct models for both associations were estimated. Correlation of patients within centres (campus or hospital) was taken into account by adding centre as a random term in the model. Categorical recognition status (coordinating breast clinic, satellite breast clinic, and no recognition for BC) and annual volume (<60, [60,124[, ≥125/year) were considered. For a selection of process indicators, a correction for patient case-mix was applied (age at diagnosis, WHO performance score, cardiovascular and respiratory diseases, diabetes, the number of inpatient bed days during the year prior to incidence date, tumour stage and tumour differentiation grade).

A logistic model was also used to examine the association between the ratio number of breast conserving surgeries (BCS) to the number of mastectomies with recognition status and campus volume. Because surgery considered for this indicator is either BCS or mastectomy, the BCS/ mastectomy ratio is in fact equal to the odds for BCS. As the logistic model directly models an odds, the percentage of BCS among operated patients was used as dependent variable in the logistic model to examine the desired associations.

### 4.7.6 Association between campus recognition status/centre volume and relative survival

The association between campus recognition status and campus volume with excess mortality was evaluated separately, i.e. distinct models for both associations were estimated. Categorical recognition status (coordinating breast clinic, satellite breast clinic, and no recognition for BC) and annual volume (<60, [60,124[, ≥125/year) were considered. Case-mix adjustment for age and combined stage at diagnosis was performed.

### 4.7.7 Interpretation of p-values and confidence intervals

As recommended by (among others) Kirkwood & Sterne,[62] precise p-values and 95% confidence intervals are reported. The results of the analyses have been interpreted in the light of both. The interpretation of the p-value, for instance, was not restricted to a binary interpretation, but was done taking into account the level of evidence against the respective null hypothesis, and in the light of potential clinical and/or policy relevance. The interpretation of the ORs was not conditional on the p-value of the overall type III test.

### 4.7.8 Statistical software

Statistical analyses were performed with SAS 9.4 (SAS Institute, Cary, NC, USA).

## 4.8 Pre-validation of available data and some methodological issues in ten hospitals

### *4.8.1 Objectives and methodology*

As was explained in section 4.1, the calculation of the process indicators was based on the linkage of Belgian Cancer Registry data (BCR data) with financial claims data from the health insurance companies (IMA – AIM data). Given that (1) it is not possible to unambiguously link the financial claims data to a (cancer) diagnosis, and (2) that procedures performed within the framework of clinical trials are not (exhaustively) present in the IMA – AIM data, and (3) that results on receptor status cannot be retrieved in the same way as the other tumour characteristics (see section 4.10), a validation study was performed before the calculation of the process indicators (hereinafter called 'pre-validation'). This pre-validation study had the following objectives:

- To validate the methodology used to allocate patients to a 'hospital of diagnosis' and a 'hospital of main treatment' (see section 4.4);
- To validate the methodology to select diagnostic and treatment procedures needed for this allocation and for the calculation of the quality indicators;
- To assess the impact of treatments given in clinical trials on the ability to define correct treatment schemes;
- To evaluate the effectiveness of the text mining algorithms to identify the receptor status (oestrogen, progesterone and HER2 receptor) from the pathology reports available at the BCR.

Medical files, financial data etc. available at the hospitals, were regarded the gold standard. Before the start, it was decided that a deviation of 5% in the total result of all hospitals would be considered acceptable.

**Based on the results of the pre-validation, no changes were made in individual files of the project database.** The pre-validation study was intended to assess the need for adaptations in the methodology and to detect programming errors, in which case corrections would be applied to the whole database.

A diverse sample of ten hospitals was selected for this pre-validation phase, taking into account (1) the recognition status as coordinating or satellite breast clinic, (2) the average annual BC treatment volume of the hospitals (high: ≥125 patients; medium: 60-124 patients; low: <60 patients), (3) academic versus non-academic hospitals, (4) their geographical location and (5) the main laboratories for anatomical pathology the hospitals work with. A diversity of laboratories for anatomical pathology was desirable since receptor status information is not transferred in a standardised format to the BCR[t]. A small fee was provided to the hospitals in order to compensate for the resources spent.

The pre-validation had to be performed at the hospital level, because the data on campus identification were not available yet at the time of the pre-validation (May-September 2021) and because the database with campus identification did not contain the patients' unique social security number (INSZ – NISS). Only the BCR team communicated with the participating hospitals on individual patient level information.

The list of the ten participating hospitals, which reviewed 885 cases in total, is provided in Appendix 9.1. The information provided to the hospitals for each assigned patient and the checks asked to be done are provided in Appendix 9.2.

[t] The quality of the (semi-)automatic extraction of receptor status information depends on how the pathology reports are structured. The ten hospitals that were selected for the pre-validation study work(ed) together with eight different laboratories for anatomical pathology.

### 4.8.2 Results

The results of the pre-validation process are provided in Appendix 9.3; they were anonymously presented to the KCE team and the participating hospitals during a dedicated meeting.

The (anonymised) results and the impact on the methodology and on the interpretation of results were also thoroughly discussed with the clinical experts, as well as the appropriate changes in the methodology.

### 4.8.3 Impact of the pre-validation on the methodology and/or interpretation of results

- The overall quality of the **diagnostic assignment algorithm** was considered as good (i.e. deviation < 5%), hence **no changes in the methodology** were indicated.
- The overall quality of the **main treatment assignment algorithm** was considered as good (i.e. deviation < 5%), hence **no changes in the methodology** were indicated. **Participation of patients in clinical trials** only had a **limited impact** on the correctness main treatment assignment algorithm.
- The **nomenclature codes for breast biopsy, breast puncture and lymph node puncture** were billed interchangeably by some hospitals, hence the results for separate categories should be done with caution since they may represent an over- or underestimation of what is actually done in clinical practice.
- Since specific nomenclature codes for **CT in preparation of radiotherapy** only became effective as from 1 August 2017[u], nomenclature codes for CT body were the only option for hospitals to invoice a preparatory CT scan before this date. The pre-validation study revealed that some CT body scans were incorrectly identified as a diagnostic or staging CT scan for BC. In order to overcome this problem, it was decided to consider CT scans that took place from the date of first treatment onwards as well as CT scans that took place within 14 days before the start of RT as CT in preparation of RT, and not as CT performed for diagnostic or staging purposes.

  In addition, for all **other imaging procedures** it was decided to **shorten the time window for inclusion to the period till the date of first treatment** in order to better omit those procedures that are done to follow-up treatment.
- Overall, the identification of the **primary treatment schemes** was considered good (i.e. deviation of 5%), hence **no changes in the methodology were indicated**.
- Since **oestrogen, progesterone and HER2 receptor status** information is not transferred to the BCR in a standardised format, this information is automatically extracted from pathology reports, using machine learning algorithms at the BCR.

  Given the high proportion of discordant cases, further optimization of the automated extraction was indicated. In order to identify the source of the discordant and completed results, the pathology reports of the validated cases which were available at the BCR were manually checked. If a result provided by BCR was changed to another result by the validating hospital, either part of information was lacking at BCR or at the validating hospital (i.e. BCR/the validating hospital did not have access to the pathology results of all specimens tested and based the final result on the incomplete information), or there was a discrepancy in how information from different specimens (biopsy versus resection tissue)

[u] The specific nomenclature codes to bill CT in preparation of radiotherapy (444614-444625, 'lokalisatie CT opname uitgevoerd bij de verstrekking 444356-444360 (eerste simulatie) en/of bij de verstrekking 444371-444382 (tweede simulatie)'/'CT de localisation effectuée lors de la prestation 444356-444360 (1re simulation) et/ou de la prestation 444371-444382 (2e simulation)') was introduced on 01/08/2017. The fee for CT in preparation for radiotherapy (nomenclature code: 444614-444625, fee in January 2022: €105.51) is lower than the fee for CT body (Nomenclature codes: 458813-458824, 459550-459561, 459572-459583 – at least 15 slices – fee in January 2022: €138.44, and 459616-459620 and 459631-459642 - at least 30 slices – fee in January 2022: €240.52).

was assembled to a final result (e.g. confirmation of a positive result based on biopsy led to a positive result indicated by BCR, but the hospital based the negative result on the resection specimen). For cases where unknown information was completed by the hospitals, the pathology reports were often not available to BCR. Especially for the HER2 ISH result, this was more frequently observed, since not all laboratories perform in situ hybridization themselves and therefore depend on external laboratories, which do not always send the pathology reports to BCR (e.g. this was the case for the hospital where 56% of cases were completed with a HER2 ISH result). For these cases, there is room for improvement of the machine learning algorithms when striving for more concordance between the two dataflows in which pathology reports on cancer diagnoses are provided to the BCR (Box 11).

Therefore, a new run of the algorithms was performed, taking into account these supplementary pathology reports. This new run led to a decrease in the percentage of unknown receptor status results for all four algorithms (i.e. to 2% for the ER and PR receptors, to 4% for the HER2 IHC receptor and to 8% for the HER2 ISH receptor). However, it did not always improve the percentage of concordant cases, since some changes caused: (1) an unknown result to become a known result, while the hospital stated a different known result or indicated that the result was unknown; (2) a known result to change to another known result and become discordant with what the hospital mentioned.

The manual check further revealed that for ER and PR some laboratories for anatomical pathology (e.g. the ones that collaborate with hospitals H6 and H8) do not always use the general Allred scoring system that is used by most Belgian laboratories, but an own internal scoring system. As these alternative scoring systems pose more difficulty for the machine learning algorithms to pick up the correct results, this led to more discordant results for e.g. hospitals H6 and H8.

Because the preliminary results of the quality indicators based on receptor status and systemic treatment were considered not reliable by the clinical experts, supplementary checks were performed with three hospitals (Cliniques universitaires Saint-Luc Bruxelles, UZ Leuven, Grand Hôpital de Charleroi) to further disentangle the discrepancies between the information that was automatically retrieved by BCR versus the information that was available at the hospitals. Still, the level of concordance remained substandard. Therefore it was concluded that these QIs could not be calculated, as there is currently **insufficient certainty about the correctness of the receptor status results on an individual patient level, available in the BCR database**.

## 4.9 Validation of the process indicators in all Belgian hospitals

### *4.9.1 Objectives and methodology*

The main objective of the validation study (May-September 2022) was to **validate the results of the process indicators**. In addition, hospitals were asked to verify whether they agreed with the **volumes** as described in their report and with the **distribution of these volumes over different campuses**, where applicable.

In previous KCE studies on quality of care, there was only one validation study and it was always limited to a selection of hospitals, just like the pre-validation study (see section 4.8). Yet, at the start of this study, KCE was informed that also VIKZ (see section 2.2.2.5) intended to assess the quality of care in BC, in Flemish hospitals. It was decided to combine forces, which implied that the validation of the quality indicator results was performed in all Belgian hospitals, since validation in all Flemish hospitals is stipulated in the VIKZ protocol.

Again, medical files, financial data etc. available at the hospitals, were regarded the gold standard. But also, **based on the results of this validation study, no changes were made in individual files of the project database.** Only the need for adaptations in the methodology and/or the programming were assessed.

Volumes and QI-results at campus level could only be validated at an aggregated level, because the database with campus identification did not contain the patients' unique social security number (INSZ – NISS). Volumes

and QI-results at the hospital level could be validated based on individual patient lists. Again, only the BCR team communicated with the hospitals.

Detailed information on the validation study is provided in Appendix 10.

### 4.9.2 Results

Overall, 85 of the hundred hospitals included in this validation phase, replied to the BCR[v]. Among those 85, 32 hospitals validated completely their results, 48 only partially and another five hospitals decided not to validate their results.

Once again, the (anonymised) results of this validation phase as well as the impact on the methodology and on the interpretation of results, were discussed in depth with the clinical experts during a dedicated meeting.

### 4.9.3 Impact of the validation study on the methodology and/or interpretation of results

- Given the non-specificity and reported mis-use of the nomenclature codes for **lymph node assessment/surgery** (see section 4.10.3), it was decided to elaborate both quality indicators on this aspect of care as a 'descriptive indicator', i.e. without target and the funnel plot replaced by a scatter plot.
- Several surgeons/hospitals voiced their concern that the **QIs just one breast surgery** in DCIS and IBC (see section 7.3.3) may create a perverse incentive for surgeons to opt more for mastectomy, as the risk of second surgeries is then logically smaller, rendering better QI results. There was consensus among the clinical experts that we should keep these QIs as it 'encompasses optimal preoperative imaging, optimal preoperative and intraoperative handling, use of oncoplastic techniques and optimal pathological examination, all concordant with guidelines'.[46] Moreover, benchmarked performance reports, and dissemination of good practices and guidelines between peers reduce re-excision rates.[63] Also, re-excisions may not only result in delays of adjuvant therapy and additional costs for patients and society, they may also adversely affect cosmetic outcomes and lead to additional physical and psychological impact for patients.[64] To address the surgeons' concern, and to provide the results in a broader context, it was decided to provide an additional graph, where the QI result is plotted against the ratio BCS/mastectomy (see section 7.3.3).
- Given the limitations of the data on the **multidisciplinary team (MDT) meeting** (see section 4.10.2), the respective QI was also changed into a 'descriptive indicator', i.e. without target and the funnel plot replaced by a scatter plot.
- Patient assignment based on the centre where **targeted and/or endocrine therapy** were prescribed, one of the final steps in the algorithm, were removed from the assignment algorithm. The validation study informed us that this resulted in the erroneous assignment of patients to campuses that do not offer BC care (e.g. patients admitted in hospital for other pathologies, who were administered their routine endocrine therapy).
- In order to reduce the number of **biopsies** with missing hospital identification, the hospital identification of the invoice of the needle (used for the biopsy) was used, if both biopsy and material were billed on the same date.
- The results on the QI '**mammography and US before the start of treatment**' (see section 7.1.1), were considered too low by several hospitals as well as by the clinical experts. This led to a further exploration and verification of invoicing rules, resulting in a broader inclusion of nomenclature codes (for more details see Appendix 13.1).

[v] According to the instructions sent to the hospitals, hospitals that didn't react, were assumed they agreed with the results provided.

## 4.10 Strengths and limitations of the study database

This study is based on data of the Belgian Cancer Registry (BCR), which were linked with administrative health insurance data (IMA – AIM), hospital discharge data (MZG – RHM), and vital status information (Crossroads Bank for Social Security). This approach had two major advantages: the Belgian Cancer Registry database covers all Belgian hospitals and more than 98% of all cancer cases in Belgium,[65] and no additional data registration by the hospitals or professionals was required.

The study cohort was diagnosed in 2014 - 2018. We admit that there may be some inconsistency with contemporary practice. On the other hand, estimating five year survival probabilities can only be performed in a robust way if the follow-up period is at least five years for the majority of the cohort.

During the selection and elaboration of process indicators, the pre-validation and validation studies, several limitations of this approach floated up to the surface. We discuss them briefly with some examples in the following paragraphs.

### *4.10.1 Valuable information not available in the consulted databases*

Several quality indicators could not be calculated because the required data were not at our disposal.

**Clinical information** on resection margins (whether or not positive), the number of resected lymph nodes and whether they were positive was not available in the database. This information is transferred to BCR in pathology reports, but as pathology reports are still not transferred in a structured and standardised format to BCR, the information is not readily available for research purposes. Moreover, currently not all complete pathology reports are transferred to BCR; the coverage depends heavily on the software system that is used by the laboratories for anatomical pathology and the extraction possibilities to define which report is transferred to BCR. Also, the nomenclature codes do not provide any information on the laterality of procedures. This limitation interfered in particular with the interpretation of multiple surgical interventions identified for the same patient: from the data it cannot be revealed whether they were performed in the same breast or in the contralateral breast (see section 7.3.3).

**Case-mix adjustment** is essential when quality of care is measured and outcomes are compared. Based on the available data, some case-mix variables were taken into account (see section 4.6). However, several other factors which have been linked to the incidence and/or prognosis of BC, could **not be captured i**n the available administrative databases. To name some: reproductive factors (e.g. age of menarche, pregnancies),[66-68] hormonal factors (e.g. contraceptive methods),[66-69] hereditary factors (e.g. mutations in the BRCA1 and BRCA2 genes),[66, 68] and lifestyle factors (e.g. overweight and obesity, smoking, alcohol consumption) were not available for the analyses.[66-68, 70, 71] Some **comorbidities** were taken into account (based on pharmaceutical information), but valuable information, e.g. on renal disease, which may also guide treatment decisions, was not available.

Another major limitation of this study was that no information on **socioeconomic status** (SES) was available for the analyses, as the SES data included in the IMA – AIM database are not routinely transferred to BCR. The role of SES in female BC has received quite some attention:[72, 73] the incidence of BC is higher in higher SES groups, patients from higher SES groups are more likely to be diagnosed at an earlier stage,[74, 75] while survival is lower in the lower SES groups.[76, 77] A Canadian population-based study revealed that also after controlling for stage and age, women with BC residing in the poorest communities had a 47% increased risk of death compared with women from the highest SES groups (HR: 1.47; 95% CI: 1.27-1.71; $p < 0.001$).[76] Also in Sweden, a country with a policy of providing equal access to health care within a National Health Care System, the risk of death was 19% lower among women with BC belonging to a household of high compared to low SES (HR: 0.81; 95% CI: 0.67-0.97), even after adjustment for tumour size and age at diagnosis.[78] We admit that not being able to adjust for SES, is a major limitation of this study.

**Patient reported outcomes (PROM)** and **experiences (PREM)** for BC treatment **were not available** either. It would also have been very informative if the available databases would have included information on the level of patient-centredness of the provided care, on the clinical decision making process, and on **patient preferences** e.g. on breast conserving

surgery versus mastectomy and on immediate breast reconstruction, but this was not the case.

The **recognition** of coordinating and satellite breast clinics is based on several **criteria** (see 2.2.2.2). But, as the available databases do not include (valid) information on structural hospital characteristics or on professional titles and individual healthcare professionals' activity, only the volume criterion could be assessed.
Also, as was explained in section 4.4.2, it was not possible to identify the campus where **diagnostic/staging procedures** were performed. Nor is it possible to discriminate **main from associated radiotherapy units**, precluding the comparative assessment of care provided in main and associated radiotherapy units.

Last, as with all administrative databases, their **correctness and completeness** depend heavily on those (responsible for) **providing data**. If nomenclature codes are not used in a correct way (e.g. because healthcare professionals consider the fee corresponding to the correct code inappropriate), this may result in an over- or underestimation of some procedures. Yet, the magnitude of these flaws cannot be assessed. When radiotherapy centres do not comply with invoicing rules and only invoice the last session, it is hard to discriminate between multi-fraction and single fraction RT schedules (and decision algorithms have to be developed, see Appendix 8.1.2). Also, if healthcare professionals/hospitals do not invoice diagnostic or therapeutic procedures, they will not be available in the database. But as the financing of Belgian healthcare professionals is mainly based on a fee-for-service system, it can be assumed that the number of non-invoiced procedures is small. Yet, administrative errors (e.g. certain fields not completed, procedures billed to the wrong patient) cannot be ruled out.

### *4.10.2 Limitations due to invoicing rules*

For **multidisciplinary team (MDT) meetings** in oncology[w] strict invoicing rules apply.[79] A 'first MDT' meeting, which is mandatory for each case of BC treated in a recognized breast clinic,[4] is reimbursed only once per calendar year. Yet, from the clinical experts as well as during the interviews, we learnt that in many hospitals patients with BC are discussed at several occasions during the care pathway (e.g. before the start of any treatment, to evaluate the effect of neoadjuvant chemotherapy, to discuss the pathology report and the need for adjuvant systemic treatment after breast surgery). From the databases we could only identify for which patients a MDT was invoiced at least once within the pre-defined time interval. In addition, it was not possible to assess the quality of the multidisciplinary meeting itself, nor whether patients benefitted from a multidisciplinary approach during the entire care pathway.

The invoicing rules further stipulate that only **one mammography** (either for diagnostic or guidance purposes) and only one **ultrasound** (either for diagnostic or guidance purposes) per patient per day can be billed. Hence, if an ultrasound of the breast is combined with an ultrasound of the abdomen or liver, only one of these can be invoiced and is thus identifiable in the IMA – AIM data. Likewise, if a breast puncture (nomenclature codes 355670-355681) is performed under US or radiographic guidance, an additional fee can be charged through nomenclature codes 355913 – 355924. However, the latter codes cannot be combined on the same day and in the same patient with an US breast or mammography breast. In order to remedy these cumulation rules, a limited list of non-breast specific ultrasound codes were included in the calculation of the QI on mammography and ultrasound of the breast (see Appendix 13.1).

For radiotherapy there is the limitation that the fee for the whole scheme is always invoiced, regardless of the number of fractions that was actually

[w] In Belgium multidisciplinary team (MDT) meetings in oncology are also known as 'multidisciplinary oncological consult', and abbreviated as MOC in Dutch and COM in French.

given. Therefore, it is not possible to identify patients who discontinued radiotherapy before it was completed.

### 4.10.3 Limitations due to the vague description of nomenclature codes

Another aspect that may limit the interpretation of (some) results is the **vagueness of some nomenclature codes**. Some nomenclature codes related to sentinel lymph node resection and/or axillary lymph node resection[x], for instance, are not specific enough: it is not clear whether patients for whom these codes were invoiced, underwent axillary lymph node resection or not. Not to mention that - according to the clinical experts – the very same codes are not by all healthcare professionals/hospitals used in the correct way (cf. supra).

A second example of non-specific nomenclature codes relates to those for hormone and HER 2 receptor status assessment. Ideally, one should be able to specify whether an ER, a PR and an HER 2 test has been performed because good quality of care includes both hormone testing and HER 2 testing before the start of systemic treatment. However, during the study period (2014 - 2018) there was neither a dedicated nomenclature code for HER2 IHC testing, nor a nomenclature code for ER and PR testing separately. In addition, exploration of the data revealed that the nomenclature codes for the combined testing of ER and PR status (546416 - 546420 and 435831- 435842) were not billed. Instead, nomenclature codes for more general immunohistochemical testing (588070 - 588081 and 588976 - 588980, describing the testing for tumour antigen) were used to bill ER-PR-HER2 IHC testing collectively[y]. It was thus impossible to disentangle whether ER as well as PR as well as HER2 IHC testing was performed.

Further, the pre-validation study (see section 4.8) revealed that in several hospitals, the nomenclature codes for breast biopsy, breast puncture and lymph node puncture are used interchangeably, hence these results should be interpreted with caution.

### 4.10.4 Limitations due to unclear or limited validity of some data

As was revealed during the pre-validation study (section 4.8), the concordance between the **hormone and HER2 receptor status** results retrieved from the BCR database and the information available in the hospitals (medical files) – based on which treatment decisions were taken – was inadequate. Consequently, the quality indicators pertaining to receptor status had to be excluded, as the results were considered unreliable by the clinical experts. This was deplored by the clinical experts, more so because the registration of hormone and HER2 receptor status in breast clinics is mandatory since 2007.[4] Many cancer registries are doing efforts in BC biomarker registration.[80]

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[x] Nomenclature code 227813-227824: Breast conserving surgery of a proven malignant breast tumour with macroscopically sufficient safety marge, and resection of the sentinel lymph node, which in case of tumour present on a preoperative anatomopathological examination is followed by axillary excision. Nomenclature code 227710-221121: Mastectomy of a proven malignant breast tumour and resection of the sentinel lymph node, which in case of tumour present on a preoperative anatomopathological examination is followed by axillary excision.

[y] The more frequently use of nomenclature codes 588070 - 588081 (fee: €28.10) and 588976 – 588980 (fee: €84.29) may be related to the fact that they can be invoiced eight times per sample.

#### *4.10.5 Treatment performed within the framework of clinical trials*

A major concern raised by several clinical experts was the participation of BC patients in clinical trials. More precisely, pharmaceuticals tested in clinical trials are not reimbursed by the health insurance. Hence, they are not included in the IMA – AIM data and may thus result in the underestimation of their use. However, the pre-validation study showed that the impact was rather limited: 2.4% of patients included in the pre-validation study received (part of) their treatment in the context of a clinical trial, but for less than 1% of included patients the fact that they participated in a clinical trial (and by consequence that part of the treatment was not billed/identified in the administrative database) had an impact on the determination of the treatment scheme (see section 4.3). However, the number of patients included in trials differs between centres, and for centres with high numbers of patients in trials, this may affect some QI results to some extent.

# 5 CHARACTERISTICS OF THE STUDY COHORT

In the present chapter a description of the study cohort is given. We start with the baseline patient and tumour characteristics of the 3 973 patients with DCIS and 46 035 with IBC, diagnosed in 2014 - 2018. In addition, a brief description is given of the main diagnostic, staging and therapeutic procedures that were recorded for these patients. Last, the observed and relative survival are presented and discussed.

## 5.1 Baseline demographics and tumour characteristics

### *5.1.1 Patient characteristics*

The mean age of women diagnosed with DCIS in 2014 - 2018 was 58.6 years (SD: 11.6;Table 4), with the majority having a WHO performance status of zero (i.e. asymptomatic; Table 61). Forty percent of them had one or more comorbidities; cardiac disease was the most prevalent comorbidity. For three in four no inpatient bed days were recorded the year before incidence.

The mean age of women diagnosed with **IBC** in the same time span was somewhat higher (62.6 years, SD: 14.3). In this group, about half of the patients was asymptomatic (according to the WHO performance status, WHO = 0; 54.3%; Table 62) and one in three was symptomatic but completely ambulatory (WHO = 1; 34.8%), according to the WHO performance status. Also in this patient group cardiac disease (42.7%) was the most prevalent comorbidity, followed by diabetes (10.1%); and for three in four no inpatient bed days were recorded the year before incidence.

Overall, 41.1% of patients with IBC for whom the campus was unknown, were diagnosed with cStage IV, while this was only 7.1% in the total study cohort (Table 65). Not surprisingly, for these patients, patient and tumour characteristics are often missing. No other apparent differences were seen between the various subgroups based on recognition status.

**Table 4 – Main patient and tumour characteristics at diagnosis**

| | DCIS (N=3 973) | | IBC (N=46 035) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Age** | | | | |
| Mean, SD (years) | 58.6 (11.6) | | 62.6 (14.3) | |
| **Number of comorbidities** | | | | |
| 0 | 2 442 | 61.5 | 24 330 | 52.9 |
| 1 | 1 207 | 30.4 | 16 362 | 35.5 |
| 2 | 301 | 7.6 | 4 938 | 10.7 |
| 3 | 23 | 0.6 | 405 | 0.9 |
| **Combined stage*ϕ** | | | | |
| (y)0 ˜ | 3 774 | 100.0 | 1 065 | 2.4 |
| yis | | | 337 | 0.7 |
| (y)IA | | | 19 104 | 42.5 |
| (y)IB | | | 1 022 | 2.3 |
| (y)IIA | | | 10 470 | 23.3 |
| (y)IIB | | | 5 037 | 11.2 |
| (y)IIIA | | | 2 914 | 6.5 |
| (y)IIIB | | | 893 | 2.0 |
| (y)IIIC | | | 1 123 | 2.5 |
| (y)IV | | | 3 009 | 6.7 |
| Unknown | 199 | 5.0 | 1 061 | 2.3 |
| **Grade** | | | | |
| I | 530 | 13.3 | 6 455 | 14.0 |
| II | 887 | 22.3 | 20 954 | 45.5 |
| III | 1 234 | 31.1 | 15 259 | 33.1 |
| Unknown$ | 1 322 | 33.3 | 3 367 | 7.3 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; SD: standard deviation; *: percentages for stages 0-IV were calculated excluding the unknown category; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0; ϕ: patients might have had neoadjuvant therapy (NAT), resulting in a ypStage in these cases. Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); the combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage$: The high proportion of grade unknown is due to the incomplete information BCR received from the oncological care programs and/or laboratories for anatomical pathology.*
*Source: BCR-IMA-HDD*

### 5.1.2 Tumour characteristics

The majority of IBCs were invasive ductal carcinoma (77.6%), followed by invasive lobular carcinoma (14.9%) and mixed ductal and lobular (3.1%; Table 63). The invasive cancer was most often situated in the upper-outer quadrant of the breast (32.5%), the upper-inner quadrant (11.1%), or the lower-outer quadrant (7.8%); for one third of IBCs (34.3%), the sub-localisation was not reported.

The number of new diagnoses of DCIS and IBC are evenly distributed over the five years under study (Table 64, Table 65). A large majority of patients with IBC with known **clinical stage** were diagnosed with an early stage of the tumour (cIA: 45.7%, cIIA: 28.1%, cIIB: 10.3%).

Among the patients with IBC who had surgery and for whom the pathological stage was reported to the BCR (N=40 233), pathological stages (y)IA (47.2%), (y)IIA (23.7%) and (y)IIB (11.6%) were the most common. Yet, we have to be mindful that these data refer to any pTNM, for instance also a pathologic staging performed after neoadjuvant therapy (systemic treatment and/or radiotherapy; ypTNM), which may have resulted in downstaging. When only operated patients are considered who were not treated with neoadjuvant therapy (N=34 257), the respective proportions are more or less comparable (pIA: 50.7%, pIIA: 24.5%, pIIB: 11.9%; ). The distribution of pStages is markedly different in the group of patients with IBC who was given neoadjuvant therapy (N=5 976; ypIA: 23.5%, y0: 21.4%, ypIIA: 18.6%; Table 68).

The combined stage[r] was unknown for 5.0% of patients with DCIS and 2.3% of patients with IBC. Note that a tumour with a missing stage can be both a tumour for which the stage was not reported to the BCR, as well as a tumour for which the stage was unknown or could not be defined. More details on clinical and pathological stage reporting are provided in section 7.1.5.

About one third of all DCIS cases were assigned grade III, 22.3% grade II and 13.3% grade I (Table 4). For one in three DCIS cases grade information was not available as this information was not (or incompletely) provided by the oncological care programs and/or laboratories for anatomical pathology to BCR. Among patients with IBC, 45.5% was given grade II, 33.1% grade III and 14.0% grade I (Table 65).

## 5.2 Main diagnostic and staging procedures

An outline of the most common diagnostic and staging procedures in the diagnostic work-up of patients with BC is provided in Table 71 - Table 74. For punctures, biopsies, cytohistological examinations and genetic testing, the time span for evaluation was confined to three months before to three months after the incidence date. A **puncture and/or biopsy** was performed in 93.9% of patients with DCIS and in 95.5% of patients with IBC (Table 71); both proportions are somewhat higher than what was observed in 2009 - 2013. **Cytohistopathological examination** was recorded for almost all patients (DCIS: 99.6%. IBC: 99.5%), also in the comparison period 2009 - 2013. **Genetic testing**, i.e. BRCA testing, was performed in 7.7% of patients with IBC within three months around incidence date; if the observation period was extended to one year before and five years after incidence, this proportion increased to 19.2%. The respective proportions for DCIS were 3.7% and 12.2%. These proportions were considerably higher than in the comparison period 2009 - 2013.

As was explained before, for all **imaging procedures**, the time span was restricted to three months around incidence date, but imaging that was performed on the date of the first treatment and from then on was excluded. For CT body, the inclusion criteria were even more strict: CT body performed within 14 days before the start of radiotherapy were also excluded (see also 4.9).

Nearly all women with DCIS or IBC had a **mammography and/or ultrasound of the breast** (94.4% and 97.5%, respectively; Table 72); for (about) half of patients a magnetic resonance imaging (MRI) was also recorded (DCIS: 47.8%, IBC: 50.0%); more detailed information on mammography and US can be found in section 7.1.1.

Additional analyses were performed to sort out **where the diagnostic procedures were performed**: in a hospital or in a private practice[z] (Table 74). With the exception of mammographies, for none of the diagnostic procedures, more than one fourth was performed outside the hospital (Table 74). For instance, for 25.2%, 8.4% and 2.9% of incision biopsies, core biopsies and vacuum assisted biopsies performed in women with IBC, the centre was unknown. The proportions of genetic testing and cytohistopathological examinations for which the centre is unknown are relatively high, as these tests are predominantly billed by laboratories, which can most of the time not be linked to one hospital.

The elaboration of the quality indicators on diagnosis and staging can be found in section 7.1.

## 5.3 Main therapeutic procedures

In patients with **DCIS**, the most prevalent treatment modality was surgery in combination with adjuvant radiotherapy (30.6%), followed by surgery only (28.9%) and by surgery in combination with radiotherapy and targeted and/or endocrine therapy (25.5%; Table 5). Among the patients with DCIS who had surgery (N=3 809), a BCS was recorded for 78.0% and a mastectomy for 28.3%.

In patients with **IBC**, the most prevalent treatment scheme was surgery followed by radiotherapy and systemic treatment (59.5%); neoadjuvant treatment followed by surgery, followed by adjuvant treatment or not was offered to 13.0%. In 11.2% of patients with IBC the treatment was confined to surgery followed by systemic therapy. Among the patients with IBC who had surgery (N=40 233), a BCS was recorded for 70.0% and a mastectomy for 33.9%. In total, 5 802 patients diagnosed with IBC were not operated: 4 861 (83.8%) of them received primary systemic and/or radiotherapy while for 941 (16.2%) patients no oncological treatment was recorded. More details on the treatment schemes offered to women with DCIS and IBC are presented in Table 75 and Table 76.

**Table 5 – Main treatment schemes in DCIS and IBC**

| Category | DCIS (N=3 973) | | IBC (N=46 035) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Surgery < adjuvant RT (no systemic Tx)** | 1 216 | 30.6 | 899 | 2.0 |
| **Surgery < adjuvant systemic Tx** | 411 | 10.3 | 5 176 | 11.2 |
| **Surgery < adjuvant RT + systemic Tx** | 1 015 | 25.5 | 27 374 | 59.5 |
| **Neoadjuvant Tx < Surgery (< adjuvant Tx)** | 20 | 0.5 | 5 976 | 13.0 |
| **Surgery only** | 1 147 | 28.9 | 808 | 1.8 |
| **Primary systemic and/or radiotherapy (no surgery)** | 55 | 1.4 | 4 861 | 10.6 |
| **No oncological treatment** | 109 | 2.7 | 941 | 2.0 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; RT: radiotherapy; Tx: treatment; <: followed by.*
*Source: BCR-IMA-HDD*

Overall, 95.9% of patients diagnosed with DCIS and 87.4% of patients with IBC had a **breast surgery** in the time frame 1 month before to 9 months

[z] Since the administrative databases do not include the identification details of private practices, a proxy approach was applied. If the RIZIV-INAMI recognition number of the hospital where the diagnostic procedure was performed, was not provided in the database, it was assumed that the procedure was performed outside a hospital. When interpreting the data, it is important to realise that this approach may have led to a small overestimation of the true number of diagnostic procedures performed in private practice, yet, for the complement proportion we are confident that the procedures were performed within the premises of a hospital.

after incidence date; these proportions were comparable in 2009 - 2013 (Table 77, Table 78). Breast conserving surgery (BCS) was offered to 74.8% of patients with DCIS and to 61.1% of patients with IBC. Mastectomy was recorded in 27.1% of patients with DCIS and in 29.6% of patients with IBC. Breast surgery, sentinel lymph node biopsy and axillary clearance are further discussed in section 7.3.

**Radiotherapy** was recorded in 57.1% of patients with DCIS and in 75.4% of patients with IBC (Table 79, Table 80); these proportions were about the same in 2009 - 2013. In the majority of cases radiotherapy was offered in the adjuvant setting.

Table 81 and Table 82 summarize the **systemic treatment** offered. **Targeted therapy** was offered to 13.4% of patients with IBC, while in 2009 - 2013 this was 10.8%; in the majority of cases it related to anti-HER2 therapy. Among the 40 233 women with IBC who received surgery, 12.6% (i.e. 8.3% + 4.3%) received targeted therapy in the adjuvant setting and 4.4% in the neoadjuvant setting. Targeted therapy was also offered to 17.5% of the 5 802 women for whom no surgical intervention was recorded.

Overall, **chemotherapy** was recorded for 39.6% of patients with IBC; more precisely, 29.7% of women with IBC who received surgery, underwent chemotherapy in the adjuvant setting and 13.4% in the neoadjuvant setting. Chemotherapy was also recorded for one in four patients with IBC who did not have breast surgery.

Last, **endocrine therapy** was offered to 79.9% of women with IBC and to 37.2% of patients with DCIS; among operated patients, it was recorded as adjuvant therapy in 37.7% of women with DCIS and 81.4% of patients with IBC. In the non-operated groups, endocrine therapy was given to 23.8% of women with DCIS and to 67.9% of patients with IBC. Again the interpretation of the above data should be done with caution since systemic treatments offered as part of clinical trials cannot be billed and are thus not always included in the administrative databases (see section 4.10.5).

Table 83 provides an **overview of systemic treatment** that was provided to **patients with non-metastatic** (i.e. combined stage 0, I, II, III) IBC. These data are further explored in Table 84 where the various classes of systemic therapy are provided.

Table 85 provides an overview of some patient and tumour characteristics of **patients from whom no oncological treatment was identified** in the administrative database. The mean age of this patient subgroup was 12.3 years higher than the overall group of patients with IBC; for the patients with DCIS this difference was less pronounced (61.5 years vs. 58.6 years). Based on follow-up data up to 1 March 2022, one in two patients with IBC who did not undergo oncological treatment had died within six months after diagnosis; in the DCIS subgroup the respective proportion was 31.6%.

## 5.4 Observed and relative survival

### *5.4.1 Patients diagnosed with IBC in 2014 - 2018*

**Five years after the diagnosis of IBC, the observed survival probability** was **83.4%** (95% CI: [83.1, 83.8]; Table 6). The survival probability was higher in patients younger than seventy years, in patients with an asymptomatic WHO performance status, and in patients without comorbidities or hospital admission the year preceding the diagnosis of BC (Table 88; Figure 21). The higher the combined stage, the lower the survival probability; the Kaplan Meier curve for patients for whom the combined stage was unknown was situated in between the curves of the patients with combined stage (y)III and (y)IV. Over the incidence years 2014 - 2018, no clear differences in survival probability were observed. In the comparison cohort of women diagnosed with IBC in 2009 - 2013 the 5-year observed survival probability was 81.9% (95% CI: [81.5, 82.2]) and the 10-year survival probability 70.2% (95% CI: [69.8, 70.7]).

**Table 6 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with IBC**

| | | Unadjusted observed survival (%, 95% CI) | | | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | **1-year** | **3-year** | **5-year** |
| **Overall** | 46 035 | 95.9 [95.7, 96.1] | 89.4 [89.1, 89.7] | 83.4 [83.1, 83.8] | 97.9 [97.8, 98.1] | 95.4 [95.1, 95.7] | 93.3 [92.9, 93.7] |
| **Age at diagnosis (years)** | | | | | <0.0001 | | |
| <40 | 2 261 | 98.8 [98.3, 99.2] | 95.3 [94.4, 96.1] | 92.1 [90.8, 93.2] | | 98.9 [98.4, 99.3] | 95.5 [94.5, 96.3] |
| 40-49 | 6 798 | 99.0 [98.7, 99.2] | 96.6 [96.1, 97.0] | 94.3 [93.7, 94.8] | | 99.1 [98.9, 99.3] | 97.1 [96.6, 97.5] |
| 50-59 | 10 580 | 98.9 [98.7, 99.1] | 96.1 [95.7, 96.5] | 93.5 [93.0, 94.0] | | 99.3 [99.0, 99.4] | 97.2 [96.8, 97.6] |
| 60-69 | 11 611 | 97.7 [97.4, 97.9] | 94.0 [93.6, 94.4] | 90.3 [89.7, 90.9] | | 98.5 [98.2, 98.8] | 96.7 [96.2, 97.1] |
| 70-79 | 8 294 | 94.6 [94.1, 95.1] | 87.1 [86.4, 87.8] | 79.1 [78.1, 80.0] | | 96.8 [96.3, 97.3] | 94.3 [93.5, 95.1] |
| 80 + | 6 491 | 85.4 [84.5, 86.2] | 63.4 [62.2, 64.6] | 45.7 [44.4, 47.0] | | 94.3 [93.3, 95.2] | 88.4 [86.8, 90.0] |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

As no national data are available on the cause of death in Belgium, BC-specific survival could not be computed. Therefore, the relative survival framework was applied to estimate the net survival. The five-year relative survival was higher than the observed survival (93.3%, 95% CI: [92.9, 93.7]), which suggests that in this cohort the probability to die is not only attributable to BC. Younger patients, asymptomatic patients, patients without comorbidities or hospital admission in the preceding year and those with a lower combined tumour stage and a tumour that was moderately or well differentiated had a better prognosis (Figure 22).

### International comparison

In the CONCORD-3 study, Belgian age-standardised 5-year net survival[aa] data for women diagnosed with IBC in 2010–2014 were good: 86.4% (95% CI: [85.9, 86.9]) versus 84.8% (95% CI: [84.1, 85.5]) in Austria, 86.1% (95% CI: [85.4, 86.9]) in Denmark, 86.7% (95% CI: [85.5, 88.0]) in France[bb], 86.0% (95% CI: [85.7, 86.4]) in Germany[cc], 86.6% (95% CI: [86.1, 87.1]) in the Netherlands, 86.2% (95% CI: [85.1, 87.3]) in Switzerland[cc], and 85.6% (95% CI: [85.4, 85.9]) in the United Kingdom.[81] In Belgium, 5-year net survival hardly increased over the years: from 84.8% (95% CI: [83.5,86.0]) in 2000-2004, over 85.3% (95% CI: [84.7, 85.8]) in 2005-2009 to 86.4% (95% CI: [85.9,86.9]) in 2010-2014; this was also observed in other Western European countries, like France and the Netherlands.[81] Several factors may contribute to the (small) differences between countries, one of which is the quality of the registration.

### Comparison between campuses

In order to allow for the differences in case-mix between campuses, **adjusted hazard ratios** were calculated. They are a measure of how much higher or lower the mortality risk in a particular campus is compared to the average over all Belgian hospital campuses, e.g. within five years after diagnosis. The following case-mix variables were included in the multivariable Cox proportional hazard models: age at diagnosis, WHO score, number of inpatient bed days, cardiovascular and respiratory diseases, diabetes, combined tumour stage and differentiation grade. No adjustment for receptor status, nor for SES background could be performed (see section 4.10.1).

Of the 135 units of analysis for which the HR could be estimated (i.e. with a minimum of forty patients treated in the campus during the five-year period, Figure 4),

- **fifteen** (twelve coordinating breast clinics and three without recognition for BC) had their confidence interval below the reference line: patients treated in these campuses had thus a **significantly lower hazard ('risk') to die than patients treated in the average campus**;
- **nine** (three coordinating breast clinics, one satellite breast clinic and five without recognition for BC) had their confidence interval above the reference line: patients treated in these campuses had a **significantly higher hazard to die** than patients treated in the average campus.

For 47 units of analysis the volume was too small to obtain robust results.

**Excess hazard ratios** were also calculated; they relate to relative survival estimates, hence to the fact that there is also a certain risk of death in the general Belgian population. Excess hazard ratios consider only the additional risk of death due to BC. Only 47 units of analysis, the majority recognised as coordinating breast clinics, were included in the analyses, as a minimum threshold of 300 assigned patients was applied (Figure 24). The analyses were adjusted for age and combined stage.

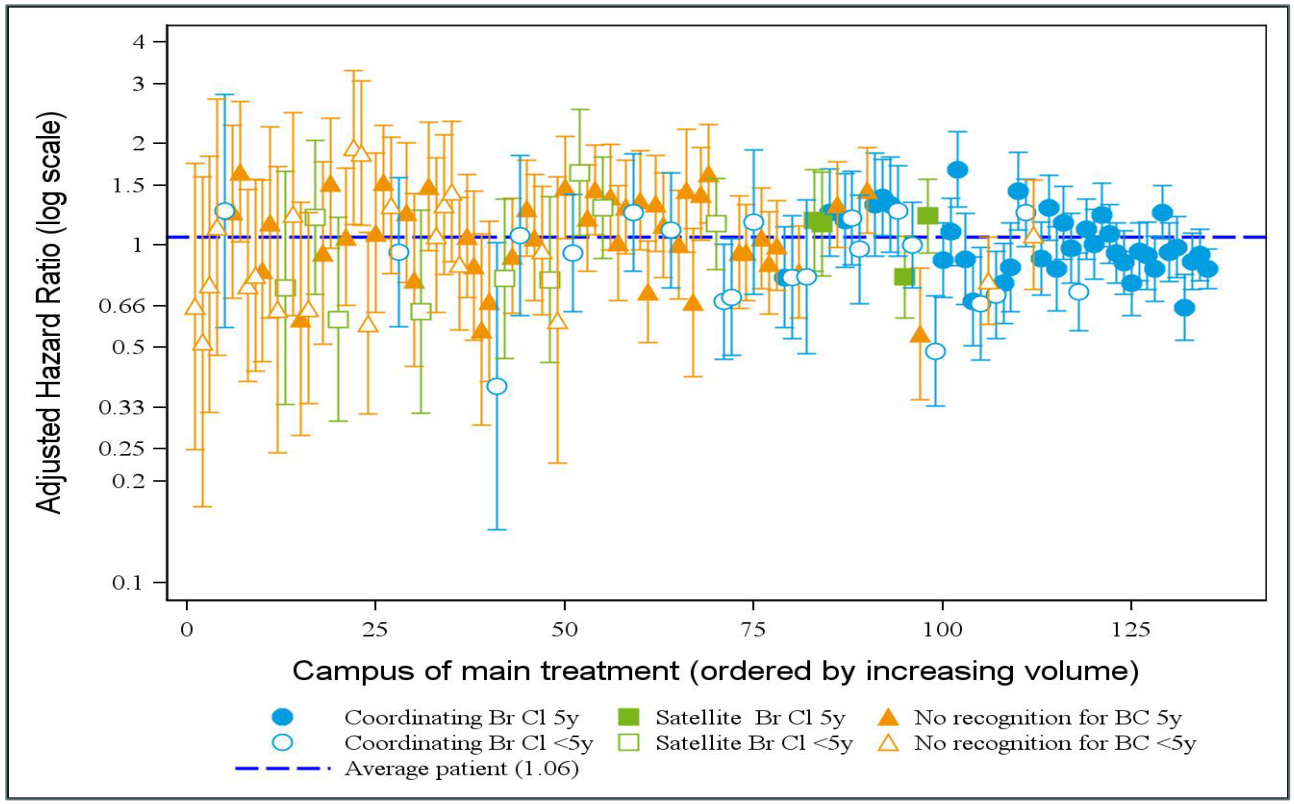
**Five** units of analysis recognised as **coordinating breast clinics** had a **significantly lower excess hazard** (the confidence interval was below the reference line), and **three** had a **significantly higher excess hazard**. However, when interpreting these data, one should realise that the volume of a campus determines the width of the CI. Many non-recognised campuses score worse, but due to their small volume the CI is very wide and includes thus the reference line.

[aa] In this study the Pohar Perme method was used to estimate 5-year net survival (i.e. the cumulative probability of surviving five years since diagnosis after correcting for background mortality), as it takes unbiased account of the higher competing risks of death in elderly.[81]

[bb] Based on the data provided by 23 cancer registries (i.e. no national coverage).

[cc] Based on the data provided by 10 cancer registries (i.e. no national coverage).

**Figure 4 – Forest plot of the adjusted hazard ratio for all-cause death in patients with IBC, by main treatment campus**




*Hazard ratios were determined over the [0,5] year survival time interval. A minimum campus size of 40 assigned patients was applied, with size referring to the number of patients available for the analysis. For 135 campuses the adjusted HR could be obtained. The hazard ratios were adjusted for age at diagnosis, WHO score, number of inpatient bed days, cardiovascular and respiratory disease, diabetes, combined tumour stage, differentiation grade.*
*Value 1.0 represents the average campus and the dashed blue line is the HR for the average patient (which equals the weighted sum of all campus HR, with the number of patients per campus as weight). The campuses are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). A HR which is lower than 1.0, indicates a lower hazard (or instantaneous risk) to die, and thus a higher survival. When the vertical lines, which represent the 95% CI on the campus HR, include value 1.0 (dashed line), the HR of that campus is not statistically significantly different from the average campus (average patient).*
*Source: BCR-IMA-HDD*

### 5.4.2 *Patients diagnosed with non-metastatic IBC in 2014 - 2018, who had surgery*

As expected, the unadjusted five-year observed survival probability in the subgroup of patients with non-metastatic IBC who underwent surgery, was higher than in the total study cohort (91.1%, 95% CI: [90.7, 91.4]; Table 7). The differences observed between the various subgroups of the total cohort, were also observed in the subgroup of non-metastatic patients. For instance, the survival probability was higher in patients younger than 70 years, but it is apparent that there was no linear trend between those younger subgroups (Table 89). The unadjusted five-year relative survival was also higher than in the whole cohort (99.5%, 95% CI: [99.1, 99.8]); interestingly, for some subgroups the relative survival proportion was higher than 100%, which suggests that for these subgroups of patients with IBC the prognosis is higher than for the general population with the same characteristics.

**Comparison between campuses**

The multivariable Cox proportional hazard models revealed that of the 127 units of analysis for which the HR could be estimated (i.e. with a minimum of forty patients treated in the campus during the five-year period):

- **seven** units of analysis (all recognised as **coordinating breast clinics**) had their confidence interval below the reference line: patients treated in these campuses had thus a **significantly lower hazard to die** than patients treated in the average campus (Figure 5)
- **sixteen other units of analysis** (six coordinating breast clinics, one satellite breast clinic and nine without recognition for BC) did **significantly worse** than the average campus.

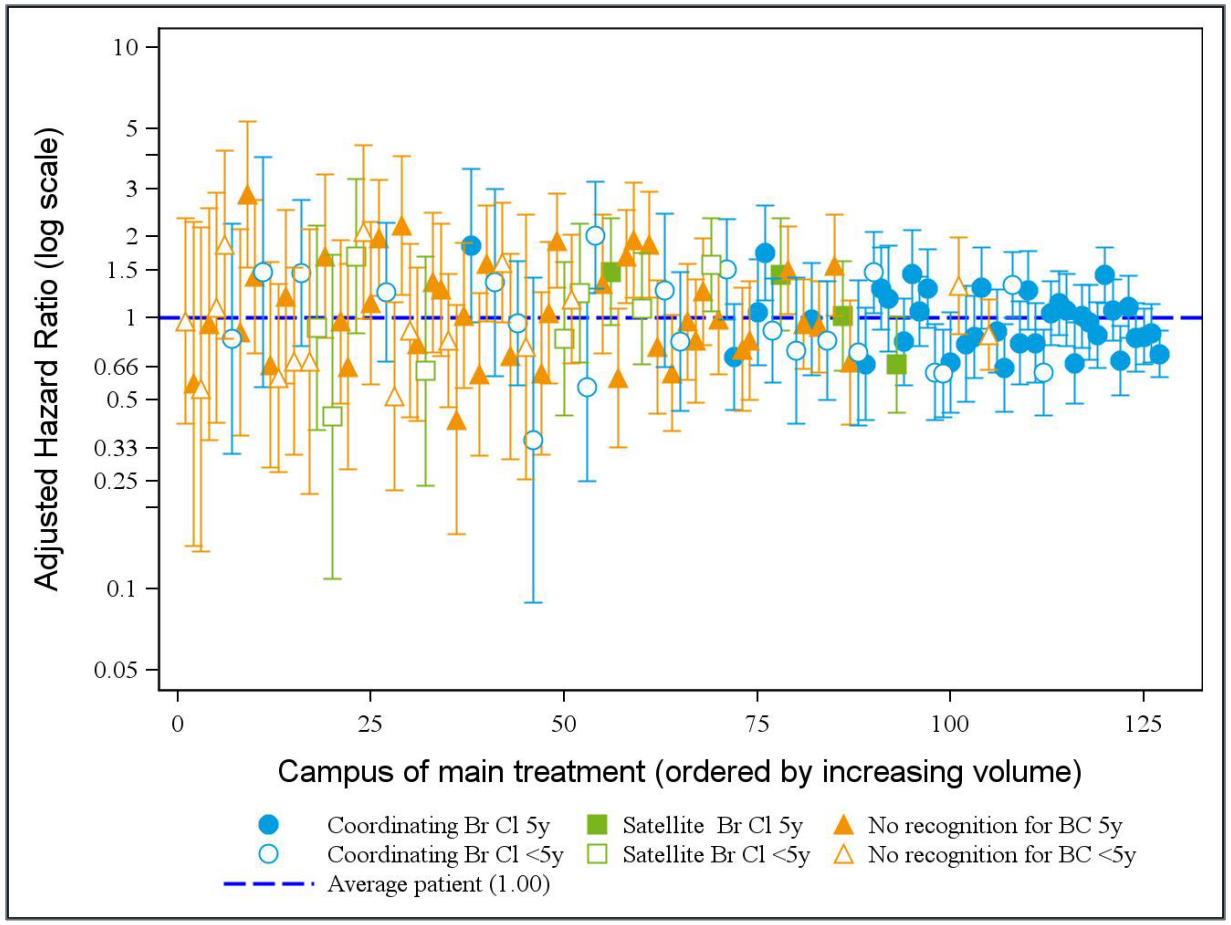
The excess hazard ratio could not be computed since there were not sufficient excess deaths to model.

**Table 7 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with non-metastatic* IBC who had surgery**

| | | Unadjusted observed survival (%, 95% CI) | | | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | **1-year** | **3-year** | **5-year** |
| **Overall** | 33 000 | 99.0 [98.9, 99.1] | 95.3 [95.1, 95.5] | 91.1 [90.7, 91.4] | 100.4 [100.3, 100.5] | 100.0 [99.8, 100.3] | 99.5 [99.1, 99.8] |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

**Figure 5 – Forest plot of the adjusted hazard ratio for all-cause death in patients with non-metastatic IBC who had surgery, by main treatment campus**




*Hazard ratios were determined over the [0,5] year survival time interval. A minimum unit size of 40 assigned patients was applied, with size referring to the number of patients available for the analysis. For 127units of analysis the adjusted HR could be obtained. The hazard ratios were adjusted for age at diagnosis, WHO score, number of previous hospital bed days, cardiovascular and respiratory disease, diabetes, combined tumour stage, differentiation grade.*

*Value 1.0 represents the average campus and the dashed blue line is the HR for the average patient (which equals the weighted sum of all campus HR, with the number of patients per campus as weight). The campuses are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). A HR which is lower than 1.0, indicates a lower hazard (or instantaneous risk) to die, and thus a higher survival. When the vertical lines, which represent the 95% CI on the campus HR, include value 1.0 (dashed line), the HR of that campus is not statistically significantly different from the average campus (average patient).*
*Source: BCR-IMA-HDD*

# 6 ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A CAMPUS AND SURVIVAL

## 6.1 Introduction

Throughout this report, analyses have been performed at the **national level**, and, where possible, also at the **level of the campuses**. If this was not feasible (e.g. in case of benchmarking based on the hospital identified as the centre of diagnosis), analyses were performed at the **level of the hospital**.

Also, the high number of non-recognised centres may give the erroneous impression that there are a lot of campuses without recognition for BC. It should be kept in mind that this number comprises campuses that were no longer active at the end of the study period as well as campuses that did not have a recognition for BC at the start of the study period, but became recognised during the study period.

## 6.2 Distribution of BC care in 2014 - 2018

In the study period 2014 - 2018, 37 out of 63 units of analysis[dd] recognised as coordinating breast clinic had an average annual campus volume of ≥125 patients (Table 8). Yet, 26 units of analysis recognised as coordinating breast clinic did not fulfil the volume criterion. Similarly, ten out of fourteen units of analysis recognised as satellite breast clinics had an average annual campus volume between 60 and 125 patients, but four did not fulfil the volume criterion.

**Table 8 – Number of campuses in 2014 - 2018, by recognition status and average annual volume**

| | Average annual campus volume* (n, %) | | | |
|---|---|---|---|---|
| | ≥125 | [60, 125[ | <60 | Total |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 37 (58.7) | 21 (33.3) | 5 (7.9) | **63** |
| **Satellite breast clinic** | 0 | 10 (71.4) | 4 (28.6) | **14** |
| **No recognition for BC** | 3 (2.8) | 17 (15.9) | 87 (81.3) | **107** |
| **Total (units of analysis at campus level)** | **40** | **48** | **96** | **184** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

Despite the legislator's initial intention to offer specialised BC care in dedicated breast clinics, 23.5% of the patients with DCIS or IBC included in the study cohort and who could be assigned to a campus of main treatment, were treated in a campus without recognition for BC (Table 9). This proportion decreased during the study period, from 30% in 2014 to 18.9% in 2018 (Appendix 12.2). The majority of patients were treated in campuses with a recognition of coordinating breast clinic (70.8%), while only 5.6% was treated in a satellite breast clinic.

But, when the average annual campus volume was also taken into account, it turned out that only about half of the patients (55.4%) was treated in a coordinating breast clinic that fulfilled the volume criterion. This proportion increased slightly from 54.2% in 2014 to 57.4% in 2018 (Appendix 12.2).

dd As the recognition status of a campus may have changed during the study period, it may appear as more than one 'unit of analysis' in the analyses and graphs. This is further explained in section 4.4.4.

During the study period, the proportion of patients treated in a satellite breast clinic that fulfilled the volume criterion increased from 2.6% in 2014 to 6.8% in 2018.

**Table 9 – Distribution of patients diagnosed with DCIS or IBC in 2014 - 2018, by recognition status and average annual volume of the campus**

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 25 928 (78.1) | 7104 (21.4) | 150 (0.5) | **33 182** (70.8) |
| **Satellite breast clinic** | 0 | 2 271 (86.0) | 370 (14.0) | **2 641** (5.6) |
| **No recognition for BC** | 1 192 (10.8) | 2 904 (26.4) | 6 919 (62.8) | **11 015** (23.5) |
| **Total** | **27 120 (57.9)** | **12 279 (26.2)** | **7 439 (15.9)** | **46 838** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; £: for each individual patient, the recognition status of the campus at the first day of the month in which the patient was treated, was taken into account.*
*Source: BCR-IMA-HDD*

## 6.3 Unadjusted association between the recognition status and volume of a campus, and observed survival since diagnosis of IBC

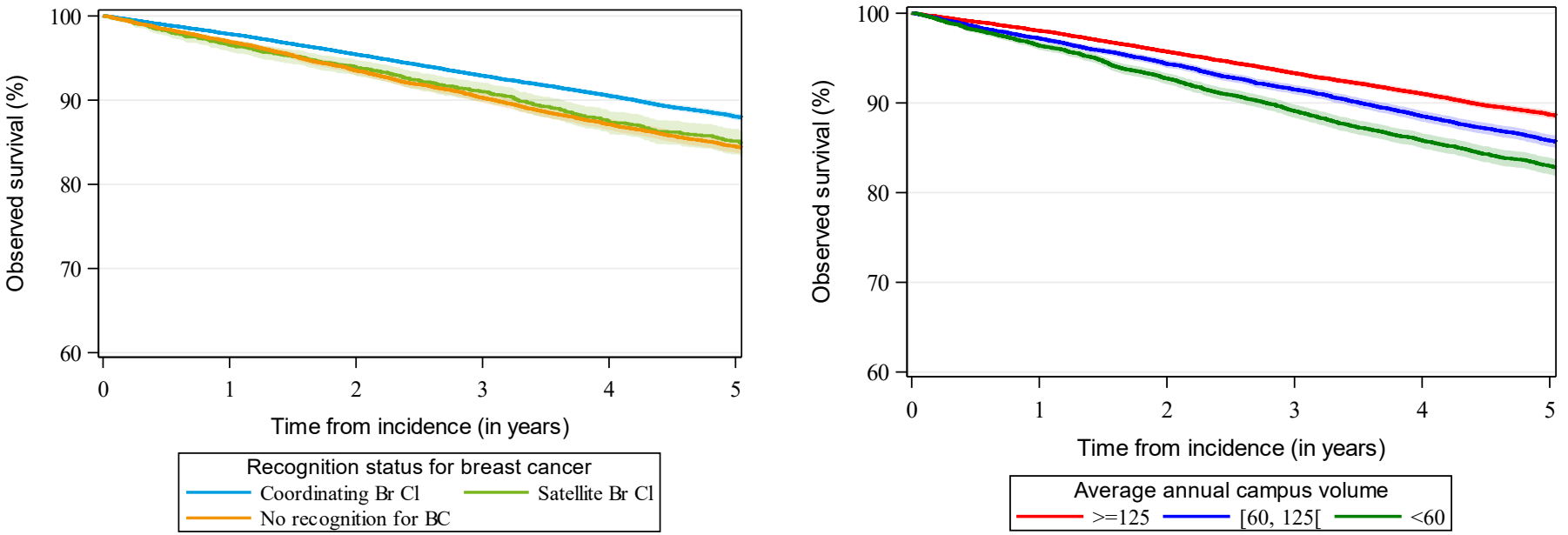
In patients with IBC, the observed survival probability five years after the diagnosis was significantly lower for the subgroups treated in campuses without recognition for BC (84.5%, 95% CI: [83.8, 85.2]) and the subgroups treated in satellite breast clinics (85.1%, 95% CI: [83.6, 86.6]), compared to the subgroup treated in coordinating breast clinics (88.0%, 95% CI: [87.6, 88.4]; Table 95, Figure 6). These analyses were not adjusted for case-mix variables and the intra-campus correlation was not taken into account either.

The Cox proportional hazards model, in which the clustering of patients within campuses was taken into account but not the case-mix, revealed that the hazard to die within 5 years after diagnosis was 40% higher (HR: 1.40, 95% CI: [1.24, 1.59]) when treated in a campus not recognised for BC and 22% higher (HR: 1.22, 95% CI: [0.98, 1.52]) when treated in a satellite breast clinic, compared to patients treated in coordinating breast clinics (Table 96). A sensitivity analysis, which also took the clustering of patients within campuses into account, indicated that the hazard to die was 39% higher (HR: 1.39, 95% CI: [1.22, 1.60]) for patients treated in a campus that treated less than 150 patients per year, compared to patients treated in campuses with an average annual caseload of 150 and more.

Similarly, five years after the diagnosis, the observed survival probability for patients with IBC treated in low-volume campuses (83.0%, 95% CI: [82.0, 83.9]) was significantly lower than the observed survival probability for patients treated in medium-volume campuses (85.8%, 95% CI: [85.1, 86.5]), which was again significantly lower than that for patients treated in high-volume campuses (88.7%, 95% CI: [88.3, 89.1]).

The hazard to die within 5 years after diagnosis, was 65% higher (HR: 1.65, 95% CI: [1.45, 1.88]) when treated in a low-volume campus and 30% higher (HR: 1.30, 95% CI: [1.14, 1.49]) when treated in a medium-volume campus, compared to patients treated in a high-volume campus. This volume effect was also observed between the high-volume and medium-volume coordinating breast clinics (p=0.014), the medium-volume and low-volume satellite breast clinics (p=0.037), as well as between the high-, medium- and low-volume campuses without recognition for BC (p<0.0001; Table 95 and Table 96).

**Figure 6 – Observed survival probability, by campus recognition status (left) and average annual campus volume (right)**




*The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 3 021 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

## 6.4 Adjusted association between the recognition status and volume of a campus, and observed survival since diagnosis

When the case-mix of campuses as well as the clustering of patients within campuses was taken into account, the Cox proportional hazard model indicated that the **hazard to die** was **12% higher** (HR: 1.12, 95% CI: [1.03, 1.23], p=0.013) for patients treated in a **campus without recognition for BC**, compared to patients treated in a **coordinating breast clinic** (Table 10). The adjusted hazard ratios are lower than the crude hazard ratios, pointing to some positive confounding by the case-mix variables (i.e. the adjusted HR is closer to the null value than the unadjusted).

Likewise, the **hazard to die** was **17% higher** (HR: 1.17, 95% CI: [1.05, 1.30], p=0.003) for patients treated in a **low-volume campus** and **14% higher** (HR: 1.14, 95% CI: [1.03, 1.26], p=0.013) for patients treated in a **medium-volume campus**, compared to **high-volume campuses**. A sensitivity analysis, which also took the case-mix of campuses and the clustering of patients within campuses into account, revealed that **the hazard to die** was **15% higher** (HR: 1.15, 95% CI: [1.04, 1.26], p=0.005) for patients treated in a campus that treated less than 150 patients per year, compared to patients treated in campuses with an average annual caseload of 150 and more.

Further analysis of the data indicated that within the group of coordinating breast clinics and within the group of campuses without recognition, no additional volume effect was observed (see Table 97). Among the satellite breast clinics, the low-volume campuses did better than the medium-volume campuses (HR: 0.60, 95% CI: [0.38, 0.94]).

**Table 10 – Observed survival, adjusted HR to die from all causes for patients with IBC, by recognition status and campus volume**

| | Adjusted# HR | 95% CI | p-value£ | p-value, type III$ |
|---|---|---|---|---|
| **Recognition status for BC** | | | | 0.045 |
| Coordinating breast clinic | 1 | [Reference] | | |
| Satellite breast clinic | 1.05 | [0.89, 1.24] | 0.544 | |
| No recognition for BC | **1.12** | [1.03, 1.23] | 0.013 | |
| **Average annual campus volume*** | | | | 0.006 |
| ≥125 | 1 | [Reference] | | |
| [60, 125[ | **1.14** | [1.03, 1.26] | 0.013 | |
| <60 | **1.17** | [1.05, 1.30] | 0.003 | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model; £: p-value from Wald test; #: adjusted for age at diagnosis, WHO performance status at diagnosis, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiovascular and respiratory diseases, diabetes), combined tumour stage and tumour differentiation grade; clustering of patients into campuses (i.e. centre of main treatment) was taken into account; 3 021 out of 45 893 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with a low volume were excluded.*

*Source: BCR-IMA-HDD*

## 6.5 Unadjusted association between the recognition status and volume of a campus, and relative survival since diagnosis

The association between the recognition status and volume of a campus with **relative survival** was estimated. The association is expressed as excess hazard ratio (EHR), which can be interpreted as the hazard ratio for an excess death (due to BC). Because the relative survival and the excess risk estimation is performed on grouped datasets (i.e. aggregated on recognition status or campus), the clustering of patients into campuses cannot be taken into account in these analyses.

**Table 11 – Relative survival, unadjusted relative excess risk to die for patients with IBC, by recognition status and campus volume**

| | Unadjusted EHR | 95% CI | p-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | <0.001 |
| Coordinating breast clinic | 1 | [Reference] | |
| Satellite breast clinic | **1.66** | [1.19, 2.30] | |
| No recognition for BC | **1.60** | [1.31, 1.95] | |
| **Average annual campus volume*** | | | <0.001 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | **1.43** | [1.14, 1.78] | |
| <60 | **2.10** | [1.69, 2.63] | |

*IBC: invasive breast cancer; EHR: excess hazard ratio; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Poisson regression model; clustering of patients into campuses (i.e. centre of main treatment) was not taken into account; 3 021 out of 45 893 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with a low volume were excluded.*

*Source: BCR-IMA-HDD*

The unadjusted **relative survival was worse in satellite breast clinics** (EHR: 1.66, 95% CI: [1.19, 2.30]) **and in campuses without recognition for breast cancer** (EHR: 1.60, **95% CI:** [1.31, 1.95]), compared to coordinating breast clinics (Table 11).

## 6.6 Adjusted association between the recognition status and volume of a campus, and relative survival since diagnosis

In a final step, the excess hazard was adjusted for age at diagnosis and combined tumour stage; the model did not allow us to adjust for more covariates.

The **risk to die from BC** was **30% higher (EHR: 1.30, 95% CI: [1.15, 1.48], p<0.001) for patients treated in a campus without recognition for BC, compared to patients treated in a coordinating breast clinic** (Table 12). The comparison of unadjusted and adjusted EHR indicate some confounding by age at diagnosis and combined tumour stage.

Likewise, the **risk to die from BC was 44% higher (EHR: 1.44, 95% CI: [1.24, 1.66]) for patients treated in a low-volume campus and 30% higher (EHR: 1.30, 95% CI: [1.14, 1.48]) for patients treated in a medium-volume campus, compared to high-volume campuses.**

**Table 12 – Relative survival, adjusted excess hazard ratios to die for patients with IBC, by recognition status and campus volume**

| | Adjusted[#] EHR | 95% CI | p-value[£] | p-value, type III[$] |
|---|---|---|---|---|
| **Recognition status for BC** | | | | <0.001 |
| Coordinating breast clinic | 1 | [Reference] | | |
| Satellite breast clinic | 1.06 | [0.84, 1.33] | 0.623 | |
| No recognition for BC | **1.30** | [1.15, 1.48] | <0.001 | |
| **Average annual campus volume*** | | | | <0.001 |
| ≥125 | 1 | [Reference] | | |
| [60, 125[ | **1.30** | [1.14, 1.48] | <0.001 | |
| <60 | **1.44** | [1.24, 1.66] | <0.001 | |

*IBC: invasive breast cancer; EHR: excess hazard ratio; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Poisson regression model; £: p-value from Wald test; #: adjusted for age at diagnosis, and combined tumour stage; clustering of patients into campuses (i.e. centre of main treatment) was not taken into account; 3 021 out of 45 893 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with a low volume were excluded.*

*Source: BCR-IMA-HDD*

## 6.7 Association between hospital volume and observed survival since diagnosis in the comparison cohort (2009 - 2013)

Ideally, difference in survival probability in BC should be assessed at **ten years after diagnosis**, given the overall good prognosis for BC. However, ten year survival probabilities could not be estimated for the study cohort, diagnosed in 2014 - 2018; ten year survival probabilities could only be estimated for the **comparison cohort**, diagnosed in 2009 - 2013.

In these analyses it was not meaningful to assess the association between recognition status and observed survival as the legislation on coordinating and satellite breast clinics was only effective in 2014. The fact that campus identification data were not available for this cohort also upset our plans: the association between volume and observed survival **could not be assessed at campus level**.

Consequently, the difference in survival probability at ten years after diagnosis of BC could only be estimated for the **comparison cohort** and at **hospital level**. Thus, when reading the results, one should be mindful that some of the centres that were categorised as high-volume centres[ee] were in reality a cluster of (potentially small) campuses. This unintentional misclassification of centres can induce bias.

Ten years after the diagnosis, the (unadjusted) observed survival probability for patients with IBC treated in low-volume hospitals (65.6%, 95% CI: [64.3, 67.0]) was significantly lower than the observed survival probability for patients treated in medium-volume (71.2%, 95% CI: [70.3, 72.2]), and high-volume hospitals (70.7%, 95% CI: [70.2, 71.3]; Table 100 andFigure 31).

When the clustering of patients within hospitals was taken into account, the hazard to die within 10 years after diagnosis, was 34% higher (HR: 1.34, 95% CI: [1.15, 1.56]; p<0.001) when treated in a low-volume hospital, compared to patients treated in a high-volume hospital (Table 101). When

[ee] For the ease of interpretation, the same volume cut-offs were applied as in the other volume analyses (i.e. >=125, [60, 125[, <60).

also the case-mix of patients was taken into account, the hazard to die was not significantly different between the volume groups (Table 102).

**Key points**

- **After adjustment for age at diagnosis and combined stage, the risk to die from BC was 30% higher (EHR: 1.30, 95% CI: [1.15, 1.48], p<0.001) for patients treated in a campus without recognition for BC, compared to patients treated in a coordinating breast clinic;**
- **After adjustment for age at diagnosis and combined stage, the risk to die from BC was 44% higher (EHR: 1.44, 95% CI: [1.24, 1.66]) for patients treated in a low-volume campus and 30% higher (EHR: 1.30, 95% CI: [1.14, 1.48]) for patients treated in a medium-volume campus, compared to high-volume campuses.**

# 7 ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A CAMPUS/HOSPITAL AND PROCESSES & OTHER OUTCOMES OF CARE

In the following sections the association between the recognition status of a hospital/campus and certain processes of care is assessed. Each section begins by providing the rationale and some contextual factors related to the calculation and/or interpretation of the process indicator. Then the national results are discussed, and the international context is briefly reviewed. The variability between campuses/hospitals is explored, before assessing the association between the recognition status and/or volume of a campus (or hospital) and the process of care. In Appendix 13 to Appendix 25 the documentation sheets, flow charts as well as tables and figures with additional results are provided.

The (average annual) campus/hospital volume is calculated as described under section 6.1. In the bubble plots, the size of the bubbles provides a relative indication of the number of patients per recognition-volume stratum.

Patient allocation was defined for each indicator, in consultation with the clinical experts. When allocation was based on the centre of diagnosis, the association between recognition status and the process of care could not be assessed (see section 4.4.2).

In each logistic regression analysis discussed in this chapter, the clustering of patients within the campuses c.q. hospitals was taken into account; this is thus not repeatedly mentioned. Whether the analyses should be adjusted for case-mix variables, was upfront discussed with the clinical experts. Where it was done, unadjusted and adjusted odds ratios are reported, as well as the case-mix variables for which adjustment was performed. When no logistic regression analysis was performed, the variability between the campuses/hospitals is presented in a funnel or scatter plot included in the respective chapter. Else, the funnel or scatter plot is provided in the respective appendix.

## 7.1 Diagnosis & staging

### *7.1.1 Mammography and sonography in patients with IBC*

The diagnosis of BC should be made by a 'triple assessment', comprising clinical assessment (patient history and physical examination), imaging and a biopsy[ff]. To allow a proper diagnostic approach and to identify size, site and possible multifocal and/or contralateral disease, imaging includes bilateral mammography and sonography (ultrasound, US) of the breast and regional lymph nodes.

Magnetic resonance imaging (MRI) of the breast is more sensitive in determining the extent of the tumour but it may also overestimate the tumour size.[82] An MRI of the breast is not routinely recommended, but should be considered in specific situations (e.g. familial BC associated with BRCA mutations, dense breasts, suspicion of multifocality/multicentricity (particularly in lobular BC)).[83] As there was no consensus among the experts whether an MRI should be included in this indicator, it was decided to not include MRI in the calculation of the main QI. Data on MRI were provided in the sensitivity analyses.

Due to the prevailing cumulation rules, stipulating that on the same day only one mammography (for one or two breasts) and only one US can be invoiced for a patient, the elaboration of the QI was somewhat complicated (see Appendix 13.1 for more details).

In Appendix 13 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

**National results**

Overall, 92.5% of patients had a mammography and breast sonography (US) before the start of any treatment (Table 103), which is somewhat below the target of 95% set by EUSOMA.[46] Women younger than forty (n=2 239) were 6% less likely to have had both imaging procedures before the start of treatment (RR: 0.94, 95% CI: [0.92, 0.95]). Further exploration of the data revealed that this subgroup was more likely to have had a combination of breast US and MRI (7.2% vs. 1.8%; data not presented) or a combination of the three imaging procedures (65.9% vs. 46.1%; data not presented) compared to older patients.

Frail women (i.e. WHO performance status 2-4) were 22% less likely having had an US and mammography before the start of the first treatment (74.9% vs. 93.1%; RR: 0.80, 95% CI: [0.78, 0.83]). The combination of mammography and US was also less frequently performed in women with clinical stage III-IV compared to women diagnosed with clinical stage 0-II (84.8% vs. 94.1%; RR: 0.90, 95% CI: [0.89, 0.91]) and in women who only received surgery (85.0% vs. 94.1%; RR: 0.90, 95% CI: [0.88, 0.93] or primary systemic and/or radiotherapy (81.5% vs. 94.1%; RR: 0.87, 95% CI: [0.85, 0.88]) compared to patients treated with a combination of surgery and/or systemic therapy and/or radiotherapy.

In nearly one in two patients with IBC who had any type of oncological treatment, a combination of mammography, US and breast MRI was performed (47.7%; Table 107) and in 44.8% of patients a combination of mammography and US without MRI was performed, while for the remaining patients either another combination of two imaging procedures or a sole imaging procedure was recorded.

**International comparison**

We did not identify population-wide data from other countries on the provision of mammography and ultrasound before the start of BC treatment. With regard to the use of MRI, in addition to standard imaging (i.e. mammography and US), the National Breast Cancer Organisation Netherlands (NABON) Breast Cancer Audit, a nation-wide audit on the quality of BC care and guideline adherence in the Netherlands, indicated that in 2018 in 28.8% of patients with DCIS and in 27.6% of patients with

[ff] A core needle biopsy is necessary; a fine-needle aspiration is insufficient and should not be performed in the breast, since it has a high rate of false results and does not allow for adequate biomarker characterisation.[34]

IBC (who did not have neo-adjuvant chemotherapy[gg]) a preoperative MRI was performed, in addition to the standard imaging.[84]

**Table 13 – Association between recognition status for BC and campus volume, and the odds of having mammography and breast sonography before any treatment in women with IBC**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.206 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.96 | [0.65, 1.41] | |
| No recognition for BC | 0.82 | [0.66, 1.02] | |
| **Average annual campus volume*** | | | 0.015 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.02 | [0.78, 1.32] | |
| <60 | **0.74** | **[0.58, 0.95]** | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first treatment) was taken into account; 3 304 patients could not be assigned to a campus, and were thus excluded from the analyses; 196 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on the algorithm for centre of first treatment) to a campus with no main treatment volume.*
*Source: BCR-IMA-HDD*

### Comparison between centres

The funnel plot indicates that there is quite some variability between the hospital campuses, with 24 out of 184 units of analysis situated below the 99% prediction interval (Figure 33).

### Association with campus volume and recognition status

The logistic regression analysis[hh] indicated a statistically significant association between average annual campus volume and the odds of having had both mammography and breast sonography before the first treatment (Table 13). The odds for having mammography and US before the start of treatment was 26% lower (OR: 0.74; 95% CI: [0.58, 0.95]) in small compared to high-volume campuses. There was no significant association with campus recognition status. Within the campuses without recognition for BC, those with a low volume did worse than those with a high volume (OR: 0.51; 95% CI: [0.26, 1.01], Table 109).

**Key points**

- **Overall, 92.5% of patients with IBC had a mammography and breast sonography before the start of any oncological treatment, which is somewhat below the EUSOMA target of 95%;**
- **The odds for having both mammography and breast sonography before the first treatment was 26% lower (OR: 0.74; 95% CI: [0.58, 0.95]) in low-volume compared to high-volume campuses.**

gg In patients with IBC who had neo-adjuvant chemotherapy, the respective proportion was 89.4%.[84]

hh Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

### 7.1.2 Assessment of histology and/or cytology before treatment[ii]

A lesion in the breast which is considered malignant following clinical examination, imaging or cytology alone should, where possible, have histopathological confirmation of the malignancy before any surgical procedure is undertaken.[85, 86] Histological type and grade are not only prognostically useful, they also show a predictive value for multifocality and metastatic pattern, and are therefore considered part of the core data set on BCs.[46]

Although the cytological assessment of breast tumours before treatment is nowadays obsolete, cytological assessment was still included in the calculation of this quality indicator because exploration of the administrative database revealed that the nomenclature codes intended for cytology are often used for a histological assessment and vice versa. In addition, the present study includes incidence years 2014 - 2018, when cytology was still being performed. The clinical experts further proposed to not restrict this quality indicator to women who had surgery, but to enlarge the target group to all women with IBC who had any type of oncological treatment.

In Appendix 14 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

**National results**

Overall, 98.0% of women with IBC had a histological or cytological assessment before any treatment, a result that was better than the pre-set target of 90% (Table 110). In the comparison period 2009 - 2013 this proportion was a bit lower (i.e. 95.8%; Table 111), but still higher than the target. There was no marked variability between the subgroups of the various patient and tumour variables, and even between the different treatment modalities. In the subgroup of women who didn't receive a surgical procedure, for instance, 96.9% had a histological or cytological assessment before their primary systemic and/or radiotherapy.

Among the 45 094 women with IBC who had an oncological treatment, two in three had the combination of a histological examination with immunohistochemical testing (IHC), and almost one third received the combination of both cytological and histological assessment with IHC testing (28.7%; Table 112).

**International comparison**

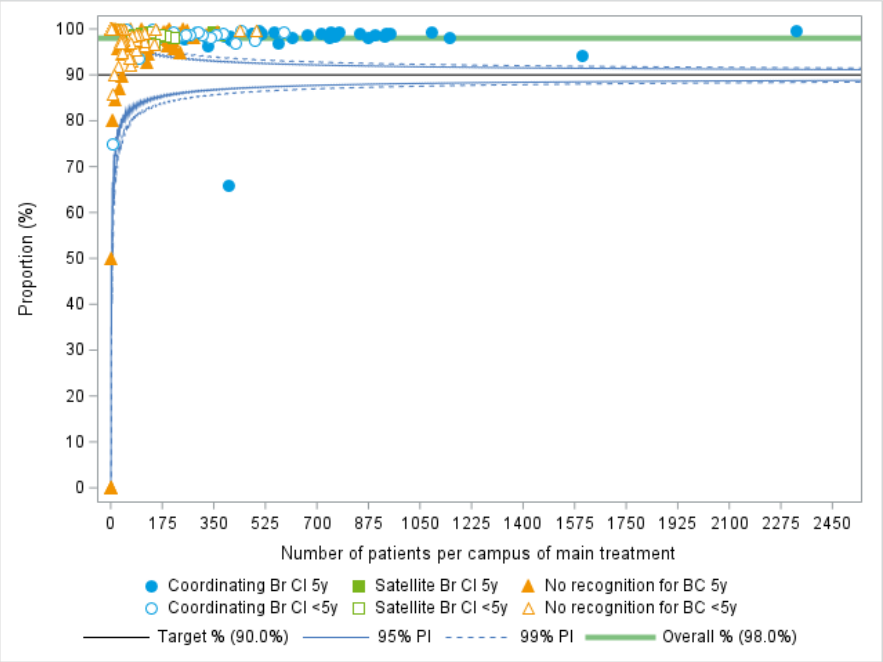
In the international literature, several reports can be found that illustrate high compliance to this quality indicator. In a French study, which included 1 560 women with primary invasive non-metastatic BC diagnosed in 2012 who were randomly selected among all incident BC cases from 16 French geographical areas covered by cancer registries, 97.6% (95% CI: 96.7-98.3) had a preoperative histologically or cytologically definitive diagnosis.[87] In Germany, the diagnosis was histologically confirmed in 98.05% of 48 754 women with DCIS or IBC before their treatment was initiated in 2018.[88] Among the 46 122 patients with invasive or in situ BC diagnosed and treated in one of the 22 EUSOMA-certified breast centres in Germany, Switzerland, Belgium, Austria, the Netherlands, Spain, Portugal and Italy in 2006-2015, 87.2% had a preoperative diagnosis; this proportion increased from 80.2% in 2006 to 91.5% in 2015.[89]

**Comparison between centres**

Irrespective of whether benchmarking was performed based on the hospital of diagnosis (Figure 35), or on the campus of main treatment (Figure 7), almost all hospitals were situated within or even above the 99% prediction interval constructed around the target of 90%.

[ii] This QI is also included in the list of QIs included in the European Quality Assurance Scheme for Breast Cancer Services, where it is focusing on women with invasive and non-IBC who had oncological treatment and where the target is set at ≥ 95%.[40]

**Figure 7 – Proportion of women with IBC with histological or cytological assessment before any treatment, by campus of main treatment**




*Note: There are 182 units of analysis reported in the funnel plot, 25 of them having less than ten patients in denominator; one unit is situated below the 99% prediction interval, while 108 are situated above the 99% prediction interval; 2 080 patients, who could not be assigned to a campus of main treatment, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

**Association with hospital volume and recognition status**

Given the low variability between the units of analysis, there was no added value of doing these analyses.

**Key points**

- **Overall, 98.0% of women with IBC had a histological or cytological assessment before any oncological treatment, which is thus better than the EUSOMA target of 90%.**

### *7.1.3 Assessment of receptor status before any systemic treatment[jj]*

Gene expression profiling in oncology (e.g. MammaPrint and Oncotype DX) has provided a new paradigm for classifying breast carcinomas, predicting response to treatment, and risk of recurrence.[90] The main drivers of classification in many of the gene expression profiling tests for BC are oestrogen receptor (ER), human epidermal growth factor 2 (HER2) receptor, and proliferation-related genes. The KCE guideline, as well as the recently updated guidelines of the American Society of Clinical Oncology (ASCO) and of the College of American Pathologists recommend HER2 and both ER and PR[kk] status testing in patients with IBC.[86, 92, 93]

While the clinical experts expressed the wish to follow the guidelines and provide data on the assessment of ER, PR and HER2 separately, this was not feasible due to the limitations of the nomenclature codes (see section 4.10.3). Last, the registration of ER, PR and HER2 is one of the legally defined recognition criteria for coordinating and satellite breast clinics.[4]

[jj] This QI is also included in the list of QIs included in the European Quality Assurance Scheme for Breast Cancer Services, where the target is set at ≥ 95%.[40]

[kk] While the role of the ER status is established, this is less clear for the PR status.[91, 92] There is a small subset of women with IBC that test ER negative and PR positive; these women may be candidates for endocrine treatment because there is no single explanation for this finding at this time.[91, 92] Taking all this in consideration, the EUSOMA working group does not take the assessment of the PR status into consideration for the calculation of its quality indicator on the completeness of recording of prognostic/predictive parameters.[46]

In Appendix 15 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

### National results

In 99.4% of women diagnosed with IBC in 2014 - 2018 and treated with systemic therapy, testing for ER and/or PR and/or HER2 status was performed before any systemic treatment (Table 113). The target of 98% was attained in the study period, but also in the period 2009 - 2013 (98.9%; Table 114). No apparent associations were observed between any of the studied variables and testing for receptor status (Table 113).

A sensitivity analysis in which the time frame was expanded to 3 months around incidence date, revealed that for nearly all women (99.6%) the receptor status was assessed (Table 115). Similarly, receptor status assessment was performed within 3 months around incidence date for almost all women (99.2%) diagnosed with IBC, irrespective of any treatment (Table 116).

### International comparison

The national results look good, also when they are compared with results from other countries. For instance, the compliance with this quality indicator was also assessed in the 22 EUSOMA-certified breast clinics located in Germany, Switzerland, Belgium, Austria, the Netherlands, Spain, Portugal and Italy in the period 2006-2015. The results revealed that the proportion of patients with IBC for whom the histological type, grading, ER/PR, stage & size was recorded, increased from 92.1% in 2006 to 97.5% in 2015.[89]

### Comparison between centres

As is illustrated in Figure 36, where benchmarking was performed based on the hospital of diagnosis, and in Figure 8, where benchmarking was performed based on the campus of main treatment, hardly any variability was observed between the various units of analysis. No unit had a proportion below the 99% prediction interval.

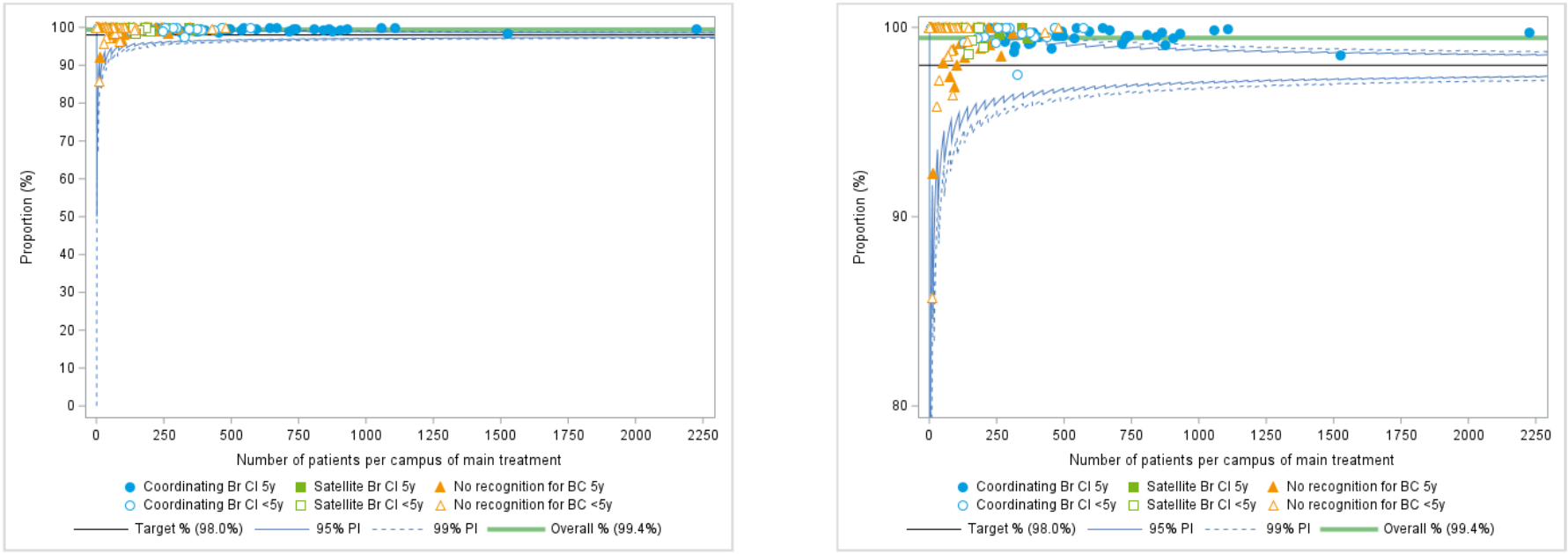
### Association with hospital volume and recognition status

Given the low variability between the units of analysis, there was no added value of doing these analyses.

**Key points**

- **Overall, in 99.4% of women with IBC an immunohistochemical assessment for either ER, PR or HER2 status was performed before the start of systemic treatment.**

**Figure 8 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status was assessed before any systemic treatment (left) and zoom on the highest proportions (right), by campus of main treatment**




*Note: There are 180 units of analysis reported in the funnel plot, 24 of them having less than ten patients in denominator; no unit is situated below the 99% prediction interval, while 30 are situated above the 99% prediction interval; 2 014 patients, who could not be assigned to a campus of main treatment, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

### 7.1.4 Multidisciplinary team (MDT) meeting

Anno 2023, it goes without saying that MDT meetings, where professionals from different specialties (among others, medical oncologists, radiologists, surgeons, radiotherapists, pathologists and nurse specialists) discuss cancer patients, have a positive impact on patient assessment and management practices. Since 2003, multidisciplinary team meetings have been reimbursed for all cancer types in Belgium.[79] Since 2010, three types of multidisciplinary team meetings are reimbursed (see Box 7).[79, 94]

**Box 7 – Types of multidisciplinary team meetings in Belgium**

The '**first MOC'** is intended for the first diagnosis and treatment plan of a newly diagnosed cancer patient.

A '**follow-up MOC'** meeting is intended to discuss the revision of a diagnosis and/or the change in an oncological treatment plan, and/or to repeat a series of irradiation within 12 months after the start of the first series of irradiation. The 'change in treatment plan' should be interpreted in a restricted way and used with parsimony: it only refers to a change in the treatment plan where a multidisciplinary decision is required. Changes in the systemic or irradiation treatment plan or in palliative care is the responsibility of the treating specialist, and does not necessarily require a follow-up MDT meeting.

A '**supplementary or second opinion MOC'** is intended for establishing the diagnosis or treatment plan in another hospital, when it was not possible to come to a diagnosis and/or treatment plan during the first MOC. A prerequisite for reimbursement is the statement of the referral hospital on in the minutes of the first MOC.

*Source: Vrijens et al., 2015[79]*

A recent systematic review of the literature (with focus on European and North American sources) reported that the target ('standard of care') for this quality indicator (proportion of BC patients to be discussed pre and postoperatively by a multidisciplinary team), ranged between 85 and 100%.[95] The clinical experts agreed to apply the EUSOMA target: 99% of BC patients should be discussed pre- and postoperatively.[46]

However, the invoicing rules threw a spanner into the works: only one 'first MDT' can be billed per patient and per calendar year (with some exceptions). Hence we could only identify for which patients at least one MDT was invoiced within the pre-defined time interval; we were not able to specify how many times a patient was discussed during the entire care pathway, nor when these MDT meetings had taken place. Therefore it was opted to not benchmark against the defined target of 99%, and to present the variability between the hospitals in a scatter plot.

For the main analysis it was opted to apply the time frame one month before up to two months after incidence date; additional sensitivity analyses are provided with increasing time periods. We should realise that the results do not provide any insights on the quality of the multidisciplinary meeting itself, nor on the multidisciplinary approach during the entire care pathway.[96]

In Belgium, a MDT meeting is mandatory for women diagnosed with BC and treated in a recognised breast clinic.[4] As it was not possible to identify the campus where the MDT was held (billed), analyses at campus level were not possible. Hence, it was not possible to verify whether for all patients diagnosed in a coordinating or satellite breast clinic a MDT was held, as is stipulated in the law.

In Appendix 16 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

### National results

Overall, **83.6% of patients with DCIS were discussed at a MDT** within the time frame of 1 month before and 2 months after incidence date (Table 117); in the comparison period 2009 - 2013 the respective proportion was 80.6% (Table 118). For **90.1% of patients diagnosed in 2014 - 2018 with IBC a MDT** was billed (Table 117), hence somewhat more than in the comparison period 2009 - 2013 (87.5%).

The sub-analyses further indicate that the proportion of patients with IBC discussed at a MDT was lowest in the over 80 years old age group (i.e. 84.6%; Table 117), in patients who had been admitted in hospital for more than 15 days in the year preceding their diagnosis of IBC (83.7%) and in the (small) subgroup for whom no oncological treatment was recorded (51.9%). It is also important to note that the proportion of women discussed at a MDT is lower in the subgroups for whom no clinical or combined stage information was available at the BCR (75.2% and 41.0%, respectively). Stated differently, **for patients with IBC whose case was not discussed in a billed MDT, there was a three times higher probability that their clinical stage information was not transferred to the BCR** (RR: 3.00, 95% CI: [2.83, 3.17]). The relative risk was smaller for patients with DCIS (RR: 1.48, 95% CI: [1.34, 1.63]).

### International comparison

Compared to the Belgian data, the results from the Netherlands are impressive. The (NABON) Breast Cancer Audit revealed that the proportion of surgically treated patients discussed in pre- and post-operative multidisciplinary team meetings increased from 83% and 91% in 2011 to 98% and 99% in 2014, respectively.[97] In 2017, 98% of women with BC were discussed during a pre- and post-operative multidisciplinary team meeting.[98] The annual reports of the German certified BC centres revealed that the proportion of patients with DCIS or IBC discussed pre-treatment was much lower: it was 75.9% in 2018; yet, postoperative case presentation was as high as 99.4%.[88] This indicator was omitted from the NABON set since it did not add any information.(*IKNL, personal communication*)

### Comparison between centres

The variability between the hospitals was large: the proportion of patients discussed during a MDT ranged between 25% and 100% for DCIS, and between 50% and 100% for patients with IBC (Figure 9). According to the clinical experts and the feedback received during the validation study, several factors may explain the low proportion in some hospitals. Some of them may invoice the MDT somewhat later, i.e. beyond the set time frame, which was confirmed in the sensitivity analysis with expanding time frames (Table 118). In addition, when patients are referred to another centre or change centre on their own initiative, this may give rise to some doubt on which centre can bill the MDT.

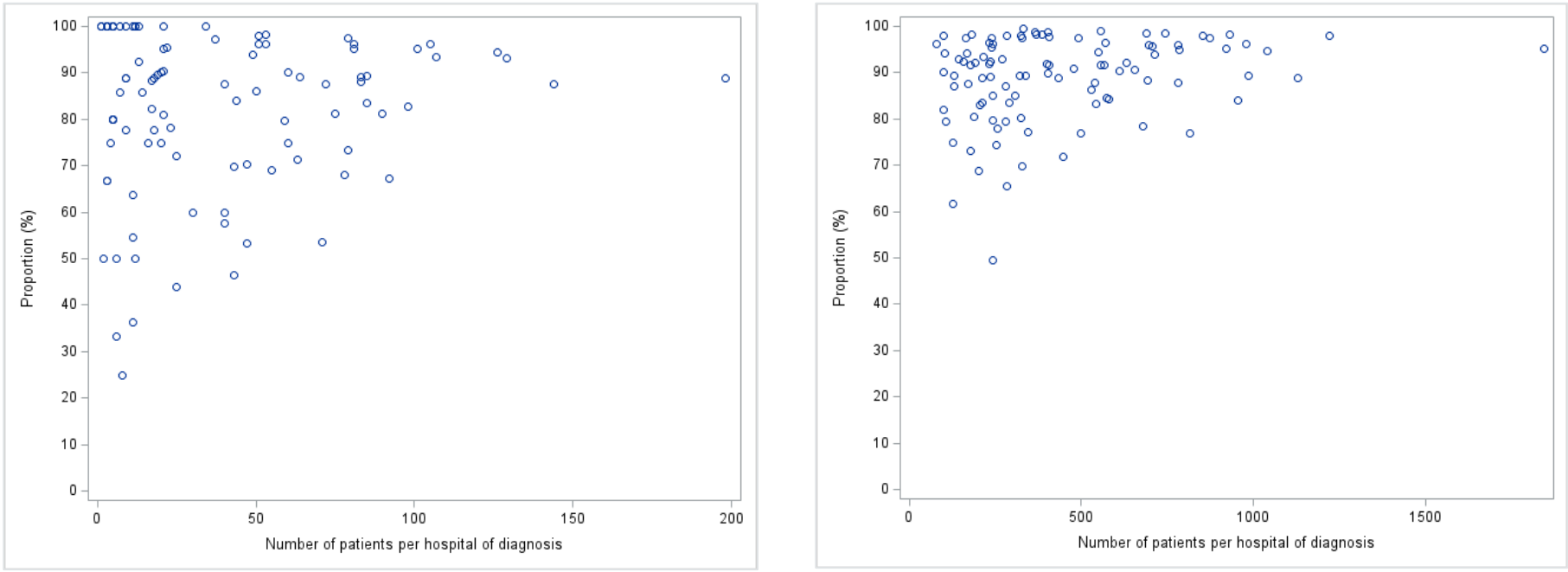
### Association with hospital volume and recognition status

In view of the fact that the available data on MDT tell little about the actual number and quality of MDT meetings held in Belgian hospitals, it was concluded that there was no added value of performing these analyses.

**Key points**

- **For 83.6% of patients with DCIS and 90.1% of patients with IBC, at least one MDT was invoiced from one month before up to two months after incidence date;**
- **The variability between the hospitals was large.**

**Figure 9 – Scatter plot of the proportion of women with DCIS (left) and IBC (right) for whom a multidisciplinary team meeting was charged within 1 month before until 2 months after incidence date, by hospital of diagnosis**




*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; Note for DCIS: There were 98 hospitals reported in the scatter plot, including 27 hospitals having less than ten patients in denominator; 138 patients, who could not be assigned to a hospital of diagnosis, are not represented in the scatter plot.*
*Note for IBC: There were 100 hospitals reported in the scatter plot; 1 859 patients, who could not be assigned to a hospital of diagnosis, are not represented in the scatter plot.*
*Source: BCR-IMA*

### 7.1.5 TNM stage reporting to the BCR

Accurate staging at diagnosis for patients with cancer, i.e. the anatomical extent of the disease at the time of diagnosis, is a crucial component in the clinical cancer pathway. It helps in guiding the selection of appropriate treatments, or the renouncement of treatment, and in predicting the patient's prognosis on the basis of the average survival of a comparable group of patients who have a similar extent of disease.[99] Stage information is also of public health importance, as it describes the overall disease burden, allows cancer surveillance, guides cancer control planning activities and helps evaluate outcomes of the healthcare system, such as screening or patient management programmes.[100, 101]

As this study is not based on medical files, but on cancer registry data linked to administrative data, a proxy approach was used to capture this information: the completeness of the data transferred to the BCR was used. In Belgium, hospitals are legally bound to transfer all new cancer diagnoses, comprising clinical and pathological stage information, to the BCR, whether or not the patient is discussed during a multidisciplinary team meeting (MDT).[102] The laboratories for anatomical pathology are the second source of information for the staging process. They encode the received specimens following the classification rules approved by the *Consilium Pathological Belgicum* and, as stated in the law, they have to transfer every (pre)malignant diagnosis together with the pathology reports to the BCR.[103]

For a good understanding of the data, it is important to mention that stages reported as TxNxMx and, for DCIS, TNM values not compatible with in situ behaviour are counted as 'not reported'; all other cTNM data are labelled as 'valid'. In case of incomplete reporting of cTNM and/or (y)pTNM, the case is categorised as reported. For instance, if only M1 is reported to the BCR, then the case is categorised as stage IV, or if only N is reported, then the case is categorised as the lowest stage compatible with this information.

In Appendix 17 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

**National results**

***a) Clinical stage***

Overall, for **66.6% of women diagnosed with DCIS** and for **88.8% of women diagnosed with IBC, valid cTNM** stage information was reported to the BCR (Table 121), which is far below the EUSOMA target of 98%.[46] Among the women with DCIS, reporting of valid cTNM stage information was lower in the older age groups (70-79 years: 63.8%, 80+ years: 55.6%), while in the group with IBC there was not much variation between age groups. Apart from the fact that cTNM stage reporting was lowest in the subgroups for whom also WHO performance status information was missing (DCIS: 44.1%, IBC: 61.5%), there was no marked association between cTNM stage reporting on the one hand, and the presence of comorbidities or the number of inpatient bed days in the year preceding incidence on the other hand. According to the experts, the suboptimal results for cTNM reporting may in part be explained by the fact that it is not always straight forward to come to a consensus with regard to the clinical staging among the members of the MDT. Arriving at a consensus is easier for (y)pTNM than for cTNM. In addition, there are several bottlenecks in this process (e.g. inferior communication between MDT and data managers, too few data managers) which may further explain the modest results.

A positive finding is that valid cTNM stage reporting increased over the years, from 56.9% in 2014 to 75.3% in 2018 in patients with DCIS and from 81.7% in 2014 to 94.5% in 2018 in patients with IBC. In the comparison period 2009 - 2013, the respective proportions were 44.7% in DCIS and 78.1% in patients with IBC (Table 122). Since 2017, the BCR has worked towards a better stage reporting with the Belgian hospitals: data sheets which report for less than 90% of their BC patients a valid cTNM stage and/or (y)pTNM stage, are returned to the hospitals for further completion. This initiative may, to some extent, explain the better results observed in 2017 and 2018.

Further, valid cTNM stage reporting was lowest in those subgroups for whom no oncological treatment was reported (DCIS: 45.0%, IBC: 65.6%) and highest in the subgroup of patients with IBC for whom neoadjuvant treatment was recorded (94.7%). As was stated before (section 7.1.2), a positive association between cTNM stage reporting and a billed MDT was

observed: the chance of not having a valid cTNM stage reported to the BCR was three and one and a half times higher when no MDT was recorded (within the time frame of 1 month before to 2 months after incidence date) in women with IBC and DCIS, respectively (RR: 3.00, 95% CI: [2.83, 3.17]; RR: 1.48, 95% CI: [1.34, 1.63]).

***b) Pathological stage***

The proportion of patients with **DCIS and IBC** who had surgery, for whom the **(y)pTNM stage was reported to the BCR was 93.4% and 96.3%**, which is close to the set target (98%; Table 124). In 2009 - 2013, (y)pTNM stage was reported for 84.7% of patients with DCIS and for 94.8% of patients with IBC who had surgery (Table 125).

The reporting of (y)pTNM stage was lowest in the subgroup of DCIS patients who only had surgery (90.7%) and in the subgroup of patients with IBC for whom neoadjuvant treatment was recorded (83.7%). In contrast to what was observed for cTNM stage, there was no marked association between (y)pTNM stage reporting and a recorded MDT.

**International comparison**

To the best of our knowledge, there are no international publications that provide contemporary (population-wide) data on the availability and/or reporting of clinical and pathological stage information in DCIS and IBC. An investigation of the data collected by the Danish Cancer Registry from 26 488 patients with a first diagnosis of BC between 2004 and 2009, showed that overall completeness of TNM registration was 85.4%.[104]

**Comparison between centres**

For DCIS, there was large variability between the hospitals with regard to cTNM stage reporting to the BCR, with some centres only reporting clinical stage information for fewer than 20% of their patients with DCIS (Figure 37). Some hospitals were situated within or on the boundaries of the 95% or 99% prediction interval around the target value, but the majority was situated well below these intervals (80.6% below the 95% prediction interval and 77.6% below the 99% prediction interval).

For IBC, the variability was less pronounced, with the least performing hospitals reporting for 50-60% of their patients the cTNM stage info to the BCR but again, the majority was situated well below the 95% and 99% prediction intervals around the target value (74% below the 95% prediction interval and 72% below the 99% prediction interval; Figure 37).

For (y)pTNM stage reporting in patients with DCIS, about 9.7% of units of analysis fell below the 99% prediction interval (Figure 39). For IBC, the respective proportion was 21.7% (Figure 39).

**Association with hospital volume, campus volume and recognition status[ll]**

The logistic regression analysis[mm], indicated that the odds for having cTNM stage information sent to BCR for patients with DCIS did not differ significantly between the three hospital volume groups (Table 14). For women with IBC, the odds for having cTNM stage information sent to BCR was 48% lower (OR: 0.52; 95% CI: [0.32, 0.86]) when they were diagnosed in a low-volume hospital compared to patients diagnosed in a high-volume hospital.

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ll For cTNM, patients were assigned to the centre of diagnosis, which is on hospital level, hence the association with volume was assessed at hospital level; the volume is based on the hospitals' main treatment volume. For (y)pTNM, patients were assigned to the campus where the main treatment took place, hence the association with volume was assessed at campus level; the volume is based on the campuses' main treatment volume.

mm Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

**Table 14 – Association between hospital volume and a valid cTNM stage reporting to the BCR**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Unadjusted OR | 95% CI | P-value, type III$ | Unadjusted OR | 95% CI | P-value, type III$ |
| **Average annual hospital volume*** | | | 0.407 | | | 0.038 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.74 | [0.44, 1.25] | | 0.67 | [0.38, 1.19] | |
| <60 | 0.76 | [0.46, 1.26] | | **0.52** | **[0.32, 0.86]** | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume groups; clustering of patients into hospitals (i.e. centre of diagnosis) was taken into account; 138 patients with DCIS and 1 859 patients with IBC could not be assigned to a hospital, and were thus excluded from these analyses.*
*Source: BCR-IMA*

With regard to the reporting of (y)pTNM stage information for patients with DCIS, the odds for having (y)pTNM stage information sent to BCR was 44% lower (OR: 0.56; 95% CI: [0.34, 0.93]) in campuses without recognition for BC compared to coordinating breast clinics. Likewise, the odds were 47% (OR: 0.53; 95% CI: [0.31, 0.92]) and 61% lower (OR: 0.39; 95% CI: [0.22, 0.68]) in medium-volume and low-volume campuses, compared with high-volume campuses (Table 15). In patients with IBC, no significant association between recognition status or campus volume on the one hand, and (y)pTNM reporting on the other was observed.

**Key points**

- **The proportion of patients with DCIS and IBC for whom cTNM stage information was transferred to the BCR was 66.6% and 88.8%, respectively, i.e. below the target of 98%;**
- **The odds for having cTNM stage information sent to BCR was 48% lower (OR: 0.52; 95% CI: [0.32, 0.86]) if patients with IBC were diagnosed in a low-volume hospital compared to a high-volume hospital;**
- **The proportion of patients with DCIS and IBC for whom (y)pTNM stage information was transferred to the BCR was 93.4% and 96.3%, respectively, thus not reaching the target of 98%;**
- **In patients with DCIS, the odds for having (y)pTNM stage information sent to BCR was 44% lower (OR: 0.56; 95% CI: [0.34, 0.93]) in campuses without recognition for BC compared to coordinating breast clinics;**
- **In patients with DCIS, the odds for having (y)pTNM stage information sent to BCR was 47% (OR: 0.53; 95% CI: [0.31, 0.92]) and 61% lower (OR: 0.39; 95% CI: [0.22, 0.68]) in medium-volume and low-volume campuses, compared with high-volume campuses.**
- **In patients with IBC, no significant association between recognition status or campus volume on the one hand, and (y)pTNM reporting on the other was observed.**

**Table 15 – Association between recognition status for BC and campus volume, and (y)pTNM stage reporting to the BCR**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Unadjusted OR | 95% CI | P-value, type III[$] | Unadjusted OR | 95% CI | P-value, type III[$] |
| **Recognition status for BC** | | | 0.078 | | | 0.948 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 0.73 | [0.30, 1.77] | | 0.93 | [0.50, 1.72] | |
| No recognition for BC | **0.56** | **[0.34, 0.93]** | | 1.03 | [0.72, 1.47] | |
| **Average annual campus volume** | | | 0.003 | | | 0.191 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | **0.53** | **[0.31, 0.92]** | | 0.78 | [0.51, 1.18] | |
| <60 | **0.39** | **[0.22, 0.68]** | | 0.69 | [0.46, 1.03] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of main treatment) was taken into account; 7 patients with DCIS and 60 patients with IBC could not be assigned to a campus, and were thus excluded from the analyses; 8 patients with DCIS and 113 patients with IBC assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

## 7.2 Time to treatment

According to EUSOMA, BC patients must start primary treatment within a maximum of four to six weeks from the first diagnostic examination in the breast centre or first consultation at the breast centre if diagnosed elsewhere. In the main analysis for this QI, a time frame of six weeks was taken into account. As the ECIBC suggests a threshold of four weeks in its respective QI, these results are provided in a sensitivity analysis.[45]

For the operationalisation of this quality indicator, date of incidence, as defined in the BCR database, was chosen as starting point, which is slightly different from EUSOMA (i.e. date of first diagnostic examination within the breast centre).[46]

In Appendix 18 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

### National results

The data illustrate that in 87.3% of women diagnosed in 2014 - 2018 with IBC the first treatment was initiated within 6 weeks (42 days) after incidence date (Table 128), which is just below the target set at 90%. When this time frame was reduced to four weeks, the respective proportion was 66.2% (Table 133). The data further indicate that for one in four patients the treatment was started within 15 days after incidence date, a quarter of patients waited 33 days or longer to start treatment (Table 129).

While in the comparison period 2009 - 2013, 90.0% of women with IBC were treated within six weeks after diagnosis (Table 130), the results of the 2014 - 2018 period show that with every incidence year, this proportion dropped slightly to 85.1% in 2018. This observation is in line with what is observed in other countries.[105-108] It has been linked with an increasing incidence of BC, partly due to systematic screening,[107] but also with demographics and preoperative components, such as imaging modalities (e.g. additional imaging[109]), biopsy type and clinician visits.[105] Also the coordination of immediate breast reconstruction after mastectomy (e.g. the availability of the breast and reconstructive surgical team) may lead to pre-operative delays.[84, 110]

Referrals and second opinions have also been suggested to impact the time to treatment. In this study 78.8% of patients who were referred between diagnosis and treatment had their first treatment within six weeks after diagnosis, while this proportion was 88.9% for patients who received their diagnosis and first treatment in the same hospital (Table 128). In other words, when diagnosis and first treatment were not performed in the same hospital, a woman with IBC had a 11.0% lower chance of being treated within six weeks after diagnosis (RR: 0.89, 95% CI: [0.87, 0.90]). Similarly, a referral during the diagnostic process also impacted the time to treatment (no referral: 88.6% vs. referral: 80.8%), but this observation should be interpreted with caution since patients whose diagnostic procedures were partly done in private practice were assigned to the group ‘no referral’, which may have affected the difference between both groups to some extent.

The sub-analyses further illustrate that the proportion of patients with IBC being treated within six weeks after diagnosis was lowest in patients over 80 years old (i.e. 80.4%; Table 128), in patients who had been admitted in hospital for more than 15 days in the year preceding their diagnosis of IBC (80.5%) and patients with two or three comorbidities (83.9% and 80.1%, respectively). The consideration of the frailty and comorbidities before starting treatment in these subgroups may explain the longer waiting times.

### International comparison

A BC audit in the Netherlands, in which 74 hospitals participated, including 13 877 patients with IBC and 1 921 patients with DCIS, recorded a median time between the date of biopsy on which the diagnosis was based (or else the date of intake when the patient was referred) and start of treatment of 27 days (range: 18-43 days);[84] in the present study the median time between diagnosis and start of treatment was 22 days. In the French Cancer Cohort for 2018 (i.e. the French National medico-administrative cancer database), 42.3% of patients underwent their first treatment within six weeks post-mammogram and 37.8% within four weeks post-biopsy, results that were significantly below the alert threshold (i.e. <80% for both).[111]

### Comparison between centres

There was considerable variability between the campuses. When benchmarking was based on the campus of first treatment, 43 campuses fell below the lower limit of the 99% prediction interval around the target (Figure 41).

When benchmarking was done based on the hospital of diagnosis (Figure 42), forty hospitals were situated below the lower limit of the 99% prediction interval.

### Association with campus volume and recognition status of the campus of first treatment

There was no significant association between the probability of starting the oncological treatment within 6 weeks after diagnosis and the campus recognition status (Table 16). Yet, the unadjusted odds for starting the oncological treatment within 6 weeks after diagnosis was 42% lower (OR: 0.58; 95% CI: [0.36, 0.91]) in low-volume campuses compared with high-volume campuses.

Part of the association between campus volume and starting the oncological treatment within 6 weeks after diagnosis could be explained by the case-mix[nn] of the campuses: after adjustment for these variables, the association between campus volume and start of treatment was no longer significant.

**Table 16 – Association between recognition status for BC and campus volume of the campus of first treatment, and start of first treatment within 6 weeks (42 days) of diagnosis of IBC**

| | Unadjusted OR | 95% CI | P-value, type III[$] | Adjusted** OR | 95% CI | P-value, type III[$] |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.406 | | | 0.529 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 1.26 | [0.61, 2.58] | | 1.35 | [0.65, 2.78] | |
| No recognition for BC | 0.83 | [0.55, 1.24] | | 0.91 | [0.60, 1.36] | |
| **Average annual campus volume** | | | 0.047 | | | 0.140 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.83 | [0.50, 1.36] | | 0.87 | [0.53, 1.44] | |
| <60 | **0.58** | **[0.36, 0.91]** | | 0.64 | [0.40, 1.02] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that all levels of a categorical predictor have the same effect on the outcome as the reference category does; **Adjusted for the following case-mix variables: age at diagnosis, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiovascular and respiratory diseases, diabetes); clustering of patients into campuses (i.e. centre of first treatment) was taken into account; 1 717 patients could not be assigned to a campus, and were thus excluded from the analyses; 141 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on algorithm for centre of first treatment) to a campus with no main treatment volume, were excluded.*
*Source: BCR-IMA-HDD*

[nn] The following case-mix variables were taken into account: age at diagnosis, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiovascular and respiratory diseases, diabetes).

**Key points**

- **In 87.3% of patients diagnosed with IBC in 2014 - 2018, the first treatment was initiated within 6 weeks (42 days) after diagnosis, which is just below the target set at 90%;**
- **There was no significant association between campus recognition status and start of treatment;**
- **After adjustment for case-mix variables[nn], there was no significant association between campus volume and start of treatment.**

## 7.3 Surgery

Surgery is a cornerstone in BC care. Two process indicators focus on the avoidance of overtreatment, more precisely ensuring adequate staging while avoiding unnecessary axillary dissection. The other two indicators assess the appropriateness of the surgical approach: the avoidance of multiple surgeries where a single intervention may be sufficient.

The clinical experts spoke against the calculation of the EUSOMA indicator on immediate reconstruction at the same time of mastectomy as the available database did not provide information on patient preferences (see section 4.10.1). Some stakeholders argued that also the quality of the surgical procedure (e.g. tumour free resection margins) should be assessed, but again, this information was not readily available.

### *7.3.1 No axillary clearance as first axillary surgery in patients with DCIS[oo]*

While lymph node evaluation is standard for women with invasive cancer, there is no demonstrated benefit for lymph node assessment in women with DCIS. It has been estimated that axillary involvement is about 1-2% in DCIS (which by definition does not metastasise); the incidence depends on grade and diameter (i.e. risk of occult invasive cancer).[46] Nevertheless, lymph node analysis is often unnecessarily performed in patients diagnosed with DCIS.[112] The additional morbidity caused by axillary evaluation is significant; axillary interventions, even limited to sentinel node biopsy, carry the risk of long term sequelae such as chronic pain, decreased strength, oedema, and sensory disorder.[113] NICE recommends to not perform SLNB routinely for women with a preoperative diagnosis of DCIS who are having BCS, unless they are considered to be at high risk of invasive disease.[114] SLNB should only be offered to women who are having a mastectomy for DCIS.[114]

The calculation of this indicator was not only troubled by the vague description of the dedicated nomenclature codes (see section 4.10.3), during the discussions with the clinical experts it was reported that these codes are not always/not in all Belgian hospitals used in a correct way. More precisely: nomenclature codes for ALND are used to attest SLNB as the fees for the former are higher. This may thus lead to an overestimation of ALND and underestimation of SLNB. An alternative approach to calculate this quality indicator was also considered: the identification of SLNB by pNsn (pathological classification of the sentinel node). But as pNsn is not reported as meticulously to the BCR by every Belgian hospital/laboratory for anatomical pathology, this approach may also have led to an underestimation of SLNB. Therefore, it was decided to elaborate this indicator as a descriptive indicator (i.e. without target and the variability between centres presented in a scatter plot). Note that the problem of incorrect coding practices of axillary procedures has also been reported in

[oo] This QI is also included in the list of QIs of the European Quality Assurance Scheme for Breast Cancer Services, where the target is set at ≥ 95%, after exclusion of patients who had mastectomy.[40]

other countries, in France, for instance, sentinel procedures were mostly coded under axillary dissection.[111]

Last, as was explained earlier, the number of lymph nodes removed and the result of the anatomopathological assessment are not available in a structured format at the BCR (see section 4.10.1).

In Appendix 19 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

### National results

Among the 3 809 patients who were diagnosed with DCIS and underwent surgery within nine months after incidence, 96.9% did not receive axillary lymph node dissection (ALND) as first axillary surgery (Table 136). Two in five patients (43.2%) who received ALND belonged to the age group 50-69 years old, i.e. the age group for whom two-yearly screening mammography is organised.

Patients who underwent mastectomy were five times more likely to have ALND compared to women who underwent BCS (8.5% vs. 1.6%, RR: 5.16, 95% CI: [3.61, 7.39]), which is in line with the guidelines.[114] In the comparison period 2009 - 2013 women with DCIS were almost twice as likely having undergone ALND compared to women diagnosed in 2014 - 2018 (5.5% vs. 3.1%, RR: 1.78, 95% CI: [1.42, 2.22]; Table 137).

### International comparison

Among the 5 190 patients with DCIS diagnosed and treated in one of the 22 EUSOMA-certified breast centres in eight European countries in 2006-2015, 93.5% did not receive axillary clearance. This proportion increased over time, from 88.8% in 2006 to 97.3% in 2015,[89] a trend that was also observed in Belgium. The Norwegian Breast Cancer Registry reported that none of the women diagnosed in 2016 with DCIS underwent ALND, but no information is provided on the size of the subgroup with DCIS.[115] In the French Cancer Cohort for 2018, only 67.5% of women with DCIS undergoing BCS, did not undergo sentinel lymph node excision or axillary dissection.[96, 111]

### Comparison between centres

The scatter plot indicates that in the majority of Belgian hospital campuses 90-100% of patients diagnosed with DCIS who had surgery, did not receive axillary lymph node dissection as first axillary surgery (Figure 44).

### Association with campus volume and recognition status

In women with DCIS, the odds[pp] for not having to undergo ALND was 56% lower (OR: 0.44; 95% CI: [0.23, 0.83]) when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic (Table 17). Likewise, the odds for not having to undergo ALND was 55% lower (OR: 0.45; 95% CI: [0.20, 1.00]) for patients with DCIS treated in a low-volume compared to a high-volume campus.

[pp] Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

**Table 17 – Association between recognition status for BC and campus volume, and the odds of not receiving ALND as first axillary surgery in women with DCIS**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.035 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.99 | [0.26, 3.77] | |
| No recognition for BC | **0.44** | **[0.23, 0.83]** | |
| **Average annual campus volume*** | | | 0.088 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.51 | [0.25, 1.06] | |
| <60 | **0.45** | **[0.20, 1.00]** | |

*BC: breast cancer; ALND: axillary lymph node dissection; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 5 patients could not be assigned to a campus, and were thus excluded from the analyses; 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

**Key points**

- **Overall, 96.9% of patients diagnosed with DCIS who had surgery, did not receive axillary lymph node dissection as first axillary surgery;**
- **The odds for not having to undergo ALND was 56% lower (OR: 0.44; 95% CI: [0.23, 0.83]) when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic;**
- **The odds for not having to undergo ALND was 55% lower (OR: 0.45; 95% CI: [0.20, 1.00]) for patients with DCIS treated in a low-volume compared to a high-volume campus.**

### *7.3.2 Sentinel lymph-node biopsy (SLNB) only, in patients with invasive pN0 BC[qq]*

The axillary nodal status is the strongest prognostic factor in BC; it tailors many loco-regional and systemic treatment decisions.[46] Therefore an adequate staging is necessary. However, an unnecessary axillary clearance must be avoided due to the associated morbidity (i.e. surgical adverse events, shoulder stiffness, pain and lymphoedema).

Several randomised trials, which compared SLNB with full axillary lymph node dissection (ALND) in patients with IBC and clinically negative lymph nodes did not reveal any difference with regard to overall survival or disease-free survival.[116-120] Yet, morbidity and quality of life were significantly better in patients who underwent SLNB alone.[46, 121] SLNB is therefore regarded as the gold standard to assess the axillary lymph node status in patients with IBC and clinically negative axilla.[46, 122]

Given the problem of incorrect coding practices of axillary procedures (see section 7.3.1), it was decided to elaborate also this indicator as a descriptive indicator (i.e. without target and the variability between centres presented in a scatter plot).

Last, women who received neoadjuvant systemic treatment were excluded from this process indicator as prediction of residual axillary involvement after neoadjuvant chemotherapy is less clear.[123]

[qq] This indicator is included in the list of QIs of the European Quality Assurance Scheme for Breast Cancer Services, where the target is set at ≥ 80%.[40]

In Appendix 20 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

### National results

Overall, 76.6% of women with IBC and clinically negative lymph nodes who underwent surgery (BCS or mastectomy) but no systemic treatment in the neoadjuvant setting, had SLNB but no axillary clearance (Table 140). Important to note is that 21.8% of patients who fulfilled the criteria for this indicator underwent ALND and for another 1.6% no lymph node surgery was reported. The incorrect use of nomenclature codes (see section 7.3.1) may to some extent have contributed to the high proportion of women undergoing ALND.

Over the years the proportion of women with IBC who underwent SLNB increased from 61.0% in 2009 - 2013 (Table 141), to 73.1% in 2014 and 80.9% in 2018. This reduction may be explained by the publication of the ACOSOG Z0011 trial, which showed that even when one or two sentinel lymph nodes were positive in women with cT1-2M0, whole-breast irradiation and adjuvant systemic therapy was not inferior to axillary clearance in terms of overall survival and disease free survival.[120, 124]

### International comparison

Among the 23 391 patients with IBC and pN0 and treated in one of the 22 EUSOMA-certified breast centres in eight European countries in 2006-2015, 87.5% received only a SLNB and no axillary clearance; this proportion increased steadily from 61.5% in 2006 to 96.7% in 2015.[89] The result for 2015 is thus better than the Belgian result when the denominator was also restricted to patients with clinically and pathologically negative axilla (cN0 and pN0), i.e. 89.0% (Table 142). Also in Germany, better results were obtained in the annual audit of the German Cancer Society (DKG): in 2018 94.7% of women with IBC and negative lymph nodes (pN0) who did not have neoadjuvant treatment, only underwent sentinel lymphadenectomy.[88] In the French Cancer Cohort for 2018, the proportion of women with pN0 nonmetastatic IBC undergoing SLNB without axillary dissection was only 30.7%. This low rate was attributed to the incorrect coding practices.[96, 111]

### Comparison between centres

The scatter plot illustrates that there is a lot of variability between the campuses; this variability is more pronounced for the campuses without recognition for BC, compared to the coordinating and satellite breast clinics (Figure 46).

### Association with campus volume and recognition status of the campus of first surgery

In women with IBC and clinically negative lymph nodes who underwent breast surgery, the odds[rr] for having SLNB only was 36% lower (OR: 0.64; 95% CI: [0.52, 0.77]) when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic (Table 18). Likewise, the odds for having SLNB only was 44% (OR: 0.56; 95% CI: [0.45, 0.71]) and 25% lower (OR: 0.75; 95% CI: [0.60, 0.95]) in low and medium-volume campuses compared to high-volume campuses. This volume effect was also observed within the group of coordinating breast clinics, with medium-volume centres obtaining significantly lower results (OR: 0.72; 95% CI: [0.54, 0.95]; Table 145).

[rr] Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

**Table 18 – Association between recognition status for BC and campus volume, and the odds of undergoing SLNB only (excluding pts who received neoadjuvant systemic treatment) in women with IBC and clinically negative axilla**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | <0.0001 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 1.08 | [0.77, 1.52] | |
| No recognition for BC | **0.64** | **[0.52, 0.77]** | |
| **Average annual campus volume*** | | | <0.0001 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | **0.75** | **[0.60, 0.95]** | |
| <60 | **0.56** | **[0.45, 0.71]** | |

*BC: breast cancer; SLNB: sentinel lymph node biopsy; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 36 patients who could not be assigned to a campus, and 20 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

**Key points**

- **76.6% of women with IBC and clinically negative lymph nodes who underwent surgery but no neoadjuvant systemic treatment, had only SNLB and no axillary clearance, which indicates ample room for improvement;**
- **The odds for having SLNB only was 36% lower (OR: 0.64; 95% CI: [0.52, 0.77]) when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic;**
- **The odds for having SLNB only was 44% (OR: 0.56; 95% CI: [0.45, 0.71]) and 25% lower (OR: 0.75; 95% CI: [0.60, 0.95]) in low and medium-volume campuses compared to high-volume campuses.**

### *7.3.3 Just one breast surgery*

Whether reoperation after BCS should be used as a quality indicator is controversial.[125] The American Society of Breast Surgeons, for example, decided not to include the re-excision rate among their quality indicators, assuming that uniformity in tumour stage distribution, margin assessment and reporting cannot be assured when data from different hospitals are compared.[126] Conversely, the EUSOMA working group decided to adopt the 'proportion of patients (invasive cancer only) who received a single (breast) operation for the primary tumour (excluding reconstruction)' and the 'proportion of patients (DCIS only) who received just one operation (excluding reconstruction)' in its set of benchmark quality indicators.[46] These QIs are also included in the set of QIs of the European Quality Assurance Scheme for Breast Cancer Services, where the target is set at ≥ 70%.[40]

Because several surgeons voiced during the validation study their concern that these QIs may create a perverse incentive for surgeons to opt more for mastectomy (see section 4.9), it was decided to provide an additional graph, where the QI result is plotted against the ratio BCS/mastectomy. When feedback is sent to the Belgian hospitals, they will also receive this additional

graph so that they can identify their QI result in relation to the ratio BCS/mastectomy for their campus.

The choice between BCS and mastectomy is based on many factors, among which patient choice, the ratio of tumour size to breast volume, age and frailty at diagnosis, the size of the DCIS component in case of IBC, as well as genetics (BRCA). In addition, preoperative MRI examination increases the mastectomy rate, although the clinical significance of the additional disease found on MRI remains controversial.[127-129]

Last, for a correct interpretation of the results, it is important to note that the nomenclature codes do not provide any information on the laterality of procedures. Hence, in case of multiple surgical interventions identified for the same patient it cannot be revealed whether they were performed in the same breast or in the contralateral breast (e.g. preventive surgery).

In Appendix 21 and Appendix 22 the documentation sheets, flow charts as well as tables and figures with additional results are provided.

#### *7.3.3.1 Just one breast surgery in DCIS*

**National results**

Overall, for 85.8% of women with DCIS who underwent surgery, no second breast surgery (without taking breast reconstruction into account) was performed within a period of six months after the initial surgery (BCS or mastectomy; Table 146). This proportion is slightly lower than the target of 90% set by EUSOMA, but somewhat higher than the result for the comparison period 2009 - 2013 (79.5%, Table 148). The results further indicate that about one in four women younger than forty years with DCIS needed a second surgical intervention. Although the results should be carefully interpreted given the rather small size of this subgroup (i.e. n=153), women younger than forty were thus 80% more likely to have to undergo a second operation, compared to women older than forty (75.2% vs. 86.2%, RR: 1.80, 95% CI: [1.35, 2.41]). This observation is in line with previous studies,[130-133] and has been put down to the reduced sensitivity of standard breast imaging in younger patients, which potentially limits the determination of the extent of disease preoperatively, as well as attempts to conserve more breast tissue in younger women.[133]

Among the 537 patients with DCIS who had a second surgery, 416 patients (77.5%) had as first surgery a BCS *stricto sensu*[ss] billed, 95 (17.7%) had as first intervention surgery for a benign lesion and 26 (4.8%) had a mastectomy. Women who had a surgical intervention for a benign lesion as first breast surgery were 42% more likely to have to undergo a second breast surgery compared to women who had a BCS *stricto sensu* (RR: 1.42, 95% CI: [1.16, 1.73]). As it was a remarkable finding that 26 women with DCIS who had mastectomy as first surgical intervention, had to undergo a second surgery, the pathology reports for these patients were investigated for further information. This revealed that in eight patients the second mastectomy was performed for preventative reasons in the contralateral breast, in another eight patients a further resection was indicated and in ten patients it related to administrative errors.

**International comparison**

The NABON Breast Cancer Audit in the Netherlands revealed slightly different results. In 2018, 69.5% of the 1 894 patients with DCIS received BCS, with 166 patients (12.4%) needing one additional resection and another 19 patients needing at least two more operations.[84] In Belgium, 74.6% (2 963/3 973) of women diagnosed in 2014 - 2018 with DCIS underwent BCS, with 17.2% of them needing at least one more surgical intervention of the breast. In the French Cancer Cohort for 2018 (i.e. the French National medico-administrative cancer database), 32% of women with DCIS who had BCS as first surgery, underwent breast reintervention.[96, 111] And among the 5 190 patients with DCIS diagnosed and treated in one of the 22 EUSOMA-certified breast centres in eight European countries in 2006-2015, 66.8% received just one operation (excluding reconstruction); this proportion varied in the time frame 2006-2015 between 56.1% and

[ss] In the calculation of the QIs on breast surgery, not only the dedicated nomenclature codes for BCS (i.e. 'BCS *stricto sensu*') were used to define BCS, but also the codes for 'surgery for benign breast lesions' and the codes for 'excision biopsy'.

82.7%.[89] The results for 2015, are thus in line with what was observed in Belgium in 2014 - 2018.

### Comparison between centres

When benchmarking was performed based on the campus of first surgery (i.e. women were assigned to the campus where the first billed breast surgery was performed), there was limited variability between the units of analysis[tt] beyond what is expected (Figure 48**)**. Nine units fell below the 99% prediction interval constructed around the target.

### Association with campus volume and recognition status of the campus of first breast surgery

When patients with DCIS were assigned to the campus where the first breast surgery was performed, no significant association[uu] was observed between recognition status and receiving just one operation, nor between average annual campus volume and receiving just one operation (Table 19).

**Table 19 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with DCIS**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.518 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.82 | [0.48, 1.41] | |
| No recognition for BC | 0.85 | [0.62, 1.16] | |
| **Average annual campus volume** | | | 0.591 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.92 | [0.66, 1.28] | |
| <60 | 0.83 | [0.57, 1.19] | |

*BC: breast cancer; DCIS: ductal carcinoma in situ; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

[tt] Note that 65 out of 155 units presented in the funnel plot, were assigned less than 10 patients with DCIS having surgery during the five year study period. This may (in part) be explained as some campuses changed recognition status during the study period or because the campus was not active during the entire study period (e.g. fusion or suspension of activities).

[uu] Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

**Association between just one breast surgery and the ratio BCS/mastectomy**

In the graph in which the campuses' QI results are plotted against their BCS/mastectomy ratio, the national QI result and the overall BCS/mastectomy ratio were used to define quadrants (Figure 50). In the south west quadrant (i.e. overall QI result < 85.8% and ratio BCS/mastectomy < 3.63), one can find six out of 53 coordinating breast clinics, three out of twelve satellite breast clinics and twelve out of 47 units without recognition for BC. In the other quadrants, the various recognition statuses are more or less evenly distributed.

The association between campus volume and recognition status of the campus of first breast surgery on the one hand, and the ratio BCS/mastectomy was further assessed in logistic regression analyses (Table 152). When the clustering of patients was taken into account, no significant associations were observed.

**Key points**

- **Overall, for 85.8% of women with DCIS who underwent surgery, no second breast surgery (without taking breast reconstruction) was performed, which is just below the target of 90%;**
- **No significant association was observed between recognition status and receiving just one operation, nor between average annual campus volume and receiving just one operation.**

### *7.3.3.2 Just one breast surgery in IBC*[vv]

**National results**

Overall, for 93.0% of women with invasive non-metastatic BC who underwent surgery, no second breast surgery (excluding reconstruction) was performed within six months after the initial surgery (Table 153); a result which is better than the target of 90% set by the EUSOMA working group.[46] There was only little variation across age groups and between incidence years, although a slight increase was observed compared to the period 2009 - 2013 (93.0% vs. 91.0%, RR: 1.02, 95% CI: [1.02, 1.03]; Table 155).

Women diagnosed with cStage 0 (i.e. tumours which were clinically assessed as in situ, but appeared to be invasive after resection) were more likely to receive a second operation than women diagnosed with cStage I-III (17.9% vs. 6.6%, RR: 2.71, 95% CI: [2.20, 3.33]). Probably, the preoperative assessment underestimated the real size of the tumour, the resection margins were not clear, or it related to DCIS or papilloma with an invasive component, indicating the need for a second breast surgery.

About two in three patients diagnosed in 2014 - 2018 with invasive non-metastatic BC received a BCS, of whom 9.3% had to undergo a second breast surgery (Table 154). As was also observed in patients with DCIS (see section 7.3.3.1), there was a small group of patients (N=182) who had to undergo a second surgery after they had received a mastectomy[ww].

**International comparison**

The Norwegian Breast Cancer Registry reported that the proportion of women with IBC who underwent one surgical intervention increased from 90% in 2014 to 94% in 2016,[115] hence results that are comparable to the Belgian data. The variability between the hospitals ranged between 86% and

[vv] This QI is also included in the list of QIs for the European Quality Assurance Scheme for Breast Cancer Services, where it focuses on T1, T2 IBC and where the target is set at ≥ 80%.[40]

[ww] This second surgery was billed as mastectomy in 55 patients, as BCS *stricto sensu* in 61 patients, and as surgery for a benign breast lesion in 66 patients. Exploration of a dozen of pathology reports revealed that the second surgery was performed because of positive resection margins (also when the first surgery was a tumorectomy), because of a hematoma, as a prophylactic surgery in the contralateral breast, or a redo without the precise rationale being mentioned.

100% in 2016.[115] In the NABON Breast Cancer Audit (the Netherlands) it was reported that in 2017, 62.2% of the 12 816 patients with IBC had initially BCS; 550 of them (6.9%) underwent one re-operation and another 44 patients (0.6%) needed two or more reoperations.[134] While the proportion of women who had BCS was lower than in Belgium (62.2% vs. 69.5%), the reoperation rate was in line with the Belgian results. Among the 38 998 patients with IBC diagnosed and treated in one of the 22 EUSOMA-certified breast centres in 8 European countries in 2006-2015, 83.5% received just one operation (excluding reconstruction); this proportion increased steadily from 80.0% in 2006 to 91.2% in 2015.[89]

### Comparison between centres

When benchmarking was performed based on the campus of first surgery, there was moderate variation between centres beyond what is expected, with 28 units above and four campuses below the 99% prediction interval constructed around the target (Figure 51). Twenty units were assigned less than 10 patients fulfilling the inclusion criteria for this QI during the five year study period.

### Association with campus volume and recognition status

The logistic regression analyses[xx] indicated that there was no significant association between recognition status and receiving just one operation in women with IBC, nor between average annual campus volume and receiving just one operation (Table 20).

**Table 20 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with IBC**

| Characteristic | | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|---|
| **Recognition status for BC** | | | | 0.583 |
| | Coordinating breast clinic | 1 | [reference] | |
| | Satellite breast clinic | 0.87 | [0.60, 1.24] | |
| | No recognition for BC | 0.91 | [0.74, 1.12] | |
| **Average annual campus volume*** | | | | 0.582 |
| | ≥125 | 1 | [reference] | |
| | [60, 125[ | 0.96 | [0.75, 1.23] | |
| | <60 | 0.88 | [0.69, 1.13] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

[xx] Based on a discussion with the experts, it was concluded that there was no justification for case-mix adjustment.

**Association between just one breast surgery and the ratio BCS/mastectomy**

In the graph in which the campuses' QI results are plotted against their BCS/mastectomy ratio, the national QI result and the overall BCS/mastectomy ratio were used to define quadrants (Figure 53). In all quadrants, the various recognition statuses are more or less evenly distributed. Yet, in the upper left quadrant (i.e. overall QI result > 85.8%, but ratio BCS/mastectomy < 3.63), one can find sixteen out of 60 coordinating breast clinics and 24 out of 81 units without recognition for BC, but no satellite breast clinics.

The association between campus volume and recognition status of the campus of first breast surgery on the one hand, and the ratio BCS/mastectomy was further assessed in logistic regression analyses (Table 160). When the clustering of patients was taken into account, there were no significant associations observed. Yet, within the group of campuses without recognition for BC, patients treated in medium-volume campuses and low-volume campuses were 40% (OR: 0.60, 95% CI: [0.38, 0.95]) and 44% (OR: 0.56, 95% CI: [0.37, 0.86]) less likely to have BCS.

**Key points**

- **Overall, for 93.0% of women with invasive M0 BC who underwent breast surgery, no second breast surgery (excluding reconstruction) was performed within six months after the initial surgery, a result that is above the target of 90%;**
- **There was no significant association between recognition status and receiving just one operation, nor between average annual campus volume and receiving just one operation.**

## 7.4 Post-operative radiotherapy in women with IBC[yy]

A meta-analysis published in 2011 indicated that radiotherapy (RT) after BCS reduced the 10-year risk of any (locoregional or distant) first recurrence from 35.0% to 19.3% (absolute reduction: 15.7%, 95% CI: 13.7-17.7) and that RT reduced the 15-year risk of BC death from 25.2% to 21.4% (absolute reduction: 3.8%, 95% CI: 1.6-6.0).[135] The authors hypothesized that killing microscopic tumour foci in the conserved breast with radiotherapy reduces the potential for both local recurrence and distant metastasis.[135]

As further studies indicated that low-risk patients, mainly elderly (age >70), who receive adjuvant endocrine therapy, have limited benefit from RT in terms of local control, and no benefit for overall survival,[46, 136] this quality indicator was restricted to patients younger than seventy years old.

In Appendix 23 the documentation sheet, flow chart as well as tables and figures with additional results are provided.

**National results**

Overall, 97.5% of women younger than seventy years old with IBC (M0) started their radiotherapy within nine months after breast conserving surgery, hence the EUSOMA target of 95% was attained (Table 161). This was also the case in 2009 - 2013 (98.0%, Table 162). There was no major variation across patient and tumour characteristics. Most patients received RT as adjuvant series only (95.1%, Table 164), and a minority received intraoperative radiotherapy (IORT) only (2.4%) or a combination of adjuvant and IORT (2.5%). Among women who underwent BCS but no chemotherapy, 97.3% started RT within three months after surgery (Table 163).

In the age group of seventy years or above, 91.4% of women started RT within 9 months after BCS (Table 165).

yy This QI is also included in the list of QIs included in the European Quality Assurance Scheme for Breast Cancer Services, but formulated more stringent: 'Number of surgically treated women with primary M0 invasive breast cancer who underwent adjuvant radiotherapy, and who started undergoing radiotherapy ≤ eight weeks after the date of surgery or the date of the last cycle of adjuvant chemotherapy (target: ≥ 80%).[40]

### International comparison

In the international literature very good results are reported for other countries as well. In a French study, for instance, which included 1 560 women with primary invasive non-metastatic BC diagnosed in 2012 who were randomly selected from 16 French geographical areas covered by cancer registries, 97.8% (95% CI: 96.7-98.6) received post-operative radiotherapy after surgical resection of the primary tumour and appropriate axillary staging/surgery in the framework of BCS.[87] In Germany, 97.02% of women with IBC (M0) received RT after breast conserving surgery in 2018.[88] Finally, among the 40 601 patients with IBC diagnosed and treated in one of the 22 EUSOMA-certified breast centres in Germany, Switzerland, Belgium, Austria, the Netherlands, Spain, Portugal and Italy in 2006-2015, 94.4% received postoperative RT after BCS; this proportion varied in the time frame 2006-2015 between 93.0% and 95.5%.[89]

### Comparison between centres

Benchmarking was performed based on the hospital of main treatment (Figure 10). There was limited variation between the centres, with all except one centre situated within or even above the 99% prediction interval around the target of 95%.

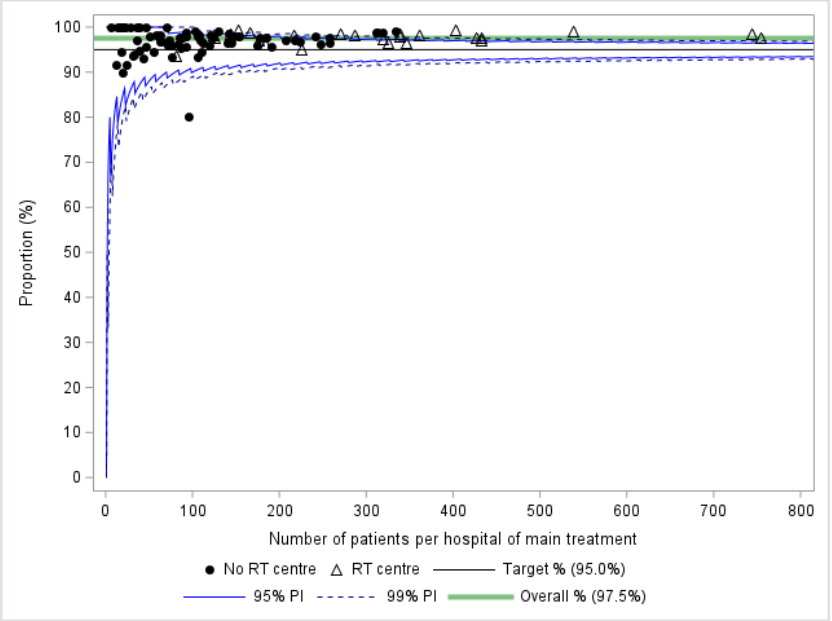
### Association with hospital volume and recognition status

Given the low variability between the hospitals, there was no added value of doing these analyses.

**Key points**

- **Overall, 97.5% of women younger than seventy years old with IBC (M0) who underwent BCS, received post-operative radiotherapy, a result that is better than the target set at 95%.**

**Figure 10 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, by hospital of main treatment**




*Note: There were 98 hospitals reported in the funnel plot, one of them having less than ten patients in the denominator; 1 out of 100 hospitals was situated below the 99% prediction interval, while sixteen were situated above the 99% prediction interval; the 25 hospitals which are recognised as RT centre, are presented as triangles.*
*Source: BCR-IMA*

## 7.5 Systemic treatment

The choice of adjuvant systemic treatment in IBC should be driven by the hormonal sensitivity, risk profile of the tumour, age, menopausal status and comorbidities of the patient.[85] As the concordance between the test results for receptor status (ER, PR, HER2) available in the BCR database and the data available in the medical files (on which medical treatment is based) was below par according to the clinical experts, several quality indicators on systemic treatment could not be calculated (Box 8).

After discussion with the clinical experts, it was concluded that this report should provide at least some insights in the way systemic treatment is provided in the Belgian setting. Therefore, two broad descriptive indicators were developed, for which no target was set and for which the variability between the hospitals is illustrated in scatter plots.

**Box 8 – Quality indicators on systemic treatment that could not be calculated due to limitations of the data**

- Proportion of women <70 years old with ER-negative (T > 1 cm or Node+) M0 IBC who received (neo-)adjuvant chemotherapy;
- Proportion of women <70 years old with ER-positive M0 IBC who received adjuvant endocrine treatment;
- Proportion of women <70 years old with HER2-positive (IHC 3+ or in situ hybridization (ISH) positive) M0 invasive carcinoma (T > 1 cm or Node+) treated with adjuvant chemotherapy who also received adjuvant anti-HER2-therapy;
- Proportion of women <70 years old with HER2-positive M0 invasive carcinoma BC treated with neoadjuvant chemotherapy who also received neoadjuvant anti-HER2-therapy;
- Proportion of women < 70 years old with cStage I-III triple negative BC receiving (neo-)adjuvant chemotherapy within 4 months of surgery;
- Proportion of women ≥ 70 years old with cStage I-III, ER+ or PR+ BC receiving (neo-)adjuvant chemotherapy within 4 months of surgery.

In Appendix 24 and Appendix 25 the documentation sheets, flow charts as well as tables and figures with additional results are provided.

### 7.5.1 Adjuvant chemotherapy and/or endocrine therapy in patients <70 years with M0 IBC

**National results**

Overall, 40.7% of women with M0 IBC, younger than 70 years old, who did not receive neoadjuvant systemic treatment, received **adjuvant chemotherapy within 4 months after surgery** (Table 166). Women diagnosed with clinical, pathological or combined stage II or III were more likely to receive adjuvant chemotherapy (Table 166). Women younger than 50 years, were 56% more likely to receive adjuvant chemotherapy (RR: 1.56, 95% CI: [1.51, 1.62]). Compared to 2009 - 2013, women were in 2014 - 2018 13% less likely to receive adjuvant chemotherapy (RR: 0.87, 95% CI: [0.85, 0.89], Table 167). A further decrease in the administration of adjuvant chemotherapy is observed during the study period: from 43.8% in 2014 to 36.7% in 2018.

Among the 8 177 women who received adjuvant chemotherapy, 88.6% also received adjuvant RT (within 9 months; Table 166). Further exploration of the systemic therapy offered during the four months following surgery, indicated that in the majority of women no other systemic treatment was offered (Table 169). Only 4.2% of women with M0 IBC received adjuvant chemotherapy and endocrine therapy.

In 2014 - 2018, 86.2% of women with M0 IBC, younger than 70 years old, who did not receive neoadjuvant systemic treatment, received **adjuvant endocrine therapy within 9 months after surgery** (Table 172). Women younger than 50 years, were 6.5% less likely to receive adjuvant endocrine therapy (RR: 0.94, 95% CI: [0.92, 0.95]). No other obvious associations with (clinical, pathological or combined) stage, year of diagnosis, or other patient characteristics were observed. Women with M0 IBC were in 2014 - 2018 4.8% more likely to receive adjuvant endocrine therapy, compared to 2009 - 2013 (RR: 1.05, 95% CI: [1.04, 1.06], Table 173).

Nine in ten women who received adjuvant endocrine therapy, also underwent radiotherapy (Table 172). During the nine months following surgery, one in four women received endocrine therapy and chemotherapy, 8.8% received endocrine, targeted and chemotherapy, while 65.4% received endocrine therapy without any other systemic treatment (Table 175).

**Comparison between centres**

When benchmarking was performed based on the campus of main treatment, the scatter plot illustrated that in the majority of campuses 30-50% of patients received adjuvant chemotherapy within 4 months after surgery (Figure 55). Likewise, in most campuses at least 80% of patients received endocrine therapy within 9 months (Figure 57).

**Association with campus volume and recognition status**

Taking the case-mix of hospitals into account as well as the intracampus correlation, the odds for receiving adjuvant chemotherapy was 27% higher (OR: 1.27, 95% CI: [1.02, 1.58], p=0.032) in campuses without recognition for BC compared to coordinating breast clinics (Table 21). There was no significant association between recognition status or average annual volume of a campus and the receipt adjuvant endocrine therapy (Table 22, Table 177).

**Table 21 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant chemotherapy within 4 months after surgery in women <70 years old with M0 IBC**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III$ | Adjusted** OR | 95% CI | P-value, type III$ |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.476 | | | 0.099 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 1.05 | [0.82, 1.34] | | 1.09 | [0.75, 1.59] | |
| No recognition for BC | 1.09 | [0.95, 1.26] | | **1.27** | **[1.02, 1.58]** | |
| **Average annual campus volume*** | | | 0.727 | | | 0.506 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 1.01 | [0.86, 1.19] | | 1.13 | [0.87, 1.46] | |
| <60 | 1.07 | [0.90, 1.26] | | 1.15 | [0.89, 1.49] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; **: adjusted for age at diagnosis, combined stage, tumour differentiation grade, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiovascular and respiratory diseases, diabetes); $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into hospital campuses (i.e. centre of main treatment) was taken into account; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded; 14 observations with combined stage X had to be deleted from the multivariable model.*
*Source: BCR-IMA-HDD*

**Table 22 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant endocrine therapy within 9 months after surgery in women <70 years old with M0 IBC**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III$ | Adjusted** OR | 95% CI | P-value, type III$ |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.278 | | | 0.183 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 0.95 | [0.72, 1.24] | | 0.97 | [0.70, 1.36] | |
| No recognition for BC | 0.88 | [0.76, 1.03] | | 0.84 | [0.69, 1.02] | |
| **Average annual campus volume*** | | | 0.174 | | | 0.227 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.96 | [0.81, 1.14] | | 0.93 | [0.74, 1.16] | |
| <60 | 0.84 | [0.71, 1.01] | | 0.82 | [0.65, 1.03] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; **: adjusted for age at diagnosis, combined stage, tumour differentiation grade, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiovascular and respiratory diseases, diabetes); $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into hospital campuses (i.e. centre of main treatment) was taken into account; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded; 14 observations with combined stage X had to be deleted for the multivariable model.*
*Source: BCR-IMA-HDD*

**Key points**

- **40.7% of women with M0 IBC, younger than 70 years old, who did not receive neoadjuvant systemic treatment, received adjuvant chemotherapy;**
- **86.2% of women with M0 IBC, younger than 70 years old, who did not receive neoadjuvant systemic treatment, received adjuvant endocrine therapy;**
- **Taking the case-mix of hospitals into account as well as the intracampus correlation, the odds for receiving adjuvant chemotherapy was 27% higher in campuses without recognition for BC compared to coordinating breast clinics;**
- **There was no significant association between recognition status or average annual volume of a campus and the receipt of adjuvant endocrine therapy.**

### *7.5.2 Adjuvant systemic therapy in patients <70 years with M1 IBC*

**National results**

Among the 31 250 women younger than 70 years old with IBC, 1 572 (5.0%) were diagnosed with combined stage IV disease (see flowchart in Appendix 25.2). Overall, 92.7% of them received any type of systemic therapy within one month before to nine months after diagnosis (Table 178). Women younger than fifty, were 4.7% more likely to receive systemic therapy, compared to older women (RR: 1.05, 95% CI: [1.02, 1.08]). The sensitivity analysis further indicated that women with metastatic BC younger than seventy years were 7.9% more likely to receive systemic therapy compared to older women (RR: 1.08, 95% CI: [1.05, 1.11], Table 180). No other obvious associations with other patient characteristics were observed.

Seven in ten patients with metastatic BC, did not undergo breast surgery, while 14.6% received a combination of neoadjuvant therapy and surgery, with or without adjuvant therapy (Table 178).

Further exploration of the systemic therapy offered within one month before to nine months after diagnosis, revealed that 62.8% received endocrine therapy, 59.2% received chemotherapy and 41.3% received targeted therapy (Table 181). One in five patients received only endocrine therapy, and 13.6% received a combination of chemo, targeted and endocrine therapy.

In 2014 - 2018, women with metastatic BC were somewhat less likely to receive systemic therapy, compared with women diagnosed in 2009 - 2013 (RR: 0.98, 95% CI: [0.96, 1.00], p= 0.049,Table 179).

**Comparison between centres**

When benchmarking was performed based on the campus of main treatment, the scatter plot illustrated that in the majority of centres all patients with metastatic BC received any type of systemic therapy (Figure 11).

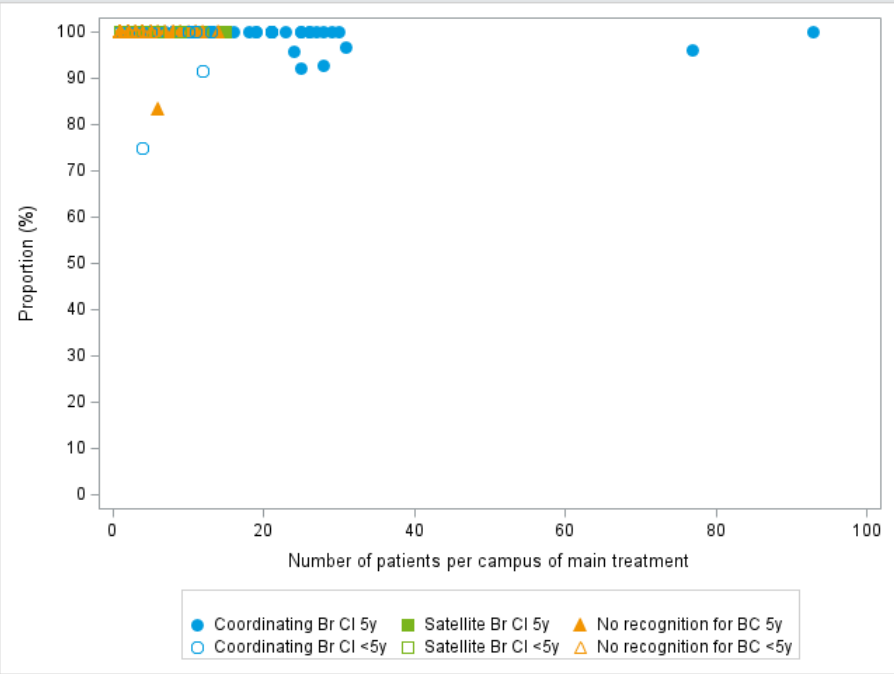
**Association with campus volume and recognition status**

According to the clinical experts, these analyses would not be meaningful, hence they were not performed.

**Key points**

- **92.7% of women with metastatic BC received any type of systemic therapy within one month before to nine months after diagnosis;**
- **Endocrine therapy was offered to 62.8% of these patients, chemotherapy to 59.2% and targeted therapy to 41.3%.**

**Figure 11 – Scatter plot of the proportion patients <70 years with M1 IBC who received systemic therapy, by campus of main treatment**




*Note: There were 141 units of analysis presented in the scatter plot, of which 100 had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 345 patients for whom the campus could not be identified, are not represented in the scatter plot.*

*Source: BCR-IMA-HDD*

# 8 DISCUSSION

In 2008, Belgium introduced the 'specialised oncological care programme for breast cancer' – in short: breast clinics - upon the advice of the European Parliament to 'roll out a network of certified multidisciplinary breast units which cover the entire population'.[1, 2, 4] Fifteen years later, after several adaptations to the legislation, which eroded step by step the initial intent to concentrate the care for patients with breast cancer in multidisciplinary high-volume settings, the result is meagre. The federated authorities did recognise 51 coordinating and 20 satellite breast clinics. But in 2018, the last year for which we have data, still 1 815 women, nearly one fifth of the study cohort diagnosed that year, was treated in a campus without recognition for breast cancer.

So, breast cancer care outside recognised breast clinics is not limited to rare cases. It is not a phenomenon in the margin, but a common practice that is legal. Yet, staffing, infrastructural and other criteria imposed on coordinating and satellite breast clinics, do not apply to these campuses. Satellite breast clinics must have a formal collaboration agreement with a coordinating breast clinic, which provides not only the medical coordination but also the chair for the multidisciplinary consultation. No such regulations apply to campuses without recognition for breast cancer. What is even more alarming, some of these campuses continue to promote themselves as 'breast clinics' or 'breast centres'. They mislead patients seeking high-quality care.

But, does it matter?

Yes, it does!

Women affected by invasive breast cancer who are treated in a **campus without recognition for BC** have a **30% higher hazard ('risk') to die** from BC, compared to women treated in a coordinating breast clinic (EHR: 1.30, 95% CI: [1.15, 1.48]; p<0.001). There was no significant difference between satellite and coordinating breast clinics. These results were obtained in analyses that controlled for intracampus correlation and for the differences in age at diagnosis and combined stage between campuses. As the models only allowed for a restricted number of case-mix variables to be added,

residual confounding, also by other potential confounders, such as socio-economic status for which we did not have data, cannot be excluded.

As at the outset of the study, the exploration of the data for December 2018 revealed that twenty of the fifty-two coordinating breast clinics and three out of the thirteen satellite breast clinics, did not fulfil the minimal volume criteria, the relationship between campus volume and observed survival was also assessed. These analyses indicated that patients with invasive breast cancer treated in a **low-volume[zz] campus** have a **44% higher hazard to die** (EHR: 1.44, 95% CI: [1.24, 1.66]; p<0.001) and patients treated in a **medium-volume** have a **30% higher hazard to die** (EHR: 1.30, 95% CI: [1.14, 1.48]; p<0.001), compared to patients treated in high-volume campuses.

These findings resonate with a vast body of evidence in the international literature. The positive relationship between provider volume (hospital and/or surgeon) and survival in breast cancer has been demonstrated numerous times, also in the Belgian context.[137-142] However, the size of the volume impact as well as the cut-off levels to discriminate high from low-volume centres, vary between studies, which complicates external validity and the definition of country specific minimum volume thresholds.[143]

The volume-outcome relationship has been attributed to various factors, among others, the multidisciplinary approach, compliance to evidence-based processes of care, level of specialization, learning-by-doing and several hospital level factors.[144, 145] Yet, in all fairness, it has to be admitted that the debate about the direction and existence of causality between hospital volume and health outcomes, is anything but settled.[144] So far, no conclusive set of explanatory factors that explain the causality of the volume-outcome relationship has been identified.[145]

In this study we also assessed the **association between campus recognition status and/or volume, and several processes of care**. An important observation that calls for action, was that in only 76.6% of women with invasive breast cancer and clinically negative lymph nodes, the first axillary intervention was confined to sentinel lymph node biopsy. The EUSOMA target for this quality indicator is set at 95%. It is clear that still far too many women have to undergo axillary clearance, which may result in significant additional morbidity and impact the quality of life. For this indicator we also observed significant recognition and volume effects: the odds for having SLNB only was 36% lower (OR: 0.64[aaa]; 95% CI: [0.52, 0.77]) when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic. The odds for patients treated in low-volume campuses was 44% lower (OR: 0.56[bbb]; 95% CI: [0.45, 0.71]) compared to women treated in high-volume campuses. Yet, as was discussed earlier in this report, the results should be interpreted with caution, given the vague description of the nomenclature codes and their reported misuse in some hospitals.

Overall, 40.7% of women with non-metastatic IBC younger than 70 years old, who did not receive neoadjuvant systemic treatment, received adjuvant chemotherapy within 4 months after surgery. Also here, an important recognition effect was found: when taking the case-mix into account, the odds for receiving adjuvant chemotherapy was 27% higher (OR: 1.27[ccc]; 95% CI: [1.02, 1.58]; p=0.032) in campuses without recognition for BC compared to campuses recognised as coordinating breast clinic.

Yet, if there is anything that this study has painfully disclosed, it is that there are **many processes of care in BC** for which it is **currently impossible to determine** whether there are differences between the various recognition

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zz The following volume categories, based on average annual campus (c.q. hospital) volume, were used in the report and in the recommendations: high-volume: ≥125, medium-volume: [60, 125[, and low-volume: <60.

aaa An OR of 0.64 corresponds to a RR of 0.89; in other words the probability for having SLNB only was 11% lower when treated in a campus without recognition for BC, compared to campuses recognised as coordinating breast clinic.

bbb An OR of 0.56 corresponds to a RR of 0.85.

ccc An OR of 1.27 corresponds to a RR of 1.14.

states, let alone to measure them *lege artis* at the national level. Some of the difficulties observed are further discussed in the following paragraphs.

The recognition of coordinating and satellite breast clinics is assigned at the campus level, not at the hospital level. Yet, **campus identification can only be deduced from hospital discharge data** ('MZG – RHM'). It implies that for procedures that are performed when patients are not admitted in hospital (e.g. many diagnostic and staging procedures, radiotherapy), only the hospital can be identified (from the invoicing data, 'IMA – AIM data'), not the campus.

Another important hurdle: **the campus identification data are currently not included in the BCR database,** only the hospital can be identified. In view of this study and the execution of its missions, BCR requested to extend its authorised transfer of hospital discharge data with campus identification data on a structural basis, but this was refused by the Information Security Committee. Only after several attempts, which took several months, authorisation was approved for the transfer of campus identification data, which was restricted to patients diagnosed with BC in 2014 - 2018. Consequently, if the federated entities inquire from BCR whether campuses (still) fulfil the mandatory volume criteria, BCR cannot provide this information. If subsequent studies want to assess the differences in processes of care and outcomes between recognised breast clinics and campuses without recognition for BC, once more authorisation for an extended MZG – RHM data transfer has to be requested, a process that is very time and labour intensive.

**Performing the analyses at hospital level, is not a valuable alternative**. First, the recognition of breast clinics is assigned at the campus level, not at the hospital level. There are many hospitals in Belgium with more than one campus. Exploratory analyses at the outset of the study revealed that performing analyses at the hospital level, assuming that as soon as one of these campuses has the recognition of coordinating or satellite breast clinic, all campuses can be categorised as coordinating or satellite breast clinic, leads to serious misclassification with respect to recognition status. Second, as a result of performing analyses at the hospital level, some hospitals that are then categorised as 'high-volume' may in reality function as a cluster of smaller campuses that each take care of a small number of patients. In these small entities patients may be denied the benefits of the 'real' high-volume centres. Hence, performing the analyses at hospital level will also result in misclassification with respect to volume, e.g. leading to attenuated differences in survival probabilities between high and low-volume centres. This may be one of the reasons why we did not observe a significant association between volume and observed survival at ten years after diagnosis in the comparison cohort (2009-2013), as these analyses were performed at the hospital level because campus identification was not possible.

**From the selected quality indicators on systemic treatment, none could be calculated**. They all required information on hormonal status (oestrogen and progesteron) and/or HER2 receptor status of the patient. The pre-validation study revealed that the receptor status information available in the BCR database does not correspond reliably with the individual medical files, based on which medical treatment is based. There are several reasons for this inferior concordance. First, receptor status information is still not transferred to BCR in a standardised and structured format. It has to be extracted from pathology reports through machine learning algorithms. Second, in the hospitals different methodologies are being used to come to the receptor status result. Third, the compulsory transfer of pathology reports to the BCR is still incomplete. Receptor status may be tested twice: on the biopsy sample and on the resection specimen. Obviously, for some patients part of that additional information is lacking at BCR. This problem is most pronounced for the HER2 ISH result: not all laboratories for anatomical pathology perform in situ hybridization, hence they have to refer to other laboratories. Apparently, the latter do not systematically transfer these results to BCR. To add some more complexity to the problem: not all laboratories use an internationally accepted scoring system for the hormone receptor status, but report based on their proper scoring system. In sum, collaborative efforts between BCR, the hospitals and the laboratories for anatomical pathology are needed to tackle these problems, so that both hospitals and BCR have faultless and comprehensive receptor status information, as is provided in the law. Similarly, BCR should explore within the field how BRCA state information can be transferred to BCR.

**Standardised and comprehensive pathology reports would also contribute to the quality assessment of surgery**, an issue that has been raised in several KCE reports.[10, 13-15] Currently, no structured data are available in the BCR database on tumour size, resection margins, multifocality, the proliferation index (Ki67), the number of lymph nodes removed and the result of their assessment. Hence, several EUSOMA quality indicators focusing on e.g. avoidance of overtreatment, could not be calculated. In addition, the IMA – AIM database does not contain information on the laterality of the surgical intervention, hence a second surgical intervention in the same breast cannot reliably be distinguished from a preventive surgical intervention in the contralateral breast. Again, standardised and structured pathology reports could provide that valuable information readily available for quality assurance programs.

The clinical experts also voiced their concern that **no data were available on the socio-economic status (SES) of the patients under study**, even though it is an important case-mix variable that should be taken into account when comparing campuses/hospitals. SES data may be derived from the IMA – AIM database, but they are not routinely transferred to BCR.

The Belgian healthcare system should also invest in the **registration of patient reported outcomes and quality of life measures.** Valuable information on shared decision-making, coordination and multidisciplinarity of care, experience with healthcare providers, information and communication, guidance and support, completion of treatment, functional recovery, and follow-up was not available, hence it could not be assessed to what extent these factors contributed to the increased survival probabilities observed in the coordinating breast clinics. Similarly, the effect of recognition status and volume could only be assessed on survival, not on other important outcome variables, such as quality of life, mental health, patient satisfaction.

The recognition of coordinating and satellite breast clinics is based on several criteria, but only the volume criterion could be assessed. Yet, we observed that this criterion is not always followed rigorously: in December 2018, for instance, twenty out of fifty-two coordinating breast clinics and three out of thirteen satellite breast clinics, did not fulfil the volume criterion. The extent to which they fulfilled the infrastructure and other recognition criteria, which are not documented in the available database, is unclear.

On the other hand, the clinical experts also realised, with us, that the **correctness and completeness of administrative databases** depends heavily on those (responsible for) providing data. The faulty use of nomenclature codes and the lack of compliance to invoicing rules (e.g. SLNB vs. ALND) hamper the correct calculation and interpretation of quality indicators. But major efforts are also indicated to improve the comprehensive reporting of cTNM and pTNM stage information to BCR, especially in low-volume campuses/hospitals. cTNM stage information, for instance, was transferred for only 66.6% of patients with DCIS and for 88.8% of patients with invasive BC, results which were well below the target of 98%. A result that is even more puzzling knowing that cancer stage reporting is one of the legal obligations of the oncological care programs.[102] In recent years, efforts are being made to improve this situation.

Importantly, as was already outlined before, the calculation and interpretation of various quality indicators was not only hindered by the **vague description of several nomenclature codes**, but also by certain **invoicing rules**. In the current major revision of the fee schedule, these issues should certainly be addressed.

Is it all sorrow and misery?

Certainly not.

It was reassuring that during the study we were assisted by **many who are eager to further improve the quality of breast cancer care in Belgium**. First of all, this study benefitted from the intense collaboration with experienced clinical experts. They provided valuable input throughout the whole process, critically reviewed and discussed documents, and ensured that the essential link with actual clinical practice was preserved. Several colleagues from the federated entities revised and validated the campus recognition information and kindly provided any other requested information. All hospitals with more than one campus, were ready to provide campus identification data for the breast cancer care that was provided in 2015, a year during which the collection of hospital discharge data was not mandatory in Belgium. During the interviews, various dedicated health

professionals explained with enthusiasm how they organised BC care at the micro-level and provided useful insights for a better interpretation of the data.

**For several quality indicators the national results were at or even above the EUSOMA target**:[46] 98.0% of women with invasive breast cancer had a histological or cytological assessment before any treatment and in 99.4% testing for ER and/or PR and/or HER2 status was performed. In 97.5% of women with non-metastatic invasive breast cancer radiotherapy was started within nine months after breast conserving surgery, and in 93.0% no second breast surgery was performed. Yet, efforts are indicated to increase the proportion of patients who have mammography and breast sonography before the start of treatment (currently: 92.5%), especially in low-volume hospitals. But also, still too many patients with DCIS have to undergo a second breast surgery (14.2%) or axillary lymph node dissection (3.1%).

In conclusion, the present study revealed that a great many patients affected by breast cancer continue to be treated outside the recognised breast clinics. These women are not only denied the (para)medical staffing and facilities that are provided for by law in the recognised breast clinics, they also have a significantly higher probability to die. Clearly, not only volume is at play. Also other factors related to the coordinating breast clinics, but on which we could not put our finger, contribute.

These observations call for adequate action. All women affected by breast cancer should be offered multidisciplinary, comprehensive and appropriate care, from the suspicion of cancer until follow-up. Campuses without recognition for BC should also be stopped to mislead patients by promoting themselves as ‘breast clinics’ or ‘breast centres’.

A profound reorganisation is imperative. This can be realised within the locoregional networks, so that a sound balance between comprehensiveness and quality of care on the one hand and regional availability and accessibility of services on the other, can be achieved.

Last but not least, auditing and quality assurance programs are essential. For that purpose, reliable and valid data on processes and outcomes are needed. Hence, tackling the many data issues raised above, is a *conditio sine qua non.*

# APPENDICES

## APPENDIX 1. THE EUROPEAN PARLIAMENT RESOLUTION 2002 – CRITERIA FOR CERTIFIED BREAST CENTRES

**Excerpt from the European parliament resolution 2002 – Criteria for certified breast centres**

- Each breast centre shall perform **a minimum of 150 primary BC operations** per year,
- Each breast centre shall operate under the direction of a highly qualified physician who specialises in breast disease, while the multidisciplinary team shall consist of physicians experienced in and performing only breast surgery, together with radiologists, oncologists, pathologists, nurses and radiographers who also specialise in breast disease, as well as a data manager,
- Multidisciplinary pre-operative and post-operative case conferences shall be held at least once a week,
- The quality of the results shall be guaranteed by means of clinical research,
- Physicians and paramedical staff shall regularly attend further training courses,
- Physicians and paramedical staff shall be required to pass a test at regular intervals to show that they have sufficient up-to-date knowledge and skills,
- Follow-up and aftercare examinations shall be carried out in close cooperation with the relevant multidisciplinary breast centre,
- Patients shall receive onco-psychological counselling, psychotherapeutic support and physiotherapy services, as well as social services.

*Source: European Parliament, 2002[1]; full text available at: https://www.europarl.europa.eu/doceo/document/TA-5-2003-0270_EN.pdf?redirect*

# APPENDIX 2. ROYAL DECREE OF 26 APRIL 2007, DEFINING THE RECOGNITION CRITERIA FOR BREAST CLINICS

## Essentials from the Royal Decree of 26 April 2007, defining the recognition criteria for breast clinics

Breast clinics focus on the diagnosis, multidisciplinary treatment, follow-up and revalidation of patients with malignant breast disorders, in accordance with the guidelines of the multidisciplinary oncology handbook.

**Care program:**

A breast clinic can only be operated as a complement to an oncology care programme (see Appendix 3), in other words: hospitals that have a care programme for basic oncological care cannot be recognised as breast clinic.

**Minimal volume:**

In order to be certified as a breast clinic, a centre must have had at least 100 new BC diagnoses, either in the year preceding the application for recognition either as an average over the three years preceding the application. After the first two years following the recognition, the minimal level of activity is **150 new BC diagnoses**[ddd], unless there is no other breast clinic within a radius of 50 km, in which case the cut-off of 100 still applied.

In order to verify this, for each new diagnosis, a copy, albeit in coded form, must be sent of:

- The report of the multidisciplinary oncological consultation (MOC/COM);
- The protocol of the main surgical intervention, with the corresponding anatomopathological protocol.

**Medical coordination:**

The medical coordination of the breast clinic is performed either by a specialist in surgery or gynaecology, or a specialist in medical oncology, or a specialist in radiotherapy-oncology; this function cannot be fulfilled by the coordinator of the oncology care program. The medical coordinator must work on a full-time basis at the hospital and spends at least eight half-days a week on the treatment of BC.

**Medical staff:**

A breast clinic must have at least the following **medical specialists**:

- Two specialists in surgery or in gynaecology with a specific expertise in BC surgery, who must perform annually at least 50 surgical interventions with regard to new diagnoses of BC;
- Two medical specialists in X-ray imaging with experience in mammography and echography of the breast as well as in the technique of breast sample biopsies; they have to assess or re-assess at least 1000 mammographies a year;
- One medical specialist in pathological anatomy with at least three years' experience in diagnosing breast pathologies; (s)he should be

ddd 'New breast cancer diagnosis' comprises any case of breast cancer, of any type and at any stage, including in situ cancers, which is diagnosed for the first time and which is treated within the breast clinic. In case the initial diagnosis was made in a centre other than the breast clinic where the first treatment was performed, the case will be included in the volume of the breast clinic. The following cases are not included in the hospital volume of the breast clinic: 1) patients referred for radiotherapy to the breast clinic; 2) patients who already received primary treatment in another hospital or in another campus of a hospital; 3) patients who are only referred for adjuvant systemic therapy; 4) patients for whom only the follow-up is organised in the breast clinic after the primary treatment has taken place in another hospital or campus of a hospital; 5) patients who were referred to another hospital or another campus after the first diagnosis had been made in the breast clinic.

available at all times and present at the campus during the surgical interventions;

- One medical specialist in radiation oncology with at least three years' experience in the treatment of BC;
- One medical specialist in medical oncology with at least three years' experience in the treatment of BC and who spends at least 8 half-days at the hospital which runs the breast clinic;
- One medical specialist in plastic, reconstructive and aesthetic surgery who has experience in the treatment of patients with BC.

They should collaborate in a coordinated and multidisciplinary way.

**Nursing staff:**

The **nursing care** of patients with BC should be coordinated by a nurse, who either holds a professional qualification in oncology or is in training to obtain this professional qualification, or who has at least five years' experience in the integral care of such patients. The nurse-coordinator should work on a full-time basis at the breast clinic.

**Psychological support:**

The breast clinic must also have a **psychologist** who must work at the breast clinic on at least a half-time basis and who has significant experience in the counselling of patients with BC; the psychosocial support of patients should be guaranteed during all stages of the disease.

**Rehabilitation staff:**

The breast clinic must have **physiotherapists** who are specialised in the prevention of post-operative and post-radio therapeutic lymphoedema and shoulder stiffness.

**Multidisciplinary consultation:**

A multidisciplinary consultation must take place every week for all newly diagnosed patients, and at least before any treatment.

At least one physician from each of the medical disciplines participating in the breast clinic (cf. supra), a nurse and a psychologist must attend the MOC-COM; if indicated, a plastic surgeon must also attend.

For each multidisciplinary consultation a report is made, which includes a comprehensive description of the primary treatment that will be proposed to the patient and a description of the proposed medical follow-up.

The medical specialist who made the diagnosis and/or the medical specialist who will perform the next phase of the treatment or monitoring of the patient, will communicate the diagnosis and the treatment plan to the patient. A psychologist and a coordinating nurse are at all times available to assist the medical specialist in communication.

**Registration:**

In addition to the registration requirements defined for the oncological care programmes, breast clinics have to register (in coded form):

- The results of analyses regarding hormonal receptors (ER and PR)
- The results of analyses regarding HER2 antigens

The breast clinic must appoint a person to coordinating data-manager.

**Training:**

The breast clinic must organise training for its staff.

**Handbook:**

In the multidisciplinary oncological handbook of the hospital a chapter should be dedicated to the breast clinic; in this chapter the procedures

for the reception and follow-up of patients are described, as well as the maximum time intervals between the different stages of the follow-up and treatment, the procedures for communicating the diagnosis and treatment to patients and referring physicians, and the modalities of referral within the framework of cooperation agreements in which the breast clinic participates.

**Breast pathology working group:**

Each breast clinic must have a breast pathology working group, chaired by the coordinator of the breast clinic and composed of a physician from

each of the medical disciplines participating in the breast clinic (cf. supra), the coordinating nurse, the psychologist, a physiotherapist, and the coordinating data-manager. The working group must assist the hospital's multidisciplinary oncology committee of the oncology care programme and must ensure the referral of patients with BC requiring complex or rare treatment to the most appropriate hospital.

**Collaboration agreements:**

The breast clinic must have a written collaboration agreement with:

- at least one recognised mammography unit;
- a recognised centre for human genetics.

The multidisciplinary team of the breast clinic takes care that collaboration agreements with patient associations active in the field of BC are made.

**Infrastructure:**

- On the site (campus) of the breast clinic, sufficient ambulatory consultations must be organised so that:
  - Every new patient with a suspicion or a proven BC who presents at the breast clinic, is seen within five days;
  - In order to ensure that these patients are offered multidisciplinary advice during these consultations, a medical specialist in surgery or gynaecology, a medical specialist in radiology, a medical specialist in radiotherapy and a medical specialist in medical oncology must be present at the campus, and if feasible, within the same unit.
  - During these consultations, a clinical examination, the necessary medical imaging examinations and the collection of breast biopsies must be possible;
  - The diagnosis and the treatment plan are communicated with the patient within a maximum of five working days from the first contact; during these consultations a nurse with experience in the management of BC and the psychologist(s) of the breast clinic must be available.
  - During the consultations organised for the multidisciplinary follow-up of BC patients during and after active treatment, a medical specialist in surgery or gynaecology, a medical specialist in radiology, a medical specialist in radiotherapy and a medical specialist in medical oncology must be present at the campus, and if feasible, within the same unit. In addition, a nurse with experience in the management of BC and the psychologist(s) of the breast clinic must be available.
- The breast clinic must have sufficient radiological and technical equipment so that a diagnosis can be made within five working days; more precisely, the breast clinic must have at least the equipment to perform a mammography, an ultrasound and MRI, and techniques for interventional medical imaging of the breast.
- The hospital's surgical infrastructure must be organised in such a way that the surgical intervention can - if indicated – take place within a period of fifteen working days from the moment the patient is informed about the surgical intervention. Breast surgery may be accompanied by immediate breast reconstruction, but the reconstruction should not cause a delay of the breast surgery.
- The breast clinic must ensure that it can offer radiotherapy within three weeks after breast surgery if no systemic treatment is required; when per-operative radiotherapy is required and the hospital does not have a radiotherapy department, the patient must be referred to a hospital with radiotherapy department and recognised breast clinic.

**Renewal of the recognition:**

To renew the approval every 3 year, a breast clinic has to demonstrate that it reached, annually, in the last year or on average over the last three years before the extension of approval, the required number of new diagnoses of BC, i.e. a minimal volume of 150 new cases of BC (whatever the cancer type and stage, and including in situ cancers), who are then treated in the breast clinic. The approval renewal is also related to compliance with the aforementioned criteria.

*Source: Royal Decree of 26 April 2007, defining the recognition criteria for breast clinics*[4]

# APPENDIX 3. CARE PROGRAMME FOR BASIC ONCOLOGICAL CARE AND ONCOLOGY CARE PROGRAMME

The care programmes for basic oncological care and oncological care have been defined in the Royal Decree of 21 March 2003.[102] Both programmes aim at reinforcing the provision of high quality care for cancer patients. The **care programmes for basic oncological care** focuses mainly on the diagnosis, less complex treatment and follow-up while in the **care programme for oncological care** more advanced diagnostic options as well as various therapeutic possibilities have to be offered. In principle, each acute hospital that does not have a recognition for an oncology care programme, has to offer a care programme for basic oncological care.

The Decree underlines the importance of a **multidisciplinary and a transversal approach**, more precisely it states that there should be coordination between care in the first line (including home care), the care programme for basic oncological care, the oncology care programme and the palliative setting. In order to get a recognition, a hospital must have a Handbook of Oncology (quality manual) that includes guidelines with respect to diagnosis, treatment and follow-up of patients, referral agreements and the identity and tasks of all personnel involved. It has to be evaluated at regular intervals and updated when indicated by the state of scientific evidence.[102]

The care programme for basic oncological care may be spread over several campuses/sites on the condition that all recognition criteria are met at each campus. Likewise, the oncology care programme may be split between several campuses/sites of the same hospital or several sites of several hospitals on the condition that all recognition criteria are met at each campus. The remaining campuses of the hospital or hospitals must meet the recognition criteria of the care programme for basic oncological care.[102]

# APPENDIX 4. ROYAL DECREE OF 2013 - ADAPTATIONS COMPARED TO THE ROYAL DECREE OF 2007

**Box 9 – Non-exhaustive list of adaptations included in the Royal Decree of 15 December 2013, defining the recognition criteria for coordinating and satellite breast clinics, compared to the initial Royal Decree of 26 April 2007**

***Recognition criteria for coordinating breast clinics:***

**Minimal volume:**

The coordinating breast clinic diagnoses annually at least 125 new BCs; the satellite breast clinic diagnoses annually at least 60 new BCs.

**Staffing:**

- A coordinating breast clinic with at least 350 new BC diagnoses a year, must have at least two full-time breast nurses; they have to coordinate the implementation of the care plan established during the multidisciplinary consultation.
- The coordinating breast clinic must have at least a half-time psychologist who has significant experience in the counselling of patients with BC. If the coordinating breast clinic has a formal collaboration with a satellite breast clinic, the coordinating breast clinic must have an additional 0.25 FTE psychologist with the aforementioned experience for each such collaboration. A coordinating breast clinic with at least 350 new BC diagnoses a year, must have at least a full-time psychologist with the aforementioned experience.

**Rehabilitation programme:**

The breast clinic shall organise a rehabilitation programme, comprising physical, psychological and social rehabilitation; the physical rehabilitation, which includes functional measurements, is always carried out by a physiotherapist.

**Registration and reporting:**

Every five years, the coordinating breast clinic must submit a report to the Minister responsible for public health, in which the hospital mortality is compared with the predicted mortality according to the patient characteristics. The model for this report will be drafted by the College of Oncology.

**Infrastructure:**

- The coordinating breast clinic has the necessary equipment and infrastructure so that the care plan can be initiated within ten working days after the diagnosis has been made.
- The coordinating breast clinic organises sufficient ambulatory consultations so that:
  - Every patient who presents at the coordinating breast clinic is seen within five days during a multidisciplinary consultation, during which both a medical specialist in surgery, a medical specialist in radiotherapy, as well as a medical specialist in oncology are available;
  - The communication of the diagnosis and the treatment plan, occurs within the shortest possible time after the first contact;
  - A multidisciplinary follow-up of the patients is possible, both during and after the treatment. During these consultations the aforementioned medical specialists, as well as a dedicated nurse and psychologist should be present;

    It is possible to follow up patients with benign breast diseases.

**The satellite breast clinic:**

- The satellite breast clinic focuses on the diagnosis, multidisciplinary treatment, rehabilitation and follow-up of multidisciplinary treatment, rehabilitation and monitoring of patients with malignant breast disease(s) in accordance with the guidelines of the multidisciplinary oncology handbook.
- The satellite breast clinic must have a formal collaboration agreement with a hospital, which has a coordinating breast clinic.

***Recognition criteria for satellite breast clinics, that differ from the recognition criteria defined for coordinating breast clinics:***

**Minimal volume:**

For the first application for recognition, an 'existing need' must be demonstrated by at least **60 new BC diagnoses**[ddd] per year, either the year before the application for recognition, or as an average during the last three years prior to the application for approval.

**Medical coordination:**

The medical coordination of the satellite breast clinic is performed by the medical specialist who also takes care of the medical coordination in the coordinating breast clinic with which the satellite breast clinic has a formal collaboration agreement.

**Medical staffing:**

The medical staffing requirements are the same as for the coordinating breast clinics.

**Nursing staff:**

The nursing staff of the satellite breast clinic consists of a half-time nurse attached to the breast clinic, who either holds a professional qualification in oncology or is in training to obtain this professional qualification, or who has at least five years' experience in the integral care of such patients.

**Psychological support:**

The obligation to have a half-time psychologist does not apply to the satellite breast clinics.

**Rehabilitation staff:**

This requirement is the same as for the coordinating breast clinics.

**Breast pathology working group:**

The satellite breast clinic does not have its own working group on breast pathology but is represented in the breast pathology working group of the coordinating breast clinic with which she has a formal collaboration agreement.

**Multidisciplinary consultation:**

The multidisciplinary consultation must take place under the chairmanship of the joint medical coordinator.

**Multidisciplinary oncology handbook:**

The satellite breast clinic uses the same multidisciplinary oncology handbook as the coordinating breast clinic with which the satellite breast clinic has a formal collaboration agreement.

**Renewal of the recognition:**

In order to remain accredited, the satellite breast clinic must demonstrate that it has during the last year or as an average during the last three years before the renewal of the approval, 60 new BC diagnoses[ddd].

# APPENDIX 5. DISTRIBUTION OF COORDINATING AND SATELLITE BREAST CLINICS OVER THE HOSPITAL NETWORKS

**Table 23 – Distribution of coordinating and satellite breast clinics over the hospital networks**

| Network | Coordinating breast clinic<br>Name (Site number) | Satellite breast clinic<br>Name (Site number) | Formal collaboration with coordinating breast clinic (site number) |
|---|---|---|---|
| **BRIANT** | - AZ Sint-Maarten, Mechelen (6170)<br>- AZ Heilig Hart, Lier (1260)<br>- Imelda Ziekenhuis, Bonheiden (2040) | / | NA |
| **Charleroi Métropole** | - Grand Hôpital de Charleroi - Notre Dame (3100)<br>- Grand Hôpital de Charleroi - Saint-Joseph (3170) | - Clinique Notre-Dame de Grace, Gosselies (3350) | - Grand Hôpital de Charleroi - Notre Dame (3100) |
| **CHORUS** | - CHU Saint-Pierre, Bruxelles / UMC Sint-Pieter, Brussel (1520)<br>- CHU/UVC Brugmann (Victor Horta), Bruxelles (Laeken; 1570)<br>- Jules Bordet Institut, Bruxelles (Anderlecht, 6220)<br>- Hôpitaux Iris Sud - Iris Ziekenhuizen Zuid, Bruxelles (Elsene; 1560)<br>- Chirec - Hôpital Delta, Bruxelles (Auderghem; 6140)<br>- Hôpital Erasme, ULB, Bruxelles (Anderlecht; 4210) | - Chirec - Hôpital Sare, St Anne-Remi (1470)<br>- Chirec - Hôpital Sare, Braine-l'alleud, Waterloo (1760) | - Chirec - Hôpital Delta (6140)<br>- Chirec - Hôpital Delta (6140) |
| **Curoz** | - Onze-Lieve-Vrouw Ziekenhuis, Aalst (1780)<br>- Universitair Ziekenhuis Brussel (4200)<br>- ASZ Aalst (1800) | / | NA |
| **E17** | - AZ Maria Middelares, Gent (1605)<br>- AZ Groeninge, Kortrijk (1090) | - St- Jozefskliniek, Izegem (1920)<br>- AZ Sint-Elisabeth, Zottegem (1900)<br>- O.L.V. Van Lourdes Ziekenhuis, Waregem (1990)<br>- AZ Glorieux, Ronse (1680) | - AZ Groeninge (1090)<br>- UZ Gent** (3850)<br>- AZ Groeninge (1090)<br>- AZ Groeninge (1090) |

| Network | Coordinating breast clinic<br>Name (Site number) | Satellite breast clinic<br>Name (Site number) | Formal collaboration with coordinating breast clinic (site number) |
|---|---|---|---|
| **ELIPSE** | - C.H.R. Verviers East Belgium (3010)<br>- Hôpital de la Citadelle, Liège (3410)<br>- CHU de Liège (3860) | / | NA |
| **GENT** | - AZ Sint-Lucas, Gent (1630)<br>- Universitair Ziekenhuis Gent (3850) | - AZ Jan Palfijn, Gent (1610) | - AZ Sint-Lucas, Gent (1630) |
| **GZA-ZNA** | - Ziekenhuisnetwerk Antwerpen, Middelheim (2000)<br>- GZA- Ziekenhuizen, St-Augustinus (1290) | - Ziekenhuisnetwerk Antwerpen, Jan Palfijn, Merksem (3360) | - Ziekenhuisnetwerk Antwerpen, Middelheim (2000) |
| **H.uni** | - Clinique Saint Pierre, Ottignies (1730)<br>- Kliniek Sint-Jan, Brussel - Clinique Saint-Jean, Bruxelles (1310)<br>- Europaziekenhuizen, Ukkel - Cliniques de l'europe, Uccle (1400)<br>- Cliniques universitaires Saint-Luc, Bruxelles (4190) | / | NA |
| **Helix** | - Universitair Ziekenhuis Antwerpen (4220)<br>- AZ Monica, Deurne (1210)<br>- AZ Klina, Brasschaat (3450) | / | NA |
| **Helora** | - CHU Tivoli, La Louvière (3220)<br>- Pôle Hospitalier Jolimont, Haine-Saint-Paul (3200)<br>- CHU Ambroise Pare, Mons (2730) | - Pôle Hospitalier Jolimont, Mons (2710) | - Pôle Hospitalier Jolimont, Haine-Saint-Paul (3200) |
| **Humani** | - CHU Charleroi (3130) | / | NA |
| **Kempen** | - AZ Turnhout, Sint-Elisabeth (1280)<br>- Ziekenhuis Geel (2690) | / | NA |
| **KOM netwerk** | - AZ Sint-Jan, Brugge (1010)<br>- AZ Sint-Lucas, Brugge (1000)<br>- AZ Damiaan, Oostende (1940) | - AZ Alma, Eeklo (1845) | - AZ Sint-Lucas, Gent (1630)** |

| Network | Coordinating breast clinic<br>Name (Site number) | Satellite breast clinic<br>Name (Site number) | Formal collaboration with coordinating breast clinic (site number) |
|---|---|---|---|
| **MIRA** | - AZ Sint-Blasius, Dendermonde (3460)<br>- Vitaz, Sint-Niklaas (1860) | / | NA |
| **MOVE** | - Groupe Santé CHC, Waremme (2930)<br>- Groupe Santé CHC, Montlégia, Liège (6200) | - Groupe Santé CHC, Hermalle (2940)<br>- Groupe Santé CHC, Heusy (2970) | - Groupe Santé CHC, Montlégia, Liège (6200)<br>- Groupe Santé CHC, Montlégia, Liège (6200) |
| **Noord-Oost Limburg** | - Ziekenhuis Oost-Limburg, Sint-Jan (3560) | - Noorderhart, Mariaziekenhuis, Pelt (3615) | - Ziekenhuis Oost-Limburg, Sint-Jan (3560) |
| **Phare** | - Centre Hospitalier Epicura, Hornu (3380)<br>- Centre Hospitalier de Wallonie Picarde (Chwapi), Tournai (2830) | - Centre Hospitalier Régional Haute Senne, Soignies (2790)<br>- Centre Hospitalier de Mouscron (2770) | - Pôle Hospitalier Jolimont, Haine-Saint-Paul (3200)**<br>- Cliniques universitaires Saint-Luc, Bruxelles (4190)** |
| **Plexus** | - UZ Gasthuisberg, Leuven (4230) | / | NA |
| **Réseau Hospitalier Namurois** | - CHU-UCL Namur, Sainte-Elisabeth (3290) | - CHR Sambre et Meuse, Namur (3300)<br>- CHU-UCL Namur, Mont-Godinne (3280)<br>- Clinique Saint-Luc, Bouge (3340) | - CHU-UCL Namur, Sainte-Elisabeth (3290)<br>- CHU-UCL Namur, Sainte-Elisabeth (3290)<br>- CHU-UCL Namur, Sainte-Elisabeth (3290) |
| **TRIaz** | - Jan Yperman Ziekenhuis, Ieper (2700)<br>- AZ Delta, Roeselare (6210) | - Sint-Andriesziekenhuis, Tielt (1170) | - AZ Delta, Roeselare (6210) |
| **Vivalia** | - / | / | NA |
| **Zuid-West Limburg** | - Jessa Ziekenhuis, Virga Jesse, Hasselt (3590) | / | NA |

***Indicates that there is a formal collaboration between a satellite breast clinic and a coordinating breast clinic from a different hospital network.*

# APPENDIX 6. SELECTION OF QUALITY INDICATORS

**Table 24 – Long list of quality indicators, their respective source and measurability**

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| **General outcome indicators** | | | | | |
| Overall 5-year survival rate by stage | x | x | | | Yes |
| Disease specific 5-year survival by stage | x | x | | | Yes |
| Disease-free 5-year survival rate by stage | x | | | | No |
| 5-year local recurrence rate after curative surgery, by stage | x | | | | No |
| **General process indicators** | | | | | |
| Proportion of women with BC who participate in clinical trials | x | | | | No |
| Median time between incidence date and start of first treatment with curative intent - Target: ≤6 weeks between first diagnostic examination and start of treatment | | | | x | Yes |
| ***Diagnosis and staging*** | | | | | |
| Proportion of women with class 3, 4 or 5 abnormal mammograms having an assessment with a specialist within 2 months of mammography | x | | | | No |
| Proportion of BC women discussed at the multidisciplinary team meeting | x | x | | x | Yes |
| Proportion of women with unknown cStage, pStage, combined stage | | x | | | Yes |
| 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 | x | | | | No |
| Proportion of newly diagnosed cStage I-III BC women who underwent two-view mammography or breast sonography within 3 months prior to surgery | x | | | x | Yes |
| *Sensitivity analysis: Proportion of newly diagnosed cStage I-III BC women who underwent two-view mammography or breast sonography or MRI within 3 months prior to surgery* | | x | | | Yes |

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| Proportion of women who received axillary ultrasonography with fine needle aspiration cytology of the axillary lymph nodes before any treatment | x | | | | No |
| Proportion of women in whom human epidermal growth factor receptor 2 status was assessed before any systemic treatment | x | x | | x | Yes |
| *Sensitivity analysis: with or without systemic treatment* | | x | | | Yes |
| Proportion of women in whom ER and PR status assessment were performed before any systemic treatment | x | x | | x | Yes |
| Proportion of BC women with cytological and/or histological assessment before surgery | x | x | | x | Yes |
| Proportion of sentinel lymph nodes biopsy in cN0 patients without contraindications | x | | | | No |
| Proportion of patients with invasive cancer and clinically negative axilla who underwent sentinel lymph-node biopsy (SLNB) only | | | | x | Yes |
| Ratio of benign to malignant diagnoses based on definitive pathology report (surgery only, non-operative biopsies excluded) | | | | x | Yes |
| Proportion of non-invasive cancer cases for which the following prognostic/predictive parameters have been recorded: Grading (according to WHO Classification of Tumours of the Breast), dominant histological pattern, size in mm (best pathology or radiology estimate if two- stage pathology), distance to nearest radial margin, ER. | | | | x | No |
| ***Surgery*** | | | | | |
| Proportion of patients (BRCA1 and BRCA2 patients excluded) with IBC not greater than 3 cm (total size, including DCIS component) who underwent BCS as primary treatment | | | | x | No |
| Proportion of patients with non-IBC not greater than 2 cm who underwent BCS | | | | x | No |
| Proportion of patients with DCIS only who do not undergo axillary clearance | | | | x | Yes |
| Proportion of BC women who underwent an ALND after positive SNLB > 2 mm | x | | | | No |
| Proportion of cStage I and II women who undergo breast-conserving surgery/mastectomy | x | | | x | Yes |
| Proportion of patients (DCIS only) who received just one operation (excluding reconstruction) | | | | x | Yes |

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| Proportion of cStage III-IV women who undergo breast surgery | | | x | | Yes |
| Proportion of women with BC recurrence after breast conserving surgery who are treated by a mastectomy | x | | | | No |
| *'Fine-tuned' definition: Proportion of cStage I and II women who undergo breast-conserving surgery followed or not by a mastectomy within 6 months* | | x | | | Yes |
| Proportion of women with reconstructive surgery after mastectomy (by age subgroups and time delays) | | x | | | Yes |
| ***Radiotherapy*** | | | | | |
| Proportion of women who received radiotherapy after breast conserving surgery | x | x | | | Yes |
| Proportion of patients with IBC (M0) who received postoperative radiation therapy (RT) after surgical resection of the primary tumour and appropriate axillary staging/surgery in the framework of BCS | | | | x | Yes |
| *Proportion of women who received radiotherapy after mastectomy (<70 years, cStage I-III)* | | | x | | Yes |
| Proportion of patients with involvement of axillary lymph nodes (≥pN2a) who received post-mastectomy radiation therapy to the chest wall and all (non-resected) regional lymph-nodes | | | | x | No |
| Proportion of women who underwent a mastectomy and having ≥ 4 positive nodes who received radiotherapy on axilla following ALND | x | | | | No |
| Proportion of patients with involvement of up to three axillary lymph nodes (pN1) who received post-mastectomy radiation therapy to the chest wall and non-resected axillary lymph-nodes, including level IV (supraclavicular), and in medially located tumours, the internal mammary lymph-nodes | | | | x | No |
| ***Systemic treatment*** | | | | | |
| Proportion of operable cT2-T3 women who received neoadjuvant systemic therapy | x | x | | | Yes |
| *Sensitivity analysis: cT1-2 cN0-1 cM0, cT3-4 cNany cM0, cTany cN2-3 cM0* | | x | | | Yes |
| *Sensitivity analysis: <70 years; neoadjuvant or adjuvant treatment within 4 months of surgery* | | | x | | Yes |

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| *Sensitivity analysis: <70 years cStage I III triple negative receiving neo adjuvant chemotherapy 4 months* | | | x | | No |
| *Sensitivity analysis: ≥75 years cStage I III, ER+ or PR+ receiving neo adjuvant chemotherapy 4 months* | | | x | | No |
| Proportion of women with a BC 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 | x | | | | No |
| Proportion of women receiving adjuvant systemic therapy after breast surgery for IBC | x | | | | Yes |
| Proportion of women receiving adjuvant systemic therapy (chemotherapy, endocrine therapy, or combination chemo and endocrine therapy) after breast surgery for IBC | | x | | | Yes |
| *Sensitivity analysis: <70 years and duration of endocrine therapy ≥4 ; 4.5; 5 years* | | | x | | Yes |
| Proportion of patients with ER- (T > 1 cm or Node+) invasive carcinoma who received adjuvant chemotherapy | | | | x | No |
| Proportion of patients with inflammatory BC (IBC) or locally advanced non-resectable ER-carcinoma who received neoadjuvant chemotherapy | | | | x | No |
| Proportion of women with hormone receptor positive IBC or DCIS who received adjuvant endocrine treatment (Tamoxifen/AI) | x | | | x | Yes |
| Proportion of women with HER2 positive, node positive or high-risk node negative BC (tumour size > 1 cm), having a left ventricular ejection fraction of ≥50-55% who received chemotherapy and Trastuzumab | | | | | No |
| Proportion of patients with HER2 positive (IHC 3+ or in situ hybridisation positive FISH-positive) invasive carcinoma (T > 1 cm or N+) treated with chemotherapy who received adjuvant trastuzumab | | | | x | No |
| Proportion of patients with HER2-positive invasive carcinoma treated with neoadjuvant chemotherapy who received neoadjuvant trastuzumab | | | | x | No |

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| Proportion of women treated by Trastuzumab in whom cardiac function is monitored every 3 months | x | | | | No |
| Proportion of women with HER2 positive metastatic BC who received Trastuzumab with/without non-anthracycline based chemotherapy or endocrine therapy as first-line treatment | x | | | | No |
| Proportion of metastatic BC women who receive systemic therapy as 1st and/or 2nd line treatment | x | x | | | Yes |
| Proportion of women with metastatic BC and lytic bone metastases who received biphosphonates | x | | | | No |
| Proportion of women ≥75 years with cStage IV BC receiving primary endocrine therapy instead of surgery | | | x | | No |
| ***Follow-up*** | | | | | |
| Proportion of women who benefit from an annual mammography after a history of BC (to add: in the first five years after primary surgery) | x | | | | Yes |
| *Proportion of women who benefit from an annual mammography/MRI after a history of BC (operated women without metastases)* | | x | | | Yes |
| Proportion of asymptomatic patients who undergo routine annual mammographic screening and 6/12 months clinical evaluation in the first 5 years after primary surgery | | | | x | No |
| ***Histopathology*** | | | | | |
| Proportion of BC 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. | x | | | | No |
| Proportion of women with IBC undergoing ALND and having 10 or more lymph nodes removed | x | | | | No |
| ***Volume*** | | | | | |
| <50 (very low) – 50-99 (low), 100-149 (medium) and >150 patients (high) | x | | | | Yes |

| Description of the QI | Source | | | | Measurable |
|---|---|---|---|---|---|
| | KCE-BCR 2010 | BCR 2012-2014 | BCR-BSMO 2010-2014 | EUSOMA 2017 | |
| b) Volume-processes<br>c) Volume-outcome (5 year survival) | | | | | |
| Volume-outcome (without grouping volumes) | | x | | | Yes |

**Table 25 – Quality indicators not selected by the clinical experts (based on relevance)**

| Quality indicators not selected |
|---|
| Ratio of benign to malignant diagnoses based on definitive pathology report (surgery only, non-operative biopsies excluded) |
| Proportion of women <70 years old with cStage I-III BC treated with mastectomy receiving adjuvant radiotherapy |

# APPENDIX 7. DEFINITION OF BREAST CANCER

**Table 26 – ICD-O-3 codes included to define IBC and DCIS**

| Cancer type | ICD-O-3 codes |
|---|---|
| IBC | Invasive ductal carcinoma (IDC): 8035/3, 8500/3, 8501/3, 8514/3, 8521/3, 8523/3 |
| | Invasive lobular carcinoma (ILC): 8520/3, 8524/3 |
| | Mixed ductal and lobular: 8522/3 |
| | Papillary & micropapillary: 8050/3, 8260/3, 8503/3, 8504/3, 8507/3, 8509/3 |
| | Mucinous: 8480/3, 8481/3 |
| | Metaplastic: 8032/3, 8033/3, 8070/3, 8560/3, 8570/3, 8571/3, 8572/3, 8573/3, 8575/3 |
| | Medullary: 8510/3, 8512/3, 8513/3 |
| | Cribriform & tubular: 8201/3, 8211/3 |
| | Inflammatory: 8530/3 |
| | Neuroendocrine: 8013/3, 8041/3, 8240/3, 8246/3, 8249/3, 8574/3 |
| | Salivary gland type: 8200/3, 8430/3, 8502/3, 8508/3, 8550/3 |
| | Apocrine: 8401/3 |
| | Other carcinoma: 8310/3, 8314/3, 8315/3, 8290/3, 8490/3, 8562/3 |
| | Carcinoma, NOS: 8000/3, 8001/3, 8010/3, 8012/3, 8020/3, 8022/3, 8030/3, 8140/3, 8147/3, 8082/3 |
| DCIS | 8201/2, 8230/2, 8500/2, 8501/2, 8503/2, 8504/2, 8507/2, 8509/2, 8522/2, 8523/2 |

*Source: RARECAREnet Information Network on Rare Cancers, List of Rare Cancers (October 2015; retrieved from http://rarecarenet.istitutotumori.mi.it/rarecarenet/index.php/cancerlist), The Surveillance, Epidemiology, and End Results (SEER) Program - Breast Solid Tumor Rules (2018, update July 2019; Retrieved from https://seer.cancer.gov/tools/solidtumor/Breast_STM.pdf), the World Health Organization Classification of Tumours Editorial Board & International Agency for Research on Cancer (2012) and personal communication with clinical experts.*

# APPENDIX 8. ANALYSIS OF CANCER REGISTRY AND OTHER AVAILABLE DATA

## Appendix 8.1. Health insurance data (IMA – AIM data)

### *Appendix 8.1.1. Linkage with the IMA – AIM database*

In Belgium, physicians are mainly paid fee-for-service. Compulsory health insurance pays for medical services on the basis of a fee schedule, called 'nomenclature', provided by the national health insurance (RIZIV-INAMI, 'Rijksinstituut voor ziekte- en invaliditeitsverzekering' – 'Institut national d'assurance maladie-invalidité'; see Box 10).

**Box 10 – The fee schedule, also known as nomenclature**

Medical and paramedical services covered by compulsory health insurance are listed in a fee schedule, called 'nomenclature', which lists more than 10 000 unique covered services. The list of reimbursable codes contains for each item the professional qualification needed to be eligible for reimbursement, a code-number, a description of the item, a key letter according to the medical speciality, a coefficient and application rules. The coefficient gives for each procedure the relative value compared to other procedures with the same key letter.

Multiplying the coefficient by the value of the key letter determines the amount of payment to the provider concerned (i.e. the fee). The type of reimbursable benefits and their amounts (total fee and reimbursement) are determined through a process of negotiations with various parties involved within RIZIV-INAMI, all within pre-set budgetary limits. The National Commission of Sickness Funds and Providers, the so-called 'Medico-Mut' negotiates on the tariffs, and more specifically, on the value of the key letter. The negotiated fee or 'convention tariff' is settled in agreements (for physicians and dentists) and conventions (for other healthcare providers).

Since 2009, the Belgian Cancer Registry is authorized to link data from its database with data on cancer-related diagnostic and therapeutic procedures and pharmaceuticals.[52] These data are obtained from all seven Belgian health insurance organisations via the Intermutualistic Agency (IMA – AIM). The linkage procedure is based on the patient's unique Social Security Identification Number (INSZ-NISS) and the incidence date as a reference. Via this linkage procedure, the BCR receives for each registered patient, health insurance data starting from the 1st of January of the year preceding the incidence year, until the 31st of December of the fifth year after the incidence year. These data are further mentioned as the IMA – AIM data.

At the start of this study, IMA – AIM data up to June 2020 were available at the BCR. From the patients selected for this study, **97.9% could be linked to the IMA – AIM database**. Patients for whom no information was available in the IMA – AIM database were excluded from the study cohort (see Appendix 8.1); they were probably not affiliated to one of the seven Belgian sickness funds (e.g. people working abroad).

### *Appendix 8.1.2. Defining diagnostic and therapeutic procedures based on health insurance data*

For each diagnostic and therapeutic procedure that was used in the calculation of one of the quality indicators, nomenclature codes were defined by the KCE-BCR research team and discussed with the clinical experts. For each procedure these codes were then selected from the IMA – AIM database and coupled to the BCR-data.

#### Time frames

**Important limitations** inherent to working with IMA – AIM data are that the codes are not directly linked with the indication (pathology) and that the description of the nomenclature is often not specific enough to identify this indication with certainty. To overcome this limitation as best we could, only interventions performed near the incidence date were selected for this study and it was decided to exclude patients for whom multiple breast or multiple invasive tumours were registered (see Appendix 8.3). This way, procedures performed for other indications could be excluded as much as possible.

Unless otherwise specified, the following **time frames** were used to link the IMA – AIM data to the cancer diagnosis in this study:

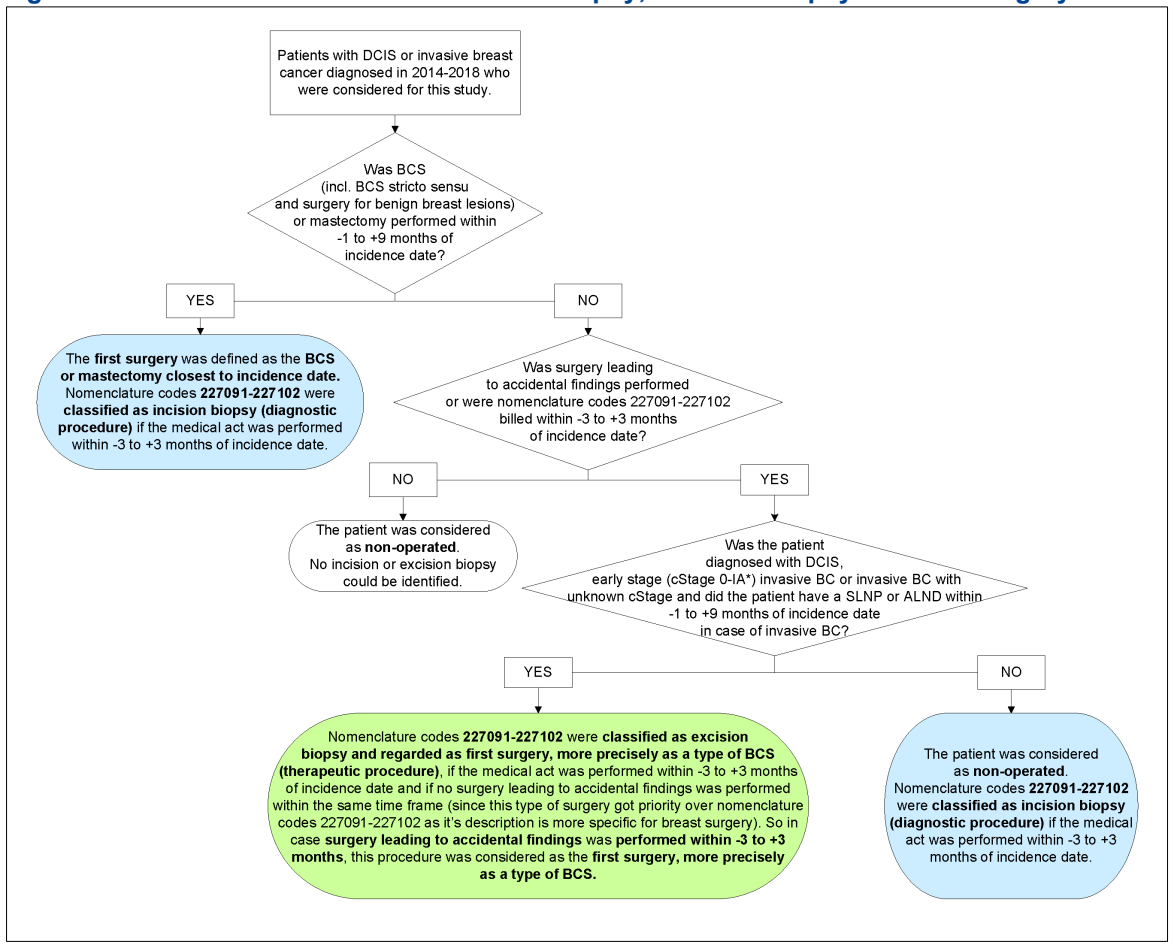
- For the **diagnostic and staging procedures**, a symmetric time frame of three months before to three months after the incidence date was considered. For imaging procedures specifically, the pre-validation phase revealed that a supplementary cut-off should be implemented to avoid taking into account procedures that are not meant for diagnostic or staging purposes (see section 4.8). Hence, imaging procedures that took place as from the start of treatment onwards, were not considered as imaging for diagnostic or staging purposes. Additionally, for CT body scans, scans that were performed as from 14 days before the start date of radiotherapy were not considered either as it was assumed that they were taken preparatory to the radiotherapy.
- For the **multidisciplinary team meeting (MDT**, 'Multidisciplinair Oncologisch Consult (MOC)' – 'Consultation Ongologique Multidisciplinaire (COM)'), an asymmetric time frame of one month before to two months after the incidence date was used;
- For **therapeutic procedures**, an asymmetric time frame of one month before to nine months after the incidence date was considered;
    - **Pre-operative treatment** (systemic therapy and in rare occasions radiotherapy) was defined as treatment initiated within one month before the incidence date until the day before the date of first breast surgery;
    - **Adjuvant treatment** was defined as treatment initiated within nine months after the first surgery (including the date of first surgery).

One month was defined as thirty days. As small deviations in the incidence date and the date of medical acts were sometimes observed in the databases, some time before incidence date was also taken into account for therapeutic procedures.

### Incision biopsy versus excision biopsy

Data exploration revealed that, in some cases, the nomenclature codes 227091-227102 were billed for incision biopsy (diagnostic purpose), while for other cases it was billed for excision biopsy (small curative surgery). To be able to consider these codes for the correct intention, a distinction was made based on tumour behaviour, clinical stage and the absence/presence of other surgical procedures to classify these codes as either diagnostic or therapeutic. Figure 12 shows the decision tree that was considered to classify these codes and to define first surgery. If nomenclature codes 227091-227102 were classified as incision biopsy, they were regarded as a type of breast biopsy.

## Figure 12 – Decision tree to define incision biopsy, excision biopsy and first surgery




** For tumours diagnosed in 2009, which are part of the comparison period 2009 - 2013, early stage IBC was defined as cStage 0-I, as the TNM 6th edition is applicable to them;[55] BCS: breast conserving surgery; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection.*

*Source: BCR – IMA*

## *Appendix 8.1.3. Diagnostic procedures*

Except for incision biopsy, all other diagnostic tests were considered for all breast tumours, regardless of their behaviour or clinical stage.

### First surgery

First surgery was defined as the first breast surgery that took place within one month before to nine months after incidence date. Priority was given to breast conserving surgery (BCS) *stricto sensu*[ss], surgery for benign breast lesions and mastectomy over excision biopsy and surgery leading to accidental findings according to the decision rules presented in Figure 12. BCS *stricto sensu*, surgery for benign breast lesions, excision biopsy and surgery leading to accidental findings were all considered as a type of BCS.

### Radiotherapy

When interpreting the results on radiotherapy (RT), the following limitations in the database must be considered:

- The start date of radiotherapy is not always available in the IMA – AIM data. According to the RIZIV-INAMI invoicing rules, hospitals should record each session separately and invoice the total RT scheme on the last day of the RT schedule.[146] A check of the IMA – AIM database revealed that 81.3% of all RT schemes were recorded according to these invoicing rules. However, in five RT centres almost none of the RT schemes were billed according to the rules. Often only the last session date was registered in the IMA – AIM database. For these cases the BCR constructed an algorithm to estimate the start date of radiotherapy based on the simulation date. If also the simulation date was not available, the start date was estimated based on the end date and on the duration of the series observed for similar patients for whom the start date was available in the IMA – AIM database.
- For those RT series for which only the last fraction was invoiced, it was impossible to distinguish multi-fraction from single fraction RT schedules. And the use of the above algorithm implied that some IORT sessions (i.e. single fraction sessions) might become categorised erroneously as multi-fraction schedules, with an incorrect start date before the date of surgery and an end date on the date of surgery. These cases were (erroneously) considered as pre-operative RT. In addition, the estimated start date of some of the adjuvant RT schedules was before the date of first breast surgery and was therefore also (erroneously) considered as a pre-operative RT scheme. This resulted in more operated patients having pre-operative radiotherapy (1 102 patients, 2.5% of operated patients) than would have been expected for the BC population under study. To limit this erroneous identification of pre-operative radiotherapy, an additional algorithm was developed to better identify IORT cases and adjust erroneously estimated start dates of adjuvant RT schemes, all of which were considered as radiotherapy in the adjuvant setting.

a. If the date of radiotherapy was within seven days before to seven days after the first breast surgery and if one or multiple fractions (i.e. hyperfractionated RT) where given on the same day, this radiotherapy was considered IORT.

b. If the start date of a RT scheme was estimated to be before the date of first surgery and the end date of the RT scheme was more than seven days after the first surgery, the RT schedule was considered adjuvant RT and the start date was equated with the end date, since the estimated start date was considered to be wrong and no other information was available in the IMA – AIM data to determine a correct start date.

c. If the start date of a RT scheme was estimated to be before the date of first surgery and the end date of the RT scheme was more than seven days before the first surgery or within seven days before to seven days after the first surgery, it was checked whether other sources of information at the BCR could confirm that RT was given in a pre-operative setting. For the majority of patients, no confirmation could be found, but it was noticed that these patients were most often (85.2%) metastasized at diagnosis (i.e. cStage IV). Therefore, metastasis was considered as the reason for pre-operative RT.

After application of the second algorithm, 27 cases (0.06% of operated patients) were considered to have pre-operative radiotherapy, 23 of them were clinically metastasized.

- Another limitation is that the fee for the whole scheme is always billed, regardless of the number of fractions that was actually given. Therefore, it is not possible to distinguish patients who completed the whole RT scheme from patients who received RT fractions but who stopped their RT treatment before it was completed.

### Systemic therapy

The list of systemic therapy products (i.e. chemotherapy, targeted therapy and endocrine therapy) relevant for BC treatment, was selected based on communication with the clinical experts. The products were then identified in the IMA – AIM database using the Anatomical Therapeutical Chemical (ATC) codes issued by the World Health Organization (WHO) (see Table 50, Table 51, Table 52).

### Included nomenclature codes

**Table 27 – Nomenclature codes for breast biopsy**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Core biopsy** | | | |
| 355213 | 355224 | 01/11/2011: * Cilinderbiopsie van de borstklier voor histologisch onderzoek | 01/11/2011 : * Biopsie en cylindre de la glande mammaire pour examen histologique |
| **Vacuum assisted biopsy** | | | |
| 355235 | 355246 | 01/11/2011: * Vacuümgeassisteerde biopsie van de borstklier voor histologisch onderzoek | 01/11/2011 : * Biopsie assistée par aspiration de la glande mammaire pour examen histologique |
| 355250 | 355261 | 01/11/2011: * Vacuümgeassisteerde biopsie van de borstklier voor histologisch onderzoek onder stereotactische geleiding | 01/11/2011 : * Biopsie assistée par aspiration de la glande mammaire pour examen histologique, effectuée sous guidance stéréotaxique |
| **Incision biopsy*** | | | |

| | | | |
|---|---|---|---|
| 227091 | 227102 | Incisie voor biopsie van de borstklier | Biopsie incisionnelle de la glande mammaire |
| **Nomenclature codes used only in view of assigning a patient to a diagnostic centre when one of the above nomenclature codes was billed on the same day but no centre could be linked to that nomenclature code** | | | |
| 161932 | 161943 | Biopsienaald aangewend ter gelegenheid van de verstrekking 355213-355224 van de nomenclatuur | Aiguille pour biopsie utilisée lors de la prestation 355213-355224 de la nomenclature |
| 698913 | 698924 | Biopsienaald aangewend ter gelegenheid van de verstrekking 355213-355224 | Aiguille pour biopsie utilisée à l'occasion de la prestation 355213-355224 |
| 161954 | 161965 | Geheel van materiaal , met uitzondering van de clip, aangewend ter gelegenheid van de verstrekkingen 355235-355246 en 355250-355261 van de nomenclatuur | Ensemble du matériel, à l'exception du clip, utilisé lors des prestations 355235-355246 et 355250-355261 de la nomenclature |
| 161976 | 161980 | Clip gebruikt in combinatie met de verstrekking 161954-161965 | Clip utilisé en combinaison avec la prestation 161954-161965 |
| 688472 | 688483 | Geheel van materiaal, met uitzondering van de clip, aangewend ter gelegenheid van de verstrekkingen 355235-355246 en 355250-355261 | Ensemble du matériel, à l'exception du clip, utilisé à l'occasion des prestations 355235-355246 et 355250-355261 |
| 688494 | 688505 | Clip gebruikt in combinatie met de verstrekking 688472 - 688483 | Clip utilisé en combinaison avec la prestation 688472 - 688483 |

** Incision biopsy is only considered as breast biopsy if no core biopsy or vacuum assisted biopsy was billed within 3 months before till 3 months after incidence date. If more than one type of breast biopsy was billed within this time frame, the closest one to incidence date was retained.*

**Table 28 – Nomenclature codes for breast puncture**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 355670 | 355681 | * Punctie van de borstklier voor cytologisch onderzoek of inspuiting | * Ponction de la glande mammaire pour examen cytologique ou injection |

**Table 29 – Nomenclature codes for lymph node puncture**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 355692 | 355703 | °* Punctie van hematopoiëtisch orgaan, exclusief lever en milt | °* Ponction d'un organe hématopoïétique, à l'exclusion du foie et de la rate |
| 220356 | 220360 | Exeresis van ganglion | Exérèse ganglionnaire |
| 355132 | 355143 | 01/09/2017: Punctie van een lymfeklier | 01/09/2017 : Ponction d'un ganglion lymphatique |

### Table 30 – Nomenclature codes for cytological examination

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 588416 | 588420 | 01/07/1999: 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 | 01/07/1999 : 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 |
| | | 01/04/2018: Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecifieerd in de verstrekkingen 589853-589864 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten, per afname | 01/04/2018: Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 589853-589864 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement |

### Table 31 – Nomenclature codes for anatomical-pathological examinations

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Biopsy specimens** | | | |
| 588114 | 588125 | Pathologisch-anatomisch onderzoek met een elektronenmicroscoop, ongeacht de aangewende techniek of technieken, ongeacht het aantal afnamen | 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 |
| 588254 | 588265 | 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 | 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 |
| **Resection specimens** | | | |
| 588011 | 588022 | 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 prelevementen die niet overeenkomen met | 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, |

| | | | |
|---|---|---|---|
| | | de prestaties 588232 - 588243, 588254 - 588265, 588276 - 588280 of 588291 - 588302 | pour les prélèvements ne correspondant pas aux prestations 588232 - 588243, 588254 - 588265, 588276 - 588280 ou 588291 - 588302 |
| 588276 | 588280 | 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) | 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, - tumorectomie mésentérique, - tumorectomie 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, - tumorectomie 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) |
| 588291 | 588302 | 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, | 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, - tumorectomie du plancher buccal avec ou sans mandibulectomie, - tumorectomie du palais avec ou sans maxillectomie, - maxillectomie totale, - gastrectomie partielle ou totale, - résection de l'intestin grêle, - colectomie partielle ou totale, - duodénopancréatectomie, - |

| | | | |
|---|---|---|---|
| | | 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 | 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 |
| **Frozen section** | | | |
| 588033 | 588044 | Peroperatoir pathologisch-anatomisch extempore onderzoek, ongeacht het aantal afnamen volgens de vriesmethode en ongeacht het aantal verrichte controle-onderzoeken na inclusie en coupe | Examen peropératoire extemporané quel que soit le nombre de prélèvements examinés par la technique de congélation et quel que soit le nombre de contrôles effectués après inclusion et coupe |

**Table 32 – Nomenclature codes for immunohistochemical examination (general)**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 588070 | 588081 | Immunohistologische onderzoeken (maximum 4 per afname) voor het aantonen van antigenen in de coupes, na incubatie met antisera, per gebruikt antiserum | Examens immunohistologiques (maximum 4 par prélèvement) pour révéler des antigènes sur des coupes, après incubation d'anticorps, par anti-sérum |
| 588976 | 588980 | 01/07/2009: 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 | 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 patients oncologiques |

**Table 33 – Nomenclature codes for oestrogen and progesterone testing**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 435831 | 435842 | 01/07/1999: Doseren van oestrogeen- en progesteronreceptoren in borsttumors, ongeacht het aantal afnamen (Maximum 1)(Cumulregel 66) Klasse 32 | 01/07/1999: 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 |
| | | 01/10/2010: Doseren van oestrogeen- en progesteronreceptoren in borsttumors, ongeacht het aantal afnamen (Maximum 1)(Cumulregel 66) | 01/10/2010 : 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) |

| | | | |
|---|---|---|---|
| 546416 | 546420 | 01/07/1999: Doseren van oestrogeen- en progesteronreceptoren in borsttumoren, ongeacht het aantal afnamen, met een immunologische methode (Maximum 1)(Cumulregel 66) Klasse 32 | 01/07/1999: Dosage des récepteurs d'oestrogènes et de progestérone dans les tumeurs mammaires, quel que soit le nombre de prélèvements, par méthode immunologique (Maximum 1)(Règle de cumul 66) Classe 32 |
| | | 01/10/2010: Doseren van oestrogeen- en progesteronreceptoren in borsttumoren, ongeacht het aantal afnamen, met een immunologische methode (Maximum 1)(Cumulregel 66) | 01/10/2010: Dosage des récepteurs d'oestrogènes et de progestérone dans les tumeurs mammaires, quel que soit le nombre de prélèvements, par méthode immunologique (Maximum 1 (Règle de cumul 66) |

*Note that the specific nomenclature codes for oestrogen and progesterone testing in breast tumours did not occur in the billing records (IMA-AIM data) of the patients considered within this study and for the defined time frame (-3 to +3 months of incidence date). Therefore, they were not reported separately in the description of the study cohort (section 5)*

### Table 34 – Nomenclature codes for HER2 in situ hybridization

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 588556 | 588560 | 01/08/2007: Opsporen van HER2 genamplificatie door een fluorescente in situ hybridatie techniek voor therapiekeuze bij mammacarcinoom in de diagnostische investigatiefase (Maximum 1) (Diagnoseregel 1) Klasse 35 | 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 (Maximum 1) (Règle diagnostique 1) Classe 35 |
| | | 01/08/2010: Opsporen van HER2 genamplificatie door een fluorescente in situ hybridatie techniek voor therapiekeuze bij mammacarcinoom in de diagnostische investigatiefase (Diagnoseregel 1, 13) | 01/08/2010 : 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) |
| | | 01/07/2011: Opsporen van HER2 genamplificatie door middel van een in situ "hybridization" techniek voor therapiekeuze bij mammacarcinoom in de diagnostische investigatiefase (Diagnoseregel 1, 13) | 01/07/2011: Dépistage d'une amplification du gène HER2 au moyen d'une technique par "hybridization" in situ dans le cadre du choix thérapeutique pour le carcinome mammaire (Règle diagnostique 1, 13) |
| | | 01/07/2017 – 30/06/2019: Opsporen van HER2 genamplificatie door middel van een in situ "hybridization" techniek (Diagnoseregel 1, 13, 21) | 01/07/2017 – 30/06/2019: Dépistage d'une amplification du gène HER2 au moyen d'une technique par "hybridization" in situ (Règle diagnostique 1, 13, 21) |
| 594436 | 594440 | 01/07/2019: Analyse van HER2 genamplificatie bij niet-gemetastaseerde borstkanker | Analyse de l'amplification du gène HER2 en cas de cancer du sein non métastatique |
| 594451 | 594462 | 01/07/2019: Analyse van HER2 genamplificatie bij gemetastaseerde borstkanker | 01/07/2019 : Analyse de l'amplification du gène HER2 en cas de cancer du sein métastatique |

**Table 35 – Nomenclature codes for BRCA test**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 565154 | 565165 | 01/01/2013: Complex moleculair cytogenetisch onderzoek (met submicroscopische, genoomwijde analyse) bij de diagnose van een maligne aandoening (Cumulregel 1) (Diagnoseregel 3, 10, 18, 19) | 01/01/2013 : Examen de cytogénétique moléculaire complexe (avec analyse sub-microscopique, pangénomique) pour le diagnostic d'une affection maligne (Règle de cumul 1) (Règle diagnostique 3, 10, 18, 19) |
| 565390 | 565401 | 01/01/2013: Moleculair onderzoek voor het opsporen van constitutionele aandoeningen of voor het bepalen van een individueel genetisch profiel met het oog op genetisch advies en/of voor diagnostische doeleinden, inclusief DNA isolatie (Diagnoseregel 10, 11, 18) | 01/01/2013 : Analyse moléculaire pour la recherche d'affections constitutionnelles ou établissement d'un profil génétique individuel à des fins de conseil génétique et/ou à des fins diagnostiques, incluant l'extraction de l'ADN (Règle diagnostique 10, 11, 18) |
| 565434 | 565445 | 01/01/2013: Predictief genetisch onderzoek naar een familiale mutatie in het kader van kanker of familiaal kankersyndroom, inclusief DNA isolatie (Diagnoseregel 12) | 01/001/2013 : Examen génétique prédictif d'une mutation familiale dans le cadre de cancer ou d'un syndrome cancéreux familial, incluant l'extraction de l'ADN (Règle diagnostique 12) |
| 565515 | 565526 | 01/01/2013: Complex moleculair genetisch onderzoek voor het opsporen van mutaties in het kader van kanker of familiaal kankersyndroom (niveau 1) (Diagnoseregel 10, 18) | 01/01/2013 : Analyse moléculaire complexe pour la recherche de mutations dans le cadre de cancer ou de syndrome cancéreux familial (niveau 1) (Règle diagnostique 10, 18) |
| 565530 | 565541 | 01/01/2013: Complex moleculair genetisch onderzoek voor het opsporen van mutaties in het kader van kanker of familiaal kankersyndroom (niveau 2) (Diagnoseregel 10, 18) | 01/01/2013 : Analyse moléculaire complexe pour la recherche de mutations dans le cadre de cancer ou de syndrome cancéreux familial (niveau 2) (Règle diagnostique 10, 18) |
| 565552 | 565563 | 01/01/2013: Complex moleculair genetisch onderzoek voor het opsporen van mutaties in het kader van kanker of familiaal kankersyndroom (niveau 3) (Diagnoseregel 10, 18) | 01/01/2013 : Analyse moléculaire complexe pour la recherche de mutations dans le cadre de cancer ou de syndrome cancéreux familial (niveau 3) (Règle diagnostique 10, 18) |
| 587915 | 587926 | 01/07/2019: Opsporen van een verworven puntmutatie door middel van een moleculair biologische methode in de diagnostische investigatiefase van een niet-lymfoïde en niet-myeloïde vaste tumor (Cumulregel 5) (Diagnoseregel 1, 13) | 01/07/2019 : Dépistage d'une mutation ponctuelle acquise au moyen d'une méthode de biologie moléculaire dans la phase d'investigation diagnostique d'une tumeur solide non lymphoïde et non-myéloïde. (Règle de cumul 5) (Règle diagnostique 1, 13) |
| 588534 | 588545 | Opsporen van een verworven chromosoom of genafwijking met uitzondering van een puntmutatie door middel van een moleculair biologische methode, in de diagnostiche investigatiefase van een niet-lymfoïde en niet-myeloïde vaste tumor ?(Cumulregel 5) (Diagnoseregel 1, 13) | Dépistage d'anomalies chromosomiques ou géniques acquises à l'exception d'une mutation ponctuelle au moyen d'une méthode de biologie moléculaire, dans la phase d'investigation diagnostique d'une tumeur solide non-lymphoïde et non-myéloïde ?(Règle de cumul 5) (Règle diagnostique 1, 13) |

**Table 36 – Nomenclature codes for mammography**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Diagnostic mammography** | | | |
| 450096 | 450100 | Mammografie per borst, inclusief de eventuele okselclichés (ongeacht het aantal clichés) | Mammographie par sein y compris les clichés axillaires éventuels (quel que soit le nombre de clichés) |
| 461090 | 461101 | Mammografie per borst, inclusief de eventuele okselclichés (ongeacht het aantal clichés) | Mammographie par sein y compris les clichés axillaires éventuels (quel que soit le nombre de clichés) |
| **Screening mammography** | | | |
| 450192 | 450203 | 01/02/2016: Mammografie van beide borsten, in het kader van een door een overheid georganiseerd bevolkingsonderzoek | 01/02/2016 : Mammographie des deux seins dans le cadre d'un examen de masse organisé par une autorité |
| 450214 | 450225 | 01/04/2018 – 01/04/2018: Tweede lezing van een screeningsmammografie van beide borsten, in het kader van een door een overheid georganiseerd bevolkingsonderzoek | 01/04/2018 – 01/04/2018: Deuxième lecture de mammographie de dépistage, des deux seins, dans le cadre d'un examen de masse organisé par une autorité |
| 450354 | 450365 | 01/04/2018 – 01/04/2018: Mammografie van beide borsten in het kader van opsporing van borstkanker bij asymptomatische vrouwen met een sterk verhoogd risicoprofiel | 01/04/2018 – 01/04/2018: Mammographie des deux seins effectuée dans le cadre du dépistage du cancer du sein chez les femmes asymptomatiques ayant un profil de risque très élevé |
| 450376 | 450380 | 01/04/2018 – 01/04/2018: Mammografie van beide borsten voor individuele opsporing van borstkanker | 01/04/2018 – 01/04/2018: Mammographie des deux seins pour dépistage individuel du cancer du sein |
| 450391 | 450402 | 01/04/2018 – 01/04/2018: Tweede lezing van een mammografie van beide borsten voor individuele opsporing van borstkanker | 01/04/2018 – 01/04/2018: Deuxième lecture d'une mammographie des deux seins pour dépistage individuel du cancer du sein |
| 461451 | 461462 | 01/04/2018 – 01/04/2018: Mammografie van beide borsten voor individuele opsporing van borstkanker | 01/04/2018 – 01/04/2018: Mammographie des deux seins pour dépistage individuel du cancer du sein |
| 461473 | 461484 | 01/04/2018 – 01/04/2018: Tweede lezing van een mammografie van beide borsten voor individuele opsporing van borstkanker | 01/04/2018 – 01/04/2018: Deuxième lecture d'une mammographie des deux seins pour dépistage individuel du cancer du sein |

**Table 37 – Nomenclature codes for breast ultrasound**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 459793 | 459804 | 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 | 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 |
| 460132 | 460143 | 01/04/2003: 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 | 01/04/2003: 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 |
| | | 01/12/2018: 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 met inbegrip van de axilla | 01/12/2018: 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 y inclus la région axillaire |
| 469394 | 469405 | 01/04/2003: Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen: Van één of beide borsten | 01/04/2003: Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes : D'un ou des deux seins |
| | | 01/12/2018: Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen: Van één of beide borsten met inbegrip van de axilla | 01/12/2018: Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes : D'un ou des deux seins y inclus la régionaxillaire |
| 461134 | 461145 | 01/02/2016: Echografie van beide borsten in het kader van opsporing van borstkanker bij asymptomatische vrouwen, met een sterk verhoogd risicoprofiel zoals bepaald in artikel 17, § 1, 1° bis | 01/02/2016 : Echographie des deux seins dans le cadre du dépistage du cancer du sein chez des femmes asymptomatiques ayant un risque très élevé comme défini à l'article 17, § 1er, 1° bis |

### Table 38 – Nomenclature codes for breast MRI

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 459476 | 459480 | NMR-onderzoek van één of beide mammae, minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager | Examen d'IRM d'un ou des deux seins, minimum 3 séquences, avec ou sans contraste, avec enregistrement sur support soit optique, soit électromagnétique |
| 459830 | 459841 | 01/02/2016: NMR van beide borsten in het kader van opsporing van borstkanker bij asymptomatische vrouwen met een verhoogd risicoprofiel, zoals bepaald in artikel 17, § 1, 1°bis | 01/02/2016 : IRM des deux seins dans le cadre du dépistage du cancer du sein chez des femmes asymptomatiques ayant un profil de risque très élevé, comme défini à l'article 17, § 1er, 1°bis |

### Table 39 – Nomenclature codes for CT body, scintigraphy, SPECT and SPECT-CT

| Outpatient | Inpatient | Dutch Description | French Description | Definition before the pre-validation phase* |
|---|---|---|---|---|
| **CT body** | | | | |
| 458813 | 458824 | Enkel beschouwd indien vóór 01/10/2010: Computergestuurde tomografie van de hals (weke delen) of van de thorax of van het abdomen, met en/of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek | Uniquement considéré avant 01/10/2010 : Tomographie commandée par ordinateur, du cou ( parties molles ) ou du thorax, ou de l'abdomen,avec et/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen | *CT body* |
| 459550 | 459561 | 01/10/2010: Computergestuurde tomografie van de thorax met of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek | 01/10/2010 : Tomographie commandée par ordinateur, du thorax avec/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen | *CT body* |
| 459572 | 459583 | 01/10/2010: Computergestuurde tomografie van het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek | 01/10/2010 : Tomographie commandée par ordinateur, de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen | *CT body* |
| 459594 | 459605 | 01/10/2010: Computergestuurde tomografie van de hals en de thorax, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek | 01/10/2010 : Tomographie commandée par ordinateur du cou et du thorax, avec/ ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen | *CT body* |

| | | | | |
|---|---|---|---|---|
| 459616 | 459620 | 01/10/2010: Computergestuurde tomografie van de thorax en het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek | 01/10/2010 : Tomographie commandée par ordinateur du thorax et de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen | *CT body* |
| 459631 | 459642 | 01/10/2010: Computergestuurde tomografie van de hals, de thorax en het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek | 01/10/2010 : Tomographie commandée par ordinateur du cou, du thorax et de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen | *CT body* |
| **Scintigraphy** | | | | |
| 442411 | 442422 | Scintigrafie van een orgaan, van een stelsel of van een deel van het lichaam | Scintigraphie d'un organe, d'un système ou d'une partie du corps | *Scintigraphy* |
| 442455 | 442466 | Scintigrafie van het ganse lichaam (de scintillogrammen moeten ten minste betrekking hebben op het hoofd, de romp, het abdomen, de schouder- en bekkengordels) | Scintigraphie du corps entier (les scintillogrammes doivent comporter la tête, le tronc, l'abdomen, les ceintures scapulaires et pelviennes au minimum) | *Scintigraphy* |
| 442610 | 442621 | 01/04/1985: Functionele scintigrafische test van een orgaan of stelsel van organen, met sequentele inzameling van de gegevens, kwantitatieve analyse met telsysteem (computer) die activiteitscurven in de tijd en/of tabellen met cijfergegevens en/of parametrische beelden omvat, met protocol en iconografische documenten | 01/04/1985: Test scintigraphique fonctionnel d'un organe ou système d'organes, avec acquisition séquentielle des données, analyse quantitative par calculateur (ordinateur) comprenant des courbes d'activité dans le temps et/ou des tableaux de données chiffrées et/ou des images paramétriques, avec protocole et documents iconographiques | *Scintigraphy* |
| | | 01/01/2016: Functioneel scintigrafisch onderzoek van een orgaan of stelsel van organen, met sequentiële (dynamische) inzameling van de gegevens die minstens drie opnames bevatten op verschillende tijdstippen, met kwantitatieve analyse ervan die activiteitscurven in de tijd en/of tabellen met cijfergegevens omvat, met protocol en iconografische documenten | 01/01/2016 : Examen scintigraphique fonctionnel d'un organe ou système d'organes, avec acquisition séquentielle (dynamique) des données qui comprend au moins trois enregistrements à différents moments, avec leur analyse quantitative comprenant des courbes d'activité dans le temps et/ou des tableaux de données chiffrées, avec protocole et documents iconographiques | |
| **SPECT** | | | | |
| 442396 | 442400 | 01/11/1998: Tomografisch onderzoek tijdens een scintigrafie, met verwerking op computer die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411-442422, 442455-442466, 442610-442621 en 442632- | 01/11/1998 : Examen tomographique lors d'une scintigraphie, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques, non cumulable avec les prestations 442411-442422, 442455-442466, 442610-442621 et 442632-442643 pour l'examen d'un | *Scintigraphy* |

| | | | | |
|---|---|---|---|---|
| | | 442643 voor het onderzoek van een zelfde orgaan of stelsel van organen dat met een zelfde gemerkt produkt wordt verricht | même organe ou système d'organes effectué au moyen d'un même produit marqué | |
| | | 01/01/2016: Tomografisch onderzoek tijdens een scintigrafie, met verwerking op computer die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten (Single-photon emission computed tomography - SPECT) | 01/01/2016: Examen tomographique lors d'une scintigraphie, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques (Single-photon emission computed tomography - SPECT) | |
| 442514 | 442525 | 01/07/1999: Tomografisch onderzoek van een streek van het lichaam tijdens een scintigrafie van het ganse lichaam, met computerverwerking, dat ten minste twee niet parallelle reconstructievlakken omvat, met protocol en iconografische documenten | 01/07/1999: Examen tomographique d'une région du corps lors d'une scintigraphie du corps entier, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques | *Scintigraphy* |
| | | 01/01/2016: Tomografisch onderzoek van een streek van het lichaam tijdens een scintigrafie van het ganse lichaam, met computerverwerking, dat ten minste twee niet parallelle reconstructievlakken omvat, met protocol en iconografische documenten (Single-photon emission computed tomography - SPECT) | 01/01/2016 : Examen tomographique d'une région du corps lors d'une scintigraphie du corps entier, avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques (Single-photon emission computed tomography - SPECT) | |
| **SPECT-CT** | | | | |
| 459351 | 459362 | 01/06/2016: Computergestuurde tomografie van het bekken en/of de wervelzuil, schedel, thorax, met of zonder contrastmiddel, met beeldfusie, bij SPECT-CT onderzoek, uitgevoerd op een SPECT-CT toestel | 01/06/2016 : Tomographie commandée par ordinateur du bassin et/ou de la colonne vertébrale, du crâne ou du thorax, avec ou sans moyen de contraste, avec fusion d'images, lors d'un examen SPECT-CT, réalisé au moyen d'un appareil SPECT-CT | *CT body* |
| 442536 | 442540 | 01/06/2016: Bijkomend honorarium voor een lokalisatie CT opname, met beeldfusie, bij een SPECT onderzoek, uitgevoerd op een SPECT-CT toestel | 01/06/2016 : Supplément d'honoraires pour l'enregistrement d'un CT de localisation, avec fusion d'images, lors d'un examen SPECT, réalisé au moyen d'un appareil SPECT-CT | *Not taken into account before the pre-validation phase* |

** During the pre-validation phase the validating hospitals made remarks on how CT body was defined. This feedback led to the revision of CT body and scintigraphy codes, together with the experts, and to the creation of separate categories for SPECT and SPECT-CT. The final definitions considered for this study are shown in this table, while the categorization into CT body and scintigraphy as it was before the pre-validation phase is shown in the far right column. Note that for CT body, the nomenclature codes 458452-458463 were no longer considered after the pre-validation phase and are therefore not represented in the table.*

**Table 40 – Nomenclature codes for PET(-CT)**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 442595 | 442606 | Enkel beschouwd indien vóór 01/01/2016: Functionele scintigrafische test die twee opeenvolgende tomografische onderzoeken omvat, met verwerking op computer, die ten minste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411 - 442422, 442455 - 442466, 442610 - 442621 en 442632 - 442643 voor het onderzoek van een zelfde functie dat met een zelfde gemerkt produkt wordt verricht | Uniquement considéré avant 01/01/2016 : Test scintigraphique fonctionnel comportant deux examens tomographiques successifs avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques, non cumulable avec les prestations 442411 - 442422, 442455 - 442466, 442610 - 442621 et 442632 - 442643 pour l'examen d'une même fonction effectué au moyen d'un même produit marqué |
| 442750 | 442761 | 01/01/2016: Positronentomografisch onderzoek door coïncidentiedetectie, met protocol en documenten, voor andere indicaties dan deze vermeld bij de verstrekkingen 442971-442982, 442676-442680, 442691-442702, 442713-442724 of 442735-442746 | 01/01/2016 : Examen tomographique à émission de positons par détection en coïncidence, avec protocole et documents, pour d'autres indications que celles mentionnées aux prestations 442971-442982, 442676-442680, 442691-442702, 442713-442724 ou 442735-442746 |
| 442971 | 442982 | 01/07/1999: Positronentomografisch onderzoek door coïncidentiedetectie met protocol en documenten, voor het geheel van het onderzoek | 01/07/1999: Tomographie à positrons par détection en coïncidence avec protocole et documents, pour l'ensemble de l'examen |
| | | 01/01/2016: Positronentomografisch onderzoek door coïncidentiedetectie met protocol en documenten, voor het geheel van het onderzoek, voor oncologische indicaties | 01/01/2016: Tomographie à émission de positons par détection en coïncidence avec protocole et documents, pour l'ensemble de l'examen, pour des indications oncologiques |
| 459874 | 459885 | 05/05/2016: Computergestuurde tomografie van de hersenen met registreren en clichés, met of zonder contrastmiddel, tegelijkertijd uitgevoerd bij een PET onderzoek, voor diagnostische doeleinden | 05/05/2016 :Tomographie du cerveau commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, effectuée simultanément avec un examen PET, à des fins diagnostiques |
| 459896 | 459900 | 05/05/2016: Computergestuurde tomografie met registreren en clichés, met of zonder contrastmiddel, tegelijkertijd uitgevoerd bij een PET onderzoek dat tenminste een opname van de halsregio tot en met het abdomen omvat, voor diagnostische doeleinden | 05/05/2016 : Tomographie commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, effectuée simultanément avec un examen PET qui comprend au moins un cliché de la région du cou jusqu'à l'abdomen, à des fins diagnostiques |
| 459911 | 459922 | 05/05/2016: Computergestuurde tomografie met registreren en clichés, met of zonder contrastmiddel, tegelijkertijd uitgevoerd bij een PET onderzoek dat tenminste een opname van de thorax omvat, voor diagnostische doeleinden | 05/05/2016 : Tomographie commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, effectuée simultanément avec un examen PET qui comprend au moins la région du thorax, à des fins diagnostiques |

### Table 41 – Nomenclature codes for X-ray of thorax

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 452690 | 452701 | Radiografie van de thorax en de inhoud ervan, één cliché | Radiographie du thorax et de son contenu, un cliché |
| 452712 | 452723 | Radiografie van de thorax en de inhoud ervan, minimum twee clichés | Radiographie du thorax et de son contenu, minimum 2 clichés |
| 463691 | 463702 | Radiografie van de thorax en de inhoud ervan, één cliché | Radiographie du thorax et de son contenu, un cliché |
| 463713 | 463724 | Radiografie van de thorax en de inhoud ervan, minimum 2 clichés | Radiographie du thorax et de son contenu, minimum 2 clichés |
| 455335* | 455346* | Radiografie van het ribrooster, minimum twee clichés | Radiographie du gril costal, minimum 2 clichés |

** This nomenclature code is added to the selection because it cannot be billed on the same day as the regular thorax X-ray codes and has a higher key value.*

### Table 42 – Nomenclature codes for brain imaging (CT scan and MRI)

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **CT scan of brain** | | | |
| 458673 | 458684 | Computergestuurde tomografie van de schedel met of zonder contrast, met registreren en clichés, minimum 10 coupes, voor het hele onderzoek | Tomographie du crâne commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, 10 coupes au minimum pour l'ensemble de l'examen |
| 458732 | 458743 | Computergestuurde tomografie van de rotsbeenderen en/of sella torsica met of zonder contrastmiddel, met registreren en clichés, in een opeenvolgende reeks coupes, gelijk aan of minder dan 2 mm: minimum 20 coupes | Tomographie des rochers et/ou de la selle turcique, commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, dans une série successive de coupes égales ou inférieures à 2 mm : 20 coupes au minimum |
| 458511 | 458522 | Verstrekkingen waarvoor de bekwaming van specialist voor röntgendiagnose (R) vereist is - Computergestuurde tomografieën: Computergestuurde tomografie van de rotsbeenderen en/of sella torsica met of zonder contrastmiddel, met registreren en clichés, in een opeenvolgende reeks coupe, gelijk aan of minder dan 2 mm: minimum 20 coupes - K.B. van 22 oktober 1992 - Pseudonomenclatuurcode ingeval de verstrekkingen verricht worden bij kinderen jonger dan 5 jaar, de betrekkelijke waarden (458732) worden verhoogd met 25% | Prestations qui requièrent la qualification de médecin spécialiste en radiodiagnostic (R) - Tomographies par ordinateur : Tomographie des rochers et/ou de la selle turcique, commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, dans une série successive de coupes égales ou inférieures à 2 mm : 20 coupes au minimum - A.R. du 22 octobre 1992 - Code pseudonomenclature lorsque les prestations sont effectuées chez des enfants de moins de 5 ans, les valeurs relatives (458732) sont augmentées de 25% |

| MRI of brain | | | |
|---|---|---|---|
| 459395 | 459406 | NMR-onderzoek van het hoofd (schedel, hersenen, rotsbeen, hypofyse, sinussen,orbita(e) of kaakgewrichten), minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager | Examen d'IRM de la tête (crâne, encéphale, rocher, hypophyse, sinus, orbite(s) ou articulations de la mâchoire), minimum 3 séquences avec ou sans contraste, avec enregistrement soit sur support optique, soit électromagnétique |

**Table 43 – Nomenclature codes for abdominal ultrasound**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 459712 | 459723 | Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd inclusief eventueel gebruik van dopplertechnieken | Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou surrénales, rétropéritoine) avec au minimum huit coupes différentes documentées, y compris l'usage éventuel de techniques doppler |
| 459793 | 459804 | 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 | 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 |
| 460154 | 460165 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen: Van het abdomen : Lever en/of galblaas, en/of galwegen | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires |
| 469416 | 469420 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen - Van het abdomen: Lever en/of galblaas en/of galwegen | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes - De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires |
| 469173 | 469184 | 01/03/2010: Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd | 01/03/2010 : Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou glandes surrénales, rétropéritoine) avec au moins huit coupes documentées différentes |

### Table 44 – Nomenclature codes for breast conserving surgery (BCS)

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **BCS without SLNB or ALND** | | | |
| 227732 | 227743 | Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge | Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante |
| 227754 | 227765 | Volledige, borstsparende, resectie van een bewezen kwaadaardig, niet voelbaar borstletsel met macroscopisch voldoende veiligheidsmarge, na localisatieprocedure | 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 |
| **BCS with SLNB, without ALND** | | | |
| 227776 | 227780 | Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier | Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante et résection du ganglion sentinelle |
| 227791 | 227802 | Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier, met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier | Résection complète, conservatrice du sein, d'une tumeur maligne démontrée, avec résection d'une marge de sécurité macroscopiquement suffisante et résection du ganglion sentinelle avec examen anatomo-pathologique peropératoire du ganglion sentinelle |
| **BCS with SLNB and possibly ALND** | | | |
| 227813 | 227824 | Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier, die wanneer tumoraal ingenomen bij peroperatoir anatomo-pathologisch onderzoek gevolgd wordt door een okseluitruiming | 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 tumoral démontré à l'examen anatomo-pathologique peropératoire est suivi d'un évidement ganglionnaire de l'aisselle |
| 227835 | 227846 | Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en een okseluitruiming | 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 |
| **Surgery for benign breast lesion** | | | |
| 227850 | 227861 | Volledige resectie van een goedaardig borstletsel | Résection complète d'une lésion bénigne du sein |
| 227872 | 227883 | Volledige resectie van een niet-voelbaar goedaardig borstletsel of met diagnostisch doeleinde, na localisatie procedure | Résection complète d'une lésion bénigne du sein non palpable ou à titre diagnostique, après procédure de localisation |

*SLNB: sentinel lymph node biopsy ; ALND: axillary lymph node dissection*

**Table 45 – Nomenclature codes for mastectomy**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Mastectomy without SLNB and ALND** | | | |
| 227894 | 227905 | Verwijderen van de volledige borstklier (mastectomie) zonder bewezen kwaadaardig letsel | Résection complète du sein (mastectomie) sans tumeur maligne démontrée |
| 227636 | 227640 | Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumor | Résection complète du sein (mastectomie) pour tumeur maligne |
| **Mastectomy with SLNB, without ALND** | | | |
| 227651 | 227662 | Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumor en resectie van schildwachtlymfeklier | Résection complète du sein (mastectomie) pour tumeur maligne et résection du ganglion sentinelle |
| 227673 | 227684 | Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumor en resectie van schildwachtlymfeklier met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier | Résection complète du sein (mastectomie) pour tumeur maligne et résection du ganglion sentinelle avec examen anatomo-pathologique peropératoire du ganglion sentinelle |
| **Mastectomy with SLNB and possibly ALND** | | | |
| 227695 | 227706 | Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumor met okseluitruiming | Résection complète du sein (mastectomie) pour tumeur maligne avec évidement axillaire |
| 227710 | 227721 | Verwijderen van de volledige borstklier (mastectomie) voor kwaadaardige tumor en resectie van schildwachtlymfeklier die wanneer tumoraal ingenomen bij peroperatoir anatomo-pathologisch onderzoek gevolgd wordt door een okseluitruiming | Résection complète du sein (mastectomie) pour tumeur maligne et résection du ganglion sentinelle qui en cas d'envahissement tumoral démontré à l'examen anatomo-pathologique peropératoire est suivi d'un évidement ganglionnaire de l'aisselle |

*SLNB: sentinel lymph node biopsy ; ALND: axillary lymph node dissection*

**Table 46 – Nomenclature codes for excision biopsy**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 227091 | 227102 | Incisie voor biopsie van de borstklier | Biopsie incisionnelle de la glande mammaire |

*These codes were considered to define first surgery according to the methodology explained supra.*

**Table 47 – Nomenclature codes for surgery leading to accidental findings**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Plastic surgery for malformations of the breast (nomenclature chapter CH05 14c/II 1. A.)** | | | |
| 251576 | 251580 | 01/04/2003: Borstplastie door implantatie van een borstprothese voor tubereuze borst, per borst | 01/04/2003: Plastie d'un sein par implantation d'une prothèse mammaire pour seins tubéreux, par sein |
| | | 01/08/2011: Borstplastie door implantatie van een borstimplantaat of een borstweefselexpander, in geval van tubereuze borst, per borst | 01/08/2011: Plastie d'un sein par implantation d'un implant mammaire ou d'un expanseur tissulaire mammaire, en cas de seins tubéreux, par sein |
| | | 01/04/2019: Eénzijdige borstplastie door implantatie van een prothese of een weefselexpander | 01/04/2019: Plastie mammaire unilatérale avec insertion d'une prothèse ou d'un expanseur tissulaire |
| 251591 | 251602 | 01/03/2006: Wegnemen van een borstprothese, omwille van gedocumenteerde complicatie, per borst | 01/03/2006: Enlèvement d'une prothèse mammaire, pour raison de complication documentée, par sein |
| | | 01/08/2011: Wegnemen van een borstimplantaat of een borstweefselexpander, omwille van gedocumenteerde complicatie, per borst | 01/08/2011: Enlèvement d'un implant mammaire ou d'un expanseur tissulaire mammaire, pour raison de complication documentée, par sein |
| | | 01/04/2019: Eénzijdige wegneming van een borstprothese of een borstweefselexpander | 01/04/2019: Retrait unilatéral d'une prothèse mammaire ou d'un expanseur tissulaire mammaire |
| 251613 | 251624 | 01/04/2003: Reducerende borstplastie wegens borsthypertrofie die functionele hinder veroorzaakt, per borst | 01/04/2003 : Plastie de réduction d'un sein pour hypertrophie mammaire entraînant une gêne fonctionnelle, par sein |
| | | 01/04/2019: Reducerende borstplastie wegens borsthypertrofie die functionele hinder veroorzaakt | 01/04/2019: Plastie de réduction d'un sein pour hypertrophie mammaire entraînant une gêne fonctionnelle |
| 251635 | 251646 | 01/04/1985: Reducerende borstplastie van de heterolaterale borst in geval van éénzijdige ernstige aangeboren hypoplastie | 01/04/1985 : Plastie de réduction du sein hétéro-latéral en cas d'hypoplasie congénitale majeure unilatérale |
| | | 01/04/2019: Reducerende borstplastie | 01/04/2019: Plastie de réduction d'un sein |
| 251650 | 251661 | 01/01/1999: Implantatie van borstprothese in geval van éénzijdige ernstige aangeboren hypoplasie | 01/01/1999: Implantation de prothèse mammaire en cas d'hypoplasie congénitale majeure unilatérale |
| | | 01/08/2011: Borstplastie door implantatie van een borstimplantaat of een borstweefselexpander, in geval van éénzijdige ernstige aangeboren hypo- of aplasie of misvorming | 01/08/2011: Plastie d'un sein par implantation d'un implant mammaire ou d'un expanseur tissulaire mammaire, en cas d'hypoplasie grave unilatérale ou d'aplasie congénitale majeure unilatérale ou de malformation |

| | | | |
|---|---|---|---|
| | | 01/04/2019: Eénzijdige borstplastie door implantatie van een prothese of een weefselexpander | 01/04/2019: Plastie mammaire unilatérale avec insertion d'une prothèse ou d'un expanseur tissulaire |
| 251790 | 251801 | 01/04/2003: Heelkundige correctie van ingetrokken tepel, per borst | 01/04/2003: Correction chirurgicale d'un mamelon invaginé, par sein |
| | | 01/04/2019: Eénzijdige heelkundige correctie van een ingetrokken tepel | 01/04/2019: Correction chirurgicale unilatérale d'une invagination mamelonnaire |
| **Reductive surgery for gynecomastia in men*** | | | |
| 227113* | 227124* | Subareolaire resectie van het borstklierweefsel bij de man | Résection sub-aréolaire de tissu mammaire chez l'homme |

*These codes were considered to define first surgery according to the methodology explained supra. *: These codes were added to the list, since for volume analysis all breast cancer patients (female and male) were considered.*

**Table 48 – Nomenclature codes for lymph node surgery (separate nomenclature codes)**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **SLNB** | | | |
| 227592 | 227603 | Resectie van schildwachtlymfeklier | Résection du ganglion sentinelle |
| 227614 | 227625 | Resectie van schildwachtlymfeklier met peroperatoir anatomo-pathologisch onderzoek van de schildwachtlymfeklier | Résection du ganglion sentinelle avec examen peropératoire anatomo-pathologique du ganglion sentinelle |
| **ALND** | | | |
| 226936 | 226940 | Okseluitruiming in het kader van de behandeling voor een bewezen kwaadaardig borstgezwel | Evidement ganglionnaire de l'aisselle dans le cadre du traitement d'une tumeur maligne du sein, démontrée |
| 226914 | 226925 | 01/04/2010: Okseluitruiming in het kader van de behandeling voor een bewezen kwaadaardig gezwel met uitzondering van het borstgezwel | 01/04/2010 : Evidement ganglionnaire de l'aisselle dans le cadre du traitement d'une tumeur maligne démontrée, à l'exception d'une tumeur du sein |

*SLNB: sentinel lymph node biopsy ; ALND: axillary lymph node dissection*

### Table 49 –Nomenclature codes for radiotherapy

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **External radiotherapy** | | | |
| 444113 | 444124 | 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 | 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 |
| 444135 | 444146 | 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 | 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 |
| 444150 | 444161 | Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 3 | Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 3 |
| 444172 | 444183 | Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 4 | Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 4 |
| **Brachytherapy** | | | |
| 444216 | 444220 | Forfaitair honorarium voor exclusieve curietherapie voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 7 | Honoraires forfaitaires pour curiethérapie exclusive chez un patient qui répond aux critères ou pathologie repris en catégorie 7 |
| 444253 | 444264 | Forfaitair honorarium voor exclusieve curietherapie voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 8 | Honoraires forfaitaires pour curiethérapie exclusive chez un patient qui répond aux critères ou pathologie repris en catégorie 8 |
| **External RT and brachytherapy combined** | | | |
| 444290 | 444301 | Forfaitair honorarium voor curietherapie gecombineerd met uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 5 | Honoraires forfaitaires pour curiethérapie combinée à une série d'irradiations externes chez un patient qui répond aux critères ou pathologie repris en catégorie 5 |
| 444312 | 444323 | 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 | Honoraires forfaitaires pour curiethérapie combinée à une série d'irradiations externes chez un patient qui répond aux critères ou pathologie repris en catégorie 6 |

**Table 50 – ATC codes for chemotherapy**

| ATC code | Substance name |
|---|---|
| **Anthracycline based** | |
| **L01DB01** | DOXORUBICIN |
| **L01DB03** | EPIRUBICIN |
| **L01DB07** | MITOXANTRONE |
| **Taxanes** | |
| **L01CD01** | PACLITAXEL |
| **L01CD02** | DOCETAXEL |
| **Platinum based** | |
| **L01XA01** | CISPLATIN |
| **L01XA02** | CARBOPLATIN |
| **Other** | |
| **L01AA01** | CYCLOPHOSPHAMIDE |
| **L01BA01**<br>**(Excluding CNK codes 0710-566, 1092-857, 1174-481, 1174-499)** | METHOTREXATE |
| **L01BC02**<br>**(Excluding CNK codes 0038-521, 0706-044)** | FLUOROURACIL |
| **L01BC05** | GEMCITABINE |
| **L01BC06** | CAPECITABINE |
| **L01CA04** | VINORELBINE |
| **L01XX41** | ERIBULINE |



**Table 51 – ATC codes for targeted therapy**

| ATC code | Substance name |
|---|---|
| **Anti-HER2 therapy** | |
| **L01XC03** | TRASTUZUMAB |
| **L01XC13** | PERTUZUMAB |
| **L01XC14** | TRASTUZUMAB-EMTANSINE |
| **L01XE07 (L01EH01)*** | LAPATINIB |
| **CDK4/6 inhibitor** | |
| **L01XE33** | PALBOCICLIB |
| **L01XE42** | RIBOCICLIB |
| **L01XE50** | ABEMACICLIB |
| **Other** | |
| **L01XC07** | BEVACIZUMAB |
| **L01XE10**<br>**(Excluding CNK codes : 0779-884, 0779-892, 0779-900, 2156-255, 2156-271, 2156-289, 7715-832, 7715-808, 7715-790, 7715-782, 7715-816, 7715-824)** | EVEROLIMUS |

** L01EH01 is a new ATC-code for lapatinib. L01EH refers to substances inhibiting both HER2 and EGFR indicated for breast cancer, while substances which are multi-targeted without a clear main target are classified in L01EX (reference: WHO ATC/DDD index; https://www.whocc.no/atc_ddd_index/?code=L01EH&showdescription=yes ). Since the RIZIV-INAMI conversion table that is used to convert Belgian CNK codes (present in the IMA-AIM data) to international ATC codes still uses the old L01XE07 code, it is listed here in this table.*

**Table 52 – ATC codes for endocrine therapy**

| ATC code | Substance name |
|---|---|
| **Selective oestrogen receptor modulators** | |
| **L02BA01** | TAMOXIFEN |
| **L02BA02** | TOREMIFENE |
| **L02BA03** | FULVESTRANT |
| **G03XC01** | RALOXIFEN |
| **Aromatase inhibitors** | |
| **L02BG03** | ANASTROZOLE |
| **L02BG04** | LETROZOLE |
| **L02BG06** | EXEMESTANE |
| **GnRH (LHRH) receptor modulators** | |
| **L02AE03** | GOSERELIN |
| **L02AE04** | TRIPTORELIN |
| **Other** | |
| **L02AB01** | MEGESTROL (ACETATE) |

**Table 53 – Non specific codes for ultrasound* used for the calculation of quality indicator on mammography and ultrasound before first treatment**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 459712 | 459723 | Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd inclusief eventueel gebruik van dopplertechnieken | Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou surrénales, rétropéritoine) avec au minimum huit coupes différentes documentées, y compris l'usage éventuel de techniques doppler |
| 459756 | 459760 | Bilateraal kleurenduplexonderzoek van de arteria carotis en van de arteria vertebralis en kleurenduplexonderzoek van de diepliggende thoracale en/of abdominale en/of pelvische bloedvaten en/of bloedvaten van de ledematen | Examen duplex couleur bilatéral des artères carotides et des artères vertébrales et examen duplex couleur des vaisseaux sanguins profonds thoraciques et/ou abdominaux et/ou pelviens et/ou des vaisseaux des membres |
| 459771 | 459782 | Bilateraal kleurenduplexonderzoek van de arteria carotis en van de arteria vertebralis en echografie van één van de volgende streken : schedelinhoud (transfontanellair), thorax, borsten, lever-galblaas, pancreas-milt, nieren-blaas, retroperitoneum, grote abdominale vaten, totale bovenbuik, mannelijk of vrouwelijk bekken | Examen duplex couleur bilatéral des artères carotides et des artères vertébrales et échographie d'une des régions suivantes : contenu du crâne (transfontanellaire), thorax, seins, foie-vésicule biliaire, pancréas-rate, reins-vessie, rétropéritoine, gros vaisseaux abdominaux, abdomen supérieur total, bassin masculin ou féminin |
| 459815 | 459826 | Bilateraal kleurenduplexonderzoek van de arteriële en/of oppervlakkige en diepe veneuze bloedvaten van de ledematen en echografie van één van de volgende streken : schedelinhoud (transfontanellair), thorax, borsten, lever-galblaas, pancreas-milt, nieren-blaas, retroperitoneum, grote abdominale vaten, totale bovenbuik, mannelijk of vrouwelijk bekken | Examen duplex couleur bilatéral des vaisseaux sanguins artériels et/ou veineux (superficiels et profonds) des membres et échographie d'une des régions suivantes : contenu du crâne (transfontanellaire), thorax, seins, foie-vésicule biliaire, pancréas-rate, reins-vessie, rétro-péritoine, gros vaisseaux abdominaux, abdomen supérieur total, bassin masculin ou féminin |
| 460110 | 460121 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen : Van de thorax | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : Du thorax |
| 460154 | 460165 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen : Van het abdomen : Lever en/of galblaas, en/of galwegen | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires |
| 460412 | 460423 | Transthoracale mono- en bidimensionele echografie (met respectievelijk ten minste 3 en 2 coupes en registratie op papier en/of magneetband) | Echographie mono- et bidimensionnelle transthoracale (avec respectivement au moins 3 et 2 coupes et enregistrement sur papier et/ou bande magnétique) |
| 460633 | 460644 | Kleurenduplexonderzoek van de diepliggende thoracale en/of abdominale en/of pelvische bloedvaten | Examen duplex couleur des vaisseaux sanguins profonds, thoraciques et/ou abdominaux et/ou pelviens |

| | | | |
|---|---|---|---|
| 469173 | 469184 | 01/03/2010: Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd | 01/03/2010 : Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou glandes surrénales, rétropéritoine) avec au moins huit coupes documentées différentes |
| 469372 | 469383 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen : Van de thorax | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes : Du thorax |
| 469416 | 469420 | Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen - Van het abdomen : Lever en/of galblaas en/of galwegen | Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes - De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires |
| 469755 | 469766 | Kleurenduplexonderzoek van de diepliggende thoracale en/of abdominale en/of pelvische bloedvaten | Examen duplex couleur des vaisseaux sanguins profonds thoraciques et/ou abdominaux et/ou pelviens |
| 469291 | 469302 | Echografie van het kleine bekken, ongeacht de toegangsweg, ongeacht de sonde, met of zonder kleurenduplexonderzoek van de pelvische bloedvaten, voorbehouden voor de gynaecologen | Echographie du petit bassin, quelle que soit la voie d'accès, quelle que soit la sonde, avec ou sans examen duplex couleur des vaisseaux sanguins pelviens, réservée aux gynécologues |

**: These codes were selected because they were billed at the same date than a mammography and due to the billing rules, we assumed the breast US was not billed*

**Table 54 – Code considered as echo-guided biopsy/puncture for the calculation of quality indicator on mammography and ultrasound before first treatment**

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| 355913 | 355924 | Bijkomend honorarium bij de verstrekkingen nrs. 355353-355364, 355375-355386, 355434-355445, 355456-355460, 355552-355563, 355596-355600, 355611-355622, 355633-355644, 355670-355681, 355714-355725, 355751-355762, 475930-475941, 475952-475963, 475974-475985, 475996-476000, wanneer zij uitgevoerd worden onder echografische of radiologische controle | Supplément aux prestations n° s 355353-355364, 355375-355386, 355434-355445, 355456-355460, 355552-355563, 355596-355600, 355611-355622, 355633-355644, 355670-355681, 355714-355725, 355751-355762, 475930-475941, 475952-475963, 475974-475985, 475996-476000, lorsque celles-ci sont effectuées sous contrôle échographique ou radiologique |

### Table 55 – Nomenclature codes for multidisciplinary team meeting (MDT)

| Outpatient | Inpatient | Dutch Description | French Description |
|---|---|---|---|
| **Basic codes** | | | |
| 350372 | 350383 | 01/02/2003: 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 | 01/02/2003 : 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 |
| | | 01/11/2010: Eerste multidisciplinair oncologisch consult (eerste MOC), geattesteerd door de geneesheer-coördinator | 01/11/2010 : Première consultation oncologique multidisciplinaire (première COM), attestée par le médecin-coordinateur |
| 350394 | 350405 | Deelname aan multidisciplinair oncologisch consult | Participation à la concertation oncologique multidisciplinaire |
| 350416 | 350420 | 01/02/2003: Deelname aan multidisciplinair oncologisch consult door de behandelende arts die geen deel uitmaakt van de ziekenhuisstaf | 01/02/2003: Participation à la concertation oncologique multidisciplinaire par le médecin traitant qui n'est pas membre de l'équipe hospitalière |
| | | 01/11/2010: Deelname aan het multidisciplinair oncologisch consult door een arts die geen deel uitmaakt van de staf van ziekenhuisgeneesheren | 01/11/2010: Participation à la concertation oncologique multidisciplinaire par un médecin qui n'est pas membre de l'équipe de médecins hospitaliers |
| **Follow-up MDT** | | | |
| 350276 | 350280 | Opvolgings-multidisciplinair oncologisch consult (opvolgings-MOC), geattesteerd door de geneesheer-coördinator | Concertation oncologique multidisciplinaire de suivi (COM de suivi), attestée par le médecin-coordinateur |
| 350291 | 350302 | Bijkomend multidisciplinair oncologisch consult (bijkomende MOC) in een ander ziekenhuis dan dit van het eerste MOC, op doorverwijzing, geattesteerd door de geneesheer-coördinator | Concertation oncologique multidisciplinaire supplémentaire (COM supplémentaire) dans un hôpital autre que celui de la première COM, sur renvoi, attestée par le médecin-coordinateur |
| **Additional fees** | | | |
| 350453 | 350464 | 01/03/2010: Bijkomend honorarium bij de verstrekking 350372-350383 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult coördineert | 01/03/2010 : Supplément d'honoraires à la prestation 350372-350383, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci coordonne la consultation oncologique multidisciplinaire |
| | | 01/11/2010: Bijkomend honorarium bij de verstrekking 350372-350383, 350276-350280 en 350291-350302 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de | 01/11/2010 : Supplément d'honoraires à la prestation 350372-350383, 350276-350280 et 350291-350302, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie |

| | | | |
|---|---|---|---|
| | | pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult coördineert | pédiatriques, lorsque celui-ci coordonne la consultation oncologique multidisciplinaire |
| 350475 | 350486 | Bijkomend honorarium bij de verstrekking 350394-350405 of 350416-350420 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult bijwoont | Supplément d'honoraires à la prestation 350394-350405 ou 350416-350420, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci assiste à la consultation oncologique multidisciplinaire |

## Appendix 8.2. Hospital discharge data - MZG – RHM data

For each patient hospitalised in a Belgian hospital (inpatient and day care), hospitals have to send administrative and medical data (more precisely, Minimal Hospital Data; 'Minimale Ziekenhuis Gegevens' / 'Résumé Hospitalier Minimum', abbreviated as MZG – RHM ) to the Federal Ministry of Health, which is defined in the Royal Decree of 27 April 2007.[147] These data contain (among other things) the principal and secondary diagnosis for hospitalisation, the procedures performed during the hospital stay and the campus where this procedure took place. Over 98% of the inpatient hospital stays charged to the health insurance are linked to MZG – RHM .

To obtain the hospital discharge data necessary for campus identification, an authorization was demanded for this study and was approved in December 2021.[53] Thanks to this authorization, linkage with MZG – RHM data with Belgian Cancer Registry database and IMA – AIM data was done on a coded level.

In 2015, the coding system for the medical data in MZG – RHM (diagnoses and procedures) passed from the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM) to the International Classification of Diseases-10th Revision-Clinical Modification (ICD-10-CM). Consequently, The transfer of MZG – RHM data was not mandatory for the transition year 2015, which was included in the study period.

Those hospitals with more than one campus, were contacted one by one and asked to provide campus identification data for procedures performed in 2015. All hospitals agreed to collaborate and to provide this important information though a sFTP-server (secure File Transfer Protocol) to the BCR. A small fee was provided to compensate the hospitals for the additional registration work.

Once the additional MZG – RHM data were obtained (December 2021), exploration of the data revealed that a great deal of hospitals had continued their MZG – RHM data transfer in 2015. Therefore, this information was considered the main data source for campus identification, also for the year 2015. Only in cases where the hospital had not transferred MZG – RHM data, the additional data, directly obtained from the hospitals, were used.

## Appendix 8.3. Identification of the study cohort in the Belgian Cancer Registry database

A total of 63 756 breast tumours, corresponding to 61 149 unique patients, with an incidence date in 2014 - 2018 were identified in the Belgian Cancer Registry (BCR) database. This selection concerned 6 219 in situ breast tumours (9.8%; ICD-10: D05) and 57 537 invasive breast tumours (90.2%; ICD-10: C50), corresponding to 6 123 and 55 603 unique patients respectively (N=577 patients have both an IBC and an in situ).

For the comparison period 2009 - 2013, there were 6 163 in situ breast tumours (10.1%; N=6 077 patients) and 54 886 invasive breast tumours (89.9%; N=53 146 patients).

For the study cohort (diagnosed in 2014 - 2018) as well as for the cohort selected for comparison (diagnosed in 2009 - 2013), it concerned all in situ and IBCs diagnosed in patients with an official residence in Belgium at the time of diagnosis, and for whom a Social Security Identification Number ('IdentificatieNummer Sociale Zekerheid' – 'Numéro d'identification de la sécurité sociale', INSZ-NISS) was available.

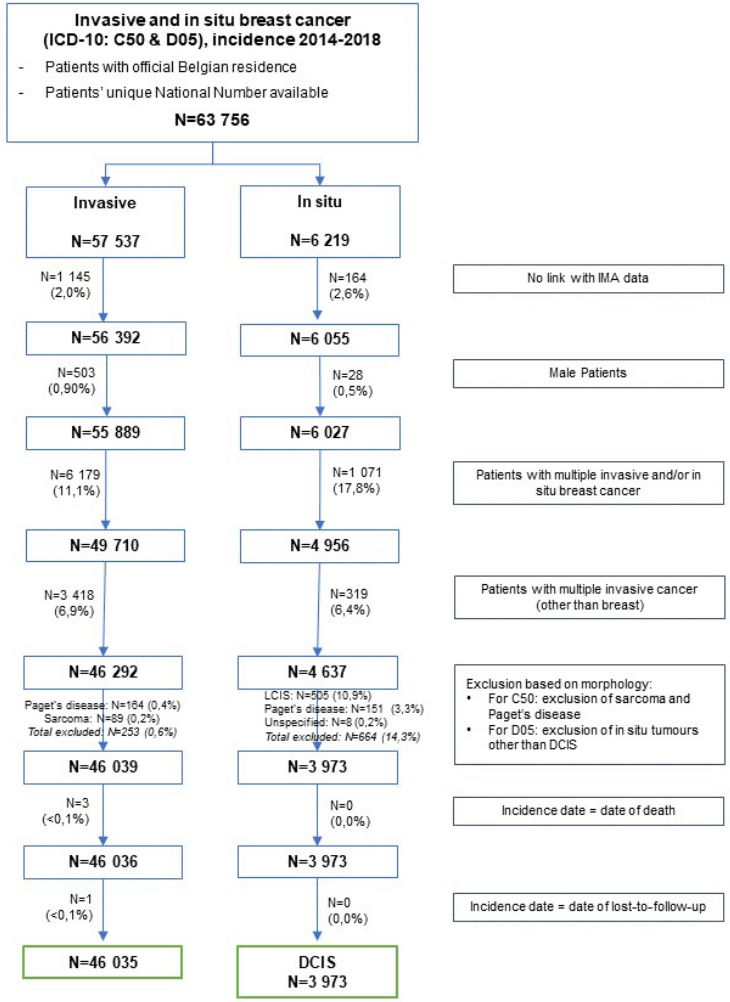
The following **exclusion criteria** were applied on both cohorts to be able to calculate the quality indicators (see Figure 13):

1. Patients for whom **no link** could be made with the **database of the Intermutualistic Agency** ('Intermutualistisch Agentschap' – 'Agence Intermutualiste', IMA – AIM), because quality indicators of care cannot be calculated without information on procedures, medications, etc;
2. Patients with **multiple invasive tumours** (breast or non-breast) and/or with **multiple breast tumours** (invasive or in situ) registered in the BCR database[eee] with a diagnosis in 2004-2018. Since it is not possible to unambiguously link a patient's diagnosis to the procedures in the health insurance data, this exclusion criterion is implemented to ensure that the population included for analyses consists only of patients with one single breast tumour, which increases the probability that the identified medical procedures were performed for that breast tumour;
3. Patients whose incidence date is the same as the date of **death**, as quality of care cannot be evaluated for those patients;
4. Patients who were **lost to follow-up** since the incidence date. These are patients who lived in Belgium at the time of diagnosis, but moved abroad when first checked for their vital status at the Crossroads Bank for Social Security ('Kruispuntbank van de Sociale Zekerheid' – 'Banque Carrefour de la Sécurité Sociale', KSZ-BCSS);
5. **In situ tumours** with an ICD-O-3 morphology **other than ductal carcinoma in situ** (DCIS) and invasive breast tumours that have an ICD-O-3 morphology corresponding with **sarcoma or Paget's disease**, since treatment can be different for these tumour types;
6. **Male patients**, since BC in men is rare and assessing quality of care in these small numbers (about 100 per year), distributed over more than 100 hospitals/campuses, is not feasible (sparse data).

Based on the above exclusion criteria, 13 748 tumours from 11 141 unique patients were excluded from the study (resp. 21.6% and 18.2%).

[eee] Note that the BCR database is considered to be complete for the national level from the year 2004 onwards.

**Figure 13 – Selection of the study cohort - flowchart**




*Source: BCR – KSZ-BCSS – IMA*

## Appendix 8.4. Assignment of each patient to one centre – assignment algorithms

### *Appendix 8.4.1. Assignment algorithm for the hospital of diagnosis*

In order to define the hospital where the diagnosis of BC was performed, the following procedures were taken into account:

- Tissue sampling (i.e. breast biopsy, breast puncture, puncture of the lymph nodes) from three months before to three months after the incidence date;
- Imaging (i.e. diagnostic mammography, breast ultrasound, breast MRI, CT body scan and PET(CT)) from three months before incidence date to three months after incidence or till 1 day before start of treatment. A CT-body that was performed within 14 days of start of radiotherapy was not considered as diagnostic imaging (but preparatory to radiation therapy). Likewise, any imaging performed after the start of any treatment was also not considered performed for diagnostic or staging purposes.

Table 56 provides an overview of the order of priority that was applied for assigning a patient to a hospital of diagnosis, with the respective cumulative percentages of assigned patients with DCIS and IBC per rule.

**Table 56 – Assignment algorithm for the hospital of diagnosis, with cumulative % per rule for patients with DCIS and IBC**

| Assignment rule | DCIS (cumulative %) | IBC (cumulative %) |
|---|---|---|
| All procedures performed in one centre | 77.6 | 79.0 |
| *If the patient underwent procedures in different centres, the following rules applied:* | | |
| Centre of breast biopsy | 95.5 | 93.9 |
| Centre of breast puncture | 96.1 | 94.9 |
| Centre of lymph node puncture | 96.1 | 95.0 |
| Centre of majority of imaging | 96.2 | 95.4 |
| Centre of diagnostic mammography | 96.3 | 95.5 |
| Centre of breast ultrasound | 96.4 | 95.5 |
| Centre of breast MRI | 96.5 | 95.9 |
| Centre of CT body | 96.5 | 96.0 |
| Hospital of diagnosis unknown | 3.5* | 4.0* |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer;*: non-cumulative proportion*
*Source: BCR - IMA*

## *Appendix 8.4.2. Assignment algorithm for the centre of main treatment*

### Allocation at hospital level

To define the centre of main treatment at hospital level, breast surgery (BCS, mastectomy), chemotherapy and radiotherapy performed during the predefined time frames were considered.

The validation study in all Belgian hospitals (see section 4.9) revealed that assignment based on the campus where targeted and/or endocrine therapy were prescribed, resulted in the erroneous assignment of patients to campuses that do not offer BC care (e.g. patients admitted in a geriatric ward who were prescribed endocrine therapy), hence these steps were removed from the assignment algorithms, both at the hospital and at the campus level.

Table 57 provides an overview of the order of priority that was applied for assigning a patient to a hospital of main treatment, with the respective cumulative percentages of assigned patients with DCIS and IBC per rule. Overall, for 0.8% of patients who received oncological treatment no main treatment centre could be identified.

**Table 57 – Assignment algorithm for the hospital of main treatment, with cumulative % per rule for patients with DCIS and IBC**

| Assignment rule | DCIS (cumulative %) | IBC (cumulative %) |
|---|---|---|
| All procedures performed in one centre | 68.6 | 50.9 |
| *If the patient underwent procedures in different centres, the following rules applied:* | | |
| Centre of first breast surgery | 96.6 | 91.2 |
| Centre of chemotherapy | 96.6 | 91.8 |
| Centre of radiotherapy | 96.6 | 91.8 |
| Centre of oncological care programme (if only one centre reported)* | 97.2 | 97.2 |
| Hospital of main treatment unknown | 2.8** | 2.8** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: To be able to assign more patients to a centre of main treatment, the oncological care programme that delivered the case to BCR was considered as the centre of main treatment, on the condition that it was the only oncological care programme that delivered the case to BCR; **: non-cumulative proportion.*
*Source: BCR - IMA*

### Allocation at campus level

In order to define the campus of main treatment, breast surgery (BCS or mastectomy) as well as chemotherapy during the predefined time frames were taken into account. It was impossible to allocate patients at campus level based on radiotherapy because this information is not available in MZG – RHM data.

Table 58 provides an overview of the order of priority that was applied for assigning a patient to a campus of main treatment, with the respective cumulative percentages of assigned patients with DCIS and IBC per rule.

**Table 58 – Assignment algorithm for the campus of main treatment, with cumulative % per rule for patients with DCIS and IBC**

| Assignment rule | DCIS (cumulative %) | IBC (cumulative %) |
|---|---|---|
| At hospital level all treatments took place in the same centre, and allocated at campus level to the campus of surgery | 67.6 | 46.9 |
| At hospital level all treatments took place in the same centre, and allocated at campus level to the campus of chemotherapy | 67.7 | 49.4 |
| At hospital level allocated based on breast surgery, and allocated at campus level to the campus of breast surgery | 95.6 | 89.6 |
| At hospital level allocated based on chemotherapy, and allocated at campus level to the campus of chemotherapy | 95.6 | 90.2 |
| Patients manually allocated to the only existing campus of one hospital* | 96.1 | 92.2 |
| Patients manually allocated to one campus, in case the hospital counts multiple campuses but BC care is only (mainly) offered in one of them* | 96.3 | 93.4 |
| Campus of main treatment unknown | 3.7** | 6.6** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: see section 4.4.3; **: non-cumulative proportion.*
*Source: BCR - IMA*

## *Appendix 8.4.3. Assignment algorithm for the centre of first treatment*

### Allocation at hospital level

For the quality indicators assessing treatment delays and the availability of a mammography and ultrasound before the start of treatment, a separate algorithm was constructed. Breast surgery (BCS or mastectomy), chemotherapy and radiotherapy were taken into account if provided within 1 month before till 9 months after incidence.

Table 59 provides an overview of the order of priority that was applied for assigning a patient to a hospital of first treatment, with the respective cumulative percentages of assigned patients with DCIS and IBC per rule. Overall, for 3.9% of patients who received oncological treatment no first treatment centre could be determined.

**Table 59 – Assignment algorithm for the hospital of first treatment, with cumulative % per rule for patients with DCIS and IBC**

| Assignment rule | DCIS (cumulative %) | IBC (cumulative %) |
|---|---|---|
| Centre of surgery | 95.4 | 74.4 |
| Centre of chemotherapy | 95.5 | 88.2 |
| Centre of radiotherapy | 96.1 | 89.2 |
| Centre of oncological care programme (if monotherapy and only one centre reported)* | 96.7 | 94.1 |
| Hospital of first treatment unknown | 2.8** | 5.9** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: To be able to assign more patients to a centre of first treatment, the oncological care programme that delivered the case to BCR was considered as the centre of first treatment, on the condition that the patient received monotherapy and that it was the only oncological care programme that delivered the case to BCR; **: non-cumulative proportion.*
*Source: BCR - IMA*

### Allocation at campus level

To define the campus of first treatment, breast surgery and chemotherapy were considered when they were performed during the predefined time. Similarly to the allocation at campus level for main treatment, it was impossible to allocate patients based on radiotherapy because this information is not available in MZG – RHM data.

Table 64 provides an overview of the order of priority that was applied for assigning a patient to a campus of first treatment, with the respective cumulative percentages of assigned patients with DCIS and IBC per rule.

**Table 60 – Assignment algorithm for the campus of first treatment, with cumulative % per rule for patients with DCIS and IBC**

| Assignment rule | DCIS (cumulative %) | IBC (cumulative %) |
|---|---|---|
| Centre of surgery | 95.1 | 74.2 |
| Centre of chemotherapy | 95.2 | 87.8 |
| Patients manually allocated to the only existing campus of one hospital* | 95.6 | 89.6 |
| Patients manually allocated to one campus, in case the hospital counts multiple campuses but BC care is only (mainly) offered in one of them* | 95.8 | 90.8 |
| Campus of first treatment unknown | 4.2** | 9.2** |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: see section 4.4.3; **: non-cumulative proportion.*
*Source: BCR - IMA*

## *Appendix 8.4.4. Assignment algorithm for the campus of first surgery*

For the quality indicators on surgery (see section 7.3), benchmarking was performed based on the campus where the first surgical procedure, BCS or mastectomy, within 1 month before till 9 months after incidence was performed.

Based on this rule 99.9% and 99.8% of the patients with DCIS and IBC, respectively, could be assigned to a campus of first surgery. For five patients with DCIS and 65 patients with IBC, the campus of first surgery was unknown.

# APPENDIX 9. PRE-VALIDATION STUDY

## Appendix 9.1. List of participating hospitals

**Brussels-Capital Region:**

- CHU Saint Pierre (Brussels)
- Institut Jules Bordet (Brussels)

**Flemish Region :**

- UZ Antwerpen (Antwerp)
- AZ Delta (Roeselare)
- Mariaziekenhuis Noord-Limburg (Pelt)
- AZ Glorieux (Ronse)

**Walloon Region :**

- CHU UCL Namur Sainte Elisabeth (Namur)
- CHR de la Citadelle (Liège)
- CHR de Mons (Mons)
- CHR de Huy (Huy)

In total, 885 cases were reviewed, with a range of 54 to 118 cases per hospital, of which 504 cases were reviewed by high volume hospitals with a coordinating breast clinic, 191 by medium volume hospitals with a satellite breast clinic and 190 by small volume hospitals who do not have a recognition for BC.

The scope of the study comprises BC diagnoses (DCIS or IBC) from 2014 until 2018, with a comparison period of 2009 till 2013. Therefore, each hospital received a list of BC patients diagnosed in a specific time period of the year 2013 and/or 2017, who were assigned to the hospital based on the diagnosis and/or main treatment algorithm (see section 4.4).The time period and number of patients to be validated depended on the volume of the hospital, the time investment that the hospital could make, the accessibility of the data for certain incidence years and the timing with which they entered the pre-validation phase. This means that the hospitals with the largest volume didn't necessarily validate the highest number of cases. However, diagnoses of the year 2017 were included for each hospital (N=644 cases in total) and six out of ten hospitals evaluated cases (N=241) diagnosed in 2013.

## Appendix 9.2. Information provided to the hospitals for each assigned patient and checks asked to be done

Patient lists contained the following information:

- Patient identifiers: social security number (INSZ – NISS), last name, first name, date of birth, a coded patient ID;
- Patient characteristics: WHO performance status at time of diagnosis;
- Tumour characteristics: incidence date, topography, morphology, behaviour, laterality, grade, clinical stage (T, N and M), pathological stage (T, N and M), anatomic site (ICD-10 code);
- Receptor status results: oestrogen receptor (ER receptor), progesterone receptor (PR receptor), HER2 receptor results obtained via immunohistochemical testing (HER2 IHC), HER2 amplification results obtained via in situ hybridization (HER2 ISH);
- Diagnostic and staging procedures that took place within a defined time frame around the incidence date (see Appendix 8.1.2): breast biopsy, breast puncture, lymph node puncture, diagnostic mammography, breast ultrasound, MRI of the breast, CT body scan, PET-CT scan;
- Information on whether the patient was assigned to the hospital based on the algorithm for hospital of diagnosis or not, and the rule used to assign the patient to the hospital, if applicable;
- Treatment procedures that were performed within a defined time frame around the incidence date or before or after date of first surgery if applicable (see Appendix 8.1.2): first surgery of the primary tumour,

chemotherapy, endocrine therapy, targeted therapy and radiotherapy. For both systemic therapy (chemo-, endocrine, targeted therapy) and radiotherapy information on the following settings was given: before first surgery of the primary tumour, after first surgery of the primary tumour, in the absence of surgery of the primary tumour;

- Information on whether the patient was assigned to the hospital based on the algorithm for hospital of main treatment or not, and the rule used to assign the patient to the hospital[fff], if applicable;
- The primary treatment scheme.

For all diagnostic and therapeutic procedures, the date of the procedure according to IMA – AIM data was provided, as well as a variable indicating whether the procedure was performed in the validating hospital or not.

Hospitals were asked to perform the following tasks:

- Verify the patient list: were these patients diagnosed and/or treated in your hospital for the defined cancer type, or not?
- Add those BC patients diagnosed in the specific period considered for validation who were incorrectly not assigned to the hospital for their diagnostic work-up, main treatment or both;
- Verify the primary treatment scheme: was it correctly defined?
- Provide information on primary treatments given in clinical trial setting
- Verify the receptor status results and provide information on the result that was used to define the patient's treatment (i.e. result determined on biopsy or resection specimen?)

[fff] At this stage of the study, targeted and endocrine therapy were still included in allocation algorithm for main treatment.

# Appendix 9.3. Results

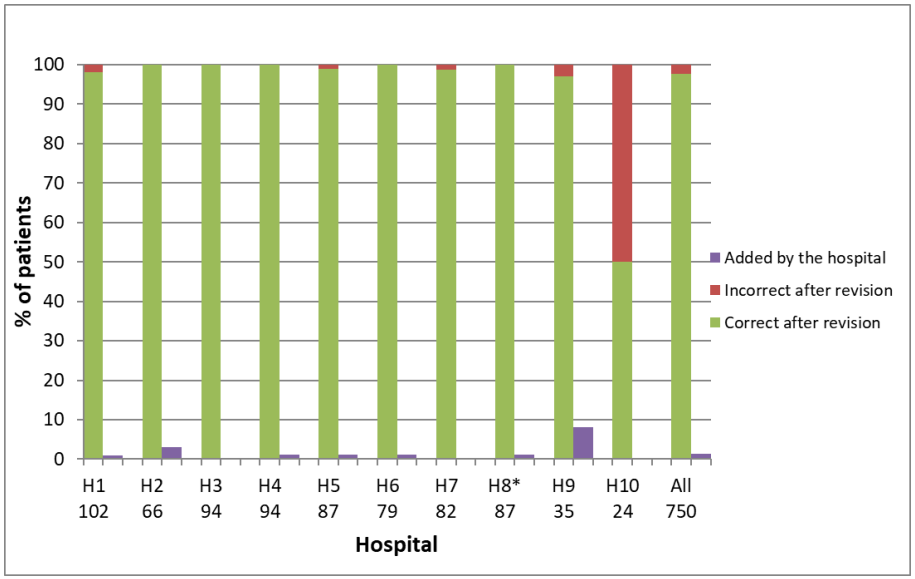
## *Appendix 9.3.1. Validation of the algorithm to assign patients to one hospital of diagnosis*

Each of the ten hospitals received a list of patients assigned to them based on the assignment algorithm for hospital of diagnosis, ranging from 24 to 102 patients per hospital and with a total number of 750 patients for the ten hospitals combined. The hospitals were asked to verify the correctness and completeness of this patient list and add information of patients who were incorrectly not assigned to them by the BCR.

**Results**

Overall, **733 patients (98%) were correctly assigned to the hospital of diagnosis**, with a range of 50% to 100% of patients over the different hospitals (Figure 14). For seventeen patients (2%), from five hospitals, the validating hospitals did not agree that they should be considered as the hospital of diagnosis for these patients. The main reason for disagreeing was that most of the diagnostic work-up was either done in a private centre or in another hospital (that wasn't always registered in the IMA – AIM data (hence categorised as 'centre unknown')), while the validating hospital only performed a minor part of the diagnostic work-up and often on request of the physician who took charge of the diagnostic work-up (16/17 cases). Most of these cases (11/16) were assigned to one hospital, that only had a total of 24 patients assigned to it. In combination with the interchangeable use of nomenclature codes for breast puncture and breast biopsy in this hospital, it resulted in the lowest percentage of correctly assigned cases (50%).

**Figure 14 – Correctness and completeness of the patient lists for hospital of diagnosis (incidence years 2013 and 2017), by hospital**




** Hospital 8 was unable to exhaustively look for additional patients.*

Ten patients (1%) were incorrectly not assigned to the validating hospitals for their diagnostic work-up, because:

- There were administrative errors in the IMA – AIM data (no centre registered, diagnostic procedure not found) or interchangeable use of nomenclature codes (puncture versus biopsy for example) by the hospitals (3/10 cases);
- The incidence date was not correct, which caused the diagnostic procedures to be outside the defined time frame (2/10 cases);
- The breast tumour was accidently found when performing a reductive surgery, which was considered as a biopsy by the validating hospital (2/10 cases);
- The BCR considered the breast tumour as a relapse of an earlier tumour with a diagnosis before 2004, instead of a new diagnosis (1/10 cases). Note that this study only excludes multiple tumours if diagnosed within the period 2004-2018 (see section 4.2). Since the oldest diagnosis dated from before 2004, the most recently diagnosed breast tumour should have been included in the study as a new primary breast tumour and should have been allocated to the validating hospital;
- The first biopsy, on which the allocation was based, had a benign result. Malignancy was shown on a later breast puncture performed by the validating hospital, which is why the patient should have been allocated to the validating hospital (1/10 cases).
- The patient was diagnosed with an ulcerative tumour. Therefore, only an oncological consultation was done at the validating hospital, but there was no further diagnostic work-up performed. So the hospital of diagnosis could not be determined (1/10 cases).

It is important to note that the correct assignment of patients to a hospital of diagnosis heavily depends on the quality and the exhaustiveness of the data that are transferred to the BCR (e.g. incidence date, identification of recurrences, TNM staging). The correct assignment of patients was further hindered by the fact that certain diagnostic procedures were performed in private centres (which are not considered in the assignment algorithm), and by the misuse/suboptimal use of some nomenclature codes, hence factors beyond the control of the study team. These barriers affect certain hospitals more than others.

### *Appendix 9.3.2. Validation of the algorithm to assign patients to one hospital of main treatment*

Each participating hospital also received a list of patients assigned to them based on the assignment algorithm for hospital of main treatment, ranging from 40 to 113 patients per hospital and with a total number of 716 patients for the ten hospitals. Again, the hospitals were asked to verify the correctness and completeness of this patient list and add information of patients who were incorrectly not assigned to them by the BCR.

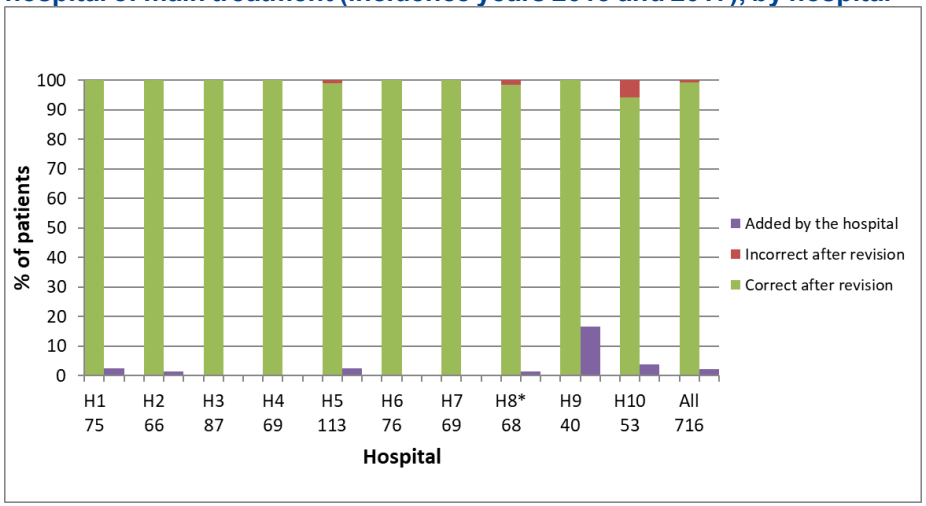
## Results

In sum, **711 patients (99%) were correctly assigned to the hospital of main treatment**, with a range of 94% to 100% of patients over the different hospitals (Figure 15). For five patients (1%), from three hospitals, the validating hospitals did not agree that they should be considered as the hospital of main treatment. Four of these patients were correctly included in the study, but the assignment to the validating hospital was not correct. For the fifth patient, the validating hospital stated that the treatment was given for an axillary relapse, so this case should have been excluded from the study.

Reasons why the allocation to the hospital of main treatment was incorrect according to the validating hospitals for four patients:

- Another hospital performed the first surgery on the primary breast tumour, but this breast surgery was not found in the IMA – AIM data (2/4 cases);
- According to the IMA – AIM data the breast surgery was performed at the validating hospital, but the hospital stated it was performed in another hospital (1/4 cases);
- The validating hospital only gave radiotherapy, while the follow-up and possible other treatments were done in another hospital but could not be retrieved in the IMA – AIM data (no information on other treatments found) (1/4 cases).

**Figure 15 – Correctness and completeness of the patient lists for hospital of main treatment (incidence years 2013 and 2017), by hospital**




** Hospital 8 was unable to exhaustively look for additional patients.*

Seventeen patients were incorrectly not assigned to the validating hospitals for their main treatment, because:

- The breast surgery performed by the validating hospital was not found in the IMA – AIM data (6/17 cases).
- Five patients only received ambulatory endocrine therapy for which no hospital was registered in the IMA – AIM data, and the cases were not registered to the BCR by a unique oncological care programme (4/17 cases) or were wrongly allocated to the centre of radiotherapy (1/17 cases).
- The breast biopsy was considered by the validating hospital as a resection with curative intent, but the procedure was considered as a regular breast biopsy by the BCR (intent of procedure was not available in BCR- IMA – AIM data) (1/17 cases).

- The breast surgery took place at the validating hospital according to the hospital, but another hospital was retrieved from the IMA – AIM data (1/17 cases).
- The BCR received the case from multiple oncological care programs (OCP), while the validating hospital stated it was the only OCP who delivered the case to the BCR (1/17 cases).
- An incorrect incidence date caused the treatment procedures to be outside the defined time frame (1/17 cases).
- BCR considered the breast tumour as a relapse of an earlier tumour with a diagnosis before 2004, instead of a new diagnosis (1/17 cases). Note that this study only excludes multiple tumours if diagnosed within the period 2004-2018 (see section 4.2). Since the oldest diagnosis dated from before 2004, the most recently diagnosed breast tumour should have been included in the study as a new primary breast tumour and should have been allocated to the validating hospital.
- The treatment was given in a clinical trial setting (1/17 cases) and hence not included in the IMA – AIM data.

Misclassifications and missing information in the IMA – AIM data were identified as important barriers to optimally assign each patient to a hospital of main treatment, which might affect certain hospitals more than others. Since endocrine therapy has a low order in the allocation algorithm used to assign a patient to a hospital of main treatment, the impact of not knowing the hospital where ambulatory endocrine therapy was prescribed is very low. Also, patients who only received ambulatory endocrine therapy were still assigned to the correct hospital if the oncological care programme of that hospital was the only source who registered the case to the BCR.

### *Appendix 9.3.3. Other issues raised for the diagnostic procedures that did not impact the allocation algorithms*

The issues raised for the diagnostic procedures that did not have an impact on the diagnostic allocation algorithm can be summarized as follows:

- Inconsistencies between the IMA – AIM data versus the information provided by the validating hospital (77 patients, 9 hospitals):
  - Diagnostic procedures mentioned by the validating hospitals could not be found in the IMA – AIM data (43 patients, 9 hospitals), or the hospital where the procedure took place was unknown or did not correspond to the information in the IMA – AIM data (e.g. procedures performed in private centres) (24 patients, 6 hospitals);
  - There were a couple of days of difference in the date of the diagnostic procedure mentioned by the validating hospital versus the information provided in the IMA – AIM data (10 patients, 4 hospitals);
- Differences in the use and billing of nomenclature codes by the validating hospitals versus how procedures were defined for this study (66 patients, 7 hospitals), for example:
  - Nomenclature codes for breast biopsy, breast puncture and/or lymph node puncture were used interchangeably by the validating hospitals (41 patients, 6 hospitals);
  - A nomenclature code for SPECT (442514-442525, see Appendix 1.1) was billed instead of a code for CT body (19 patients, 2 hospitals);
- Differences in the selected diagnostic procedures (biopsy, puncture, imaging) for this study, because the diagnostic procedure mentioned by the validation hospital took place outside the defined time frame or was not the procedure closest to incidence date (27 patients, 5 hospitals);
- Procedures that were not performed for the diagnosis of the primary breast tumour (8 patients, 5 hospitals). For example:

- Malignancy was not shown on the procedure that was closest to incidence date. A subsequent procedure confirmed the presence of a breast tumour;
- The procedure was performed for another reason (e.g. CT body for preparation of radiotherapy).

Other discrepancies were noted for a limited number of patients (minimum 1, maximum 10), but they had no impact on the allocation of patients to a hospital of diagnosis, nor did they provide new insights for the methodology applied for this study.

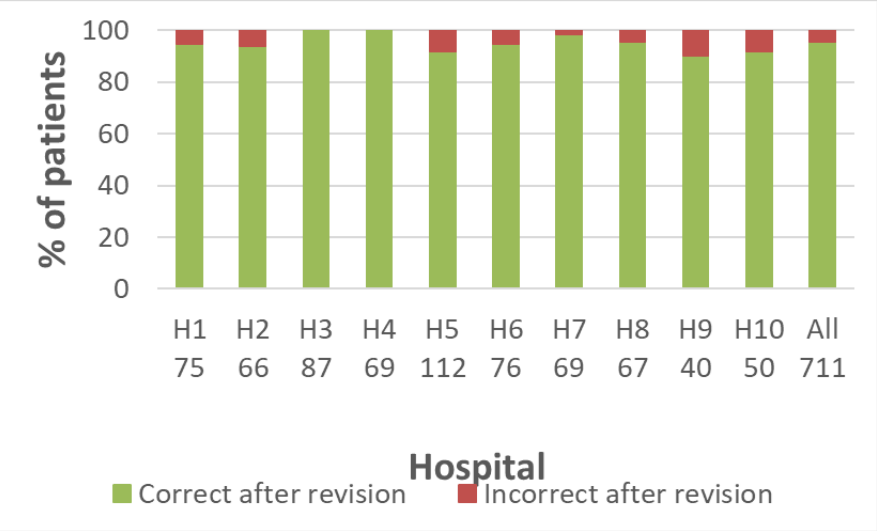
### *Appendix 9.3.4. Validation of the primary treatment scheme and the impact of treatments given in clinical trial setting*

The patient lists sent to the ten validating hospitals provided information on the primary treatment scheme that was defined based on the treatment procedures and time frames discussed in section 4.3. The hospitals were asked to focus on the 1st line treatment (i.e. no treatment for disease progression or recurrences) when validating these treatment schemes and to provide supplementary information on treatment procedures given in clinical trial setting if applicable. The results shown in this section only apply to the 711 patients for whom the validating hospitals agreed to be the hospital of main treatment.

**Results**

Overall, **the primary treatment scheme was correctly defined for 678 patients (95%)**, with a range of 90% to 100% over the different hospitals (Figure 16). For thirty-three patients (5%), from eight hospitals, the validating hospitals did not agree on the treatment scheme. The main reason for disagreeing was that adjuvant endocrine therapy was started beyond the defined time window (i.e. more than nine months after the first breast surgery; 10 patients, 6 hospitals).

**Figure 16 – Correctness of the primary treatment schemes, by hospital**




The validating hospitals disagreed with the treatment scheme that was provided for 33 patients, because:

- Adjuvant endocrine therapy was started more than nine months after the first breast surgery (outside the defined time frame) but was still part of the primary treatment according to the validating hospital (8/33 patients);
- The treatment procedure (e.g. systemic therapy, radiotherapy) mentioned by the validating hospital could not be found in the IMA – AIM data, because the treatment was given abroad (1/33 patients), and for 8/33 patients the reason of discrepancy with the IMA – AIM data was unknown;
- The treatment, or a part of it, was given in clinical trial setting, which is why the information was not available in the IMA – AIM data (6/33 patients);

- The validating hospitals found no evidence of systemic therapy (e.g. endocrine therapy, chemotherapy) that was retrieved from the IMA – AIM data (4/33 patients);
- The treatment was not intended as primary treatment for the breast tumour (e.g. chemotherapy was given as second line treatment for metastatic BC, radiotherapy was given for a recurrence; 2/33 patients);
- Ambulatory endocrine therapy started earlier according to the validation hospital and should have been considered as primary treatment (i.e. within the defined time frame; 1/33 patients);
- For three patients, more than one of the reasons mentioned above applied.

Other major remarks reported by the hospitals for treatment procedures were:

- The hospital where the ambulatory endocrine therapy was prescribed couldn't be retrieved from the IMA – AIM data. Six hospitals noted that the ambulatory endocrine therapy should have been considered as administered by them, since they prescribed it (169 patients, 6 hospitals), while one hospital just confirmed it was taken ambulatory (32 patients). Note that it was not commented on for all patients listed with ambulatory endocrine therapy, since it wasn't explicitly asked for this pre-validation phase.
- A discrepancy between the start date of the treatment found in the IMA – AIM data versus the information available to the hospital.
    - For systemic therapy this was mentioned by seven hospitals for a total of fifty-nine patients. For fifty-six patients this was due to a delay between the prescription date of ambulatory endocrine therapy and the date of pick up at the pharmacy. Note that the validating hospitals often consider the prescription date as the start date of ambulatory endocrine therapy, while the prestation date present in the IMA – AIM data is the date on which the patient purchased the endocrine therapy at the pharmacy. Patients might also have been offered a sample during consultation, which causes a delay in the first purchase of the product and the first appearance in the IMA – AIM data. However, according to the experts consulted for this study, this is a rare practice.
    - For radiotherapy this was reported by six hospitals for a total of fifty-two patients. Mostly this was due to an incorrect billing of the radiotherapy series, i.e. not in line with the RIZIV – INAMI instructions.
    - For surgery, this was noted by three hospitals for three patients and this was confined to one or two days of difference.

Other discrepancies were noted for a limited number of patients (minimum 1, maximum 3), but they had no impact on the allocation of patients to a hospital of main treatment nor on the treatment scheme, nor did they provide new insights for the methodology applied for this study.

A total of **17 patients (2%) received (part of) their treatment in a clinical trial setting**. Although procedures performed in a clinical trial setting are normally not registered in the IMA – AIM data, for only six patients (<1%) this led to an incorrect definition of the primary treatment scheme.

Since the main reason for disagreeing with the treatment scheme was the rather short time frame for adjuvant endocrine therapy, it was explored whether a larger time frame should be applied. When enlarging the time frame for adjuvant endocrine therapy to twelve months, the gain was only 1 percentage point (from 78% of operated patients having adjuvant endocrine therapy within 9 months after first breast surgery to 79% when the time frame was expanded to 12 months). Since the risk of taking into account endocrine therapies that are not meant as primary treatment for the breast tumour becomes larger when expanding the time frame, it was decided to keep the time frame for adjuvant endocrine therapy on a maximum of 9 months after the first breast surgery.

## *Appendix 9.3.5. Validation of automatically extracted receptor status*

Since oestrogen, progesterone and HER2 receptor status information is not transferred to the BCR in a standardised format, this information is automatically extracted by using machine learning algorithms at the BCR. In order to evaluate the correctness and completeness of these automatically generated data, the validating hospitals were asked to compare these results with the information available in their medical files.

**Results**

The oestrogen and progesterone receptor status information was validated for a total of 882 patients (DCIS and IBC combined), while the results for the HER2 receptor were only presented for the 809 patients diagnosed with IBC, since HER2 testing is not relevant for DCIS tumours.

Figure 17 to Figure 20 present the correctness and completeness of the oestrogen, progesterone and HER2 receptor status results respectively. Based on the comments received by the validating hospitals, the patients listed were categorized into three groups:

- Group 1: Patients for whom the receptor status result was concordant (green bar);
- Group 2: Patients for whom a receptor status result known to BCR was changed or could not be confirmed (unknown) by the validating hospital (i.e. discordant cases; brown bar);
- Group 3: Patients for whom the receptor status result was unknown to BCR but was completed by the validating hospital (purple bar).

The percentage of concordant and discordant cases is calculated on the total for groups 1 and 2, while the percentage of cases completed by the validating hospitals is calculated on the total for groups 1, 2 and 3.

For the HER2 receptor, two algorithms were constructed, one for the HER2 result obtained via immunohistochemical testing and one for the HER2 amplification result obtained via in situ hybridisation.

**Figure 17 – Correctness of oestrogen receptor status result, by hospital**

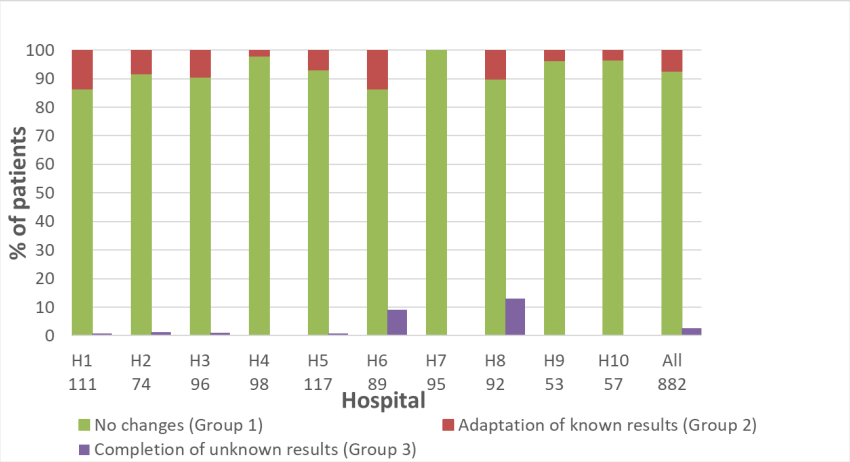



**Figure 18 – Correctness of progesterone receptor status result, by hospital**

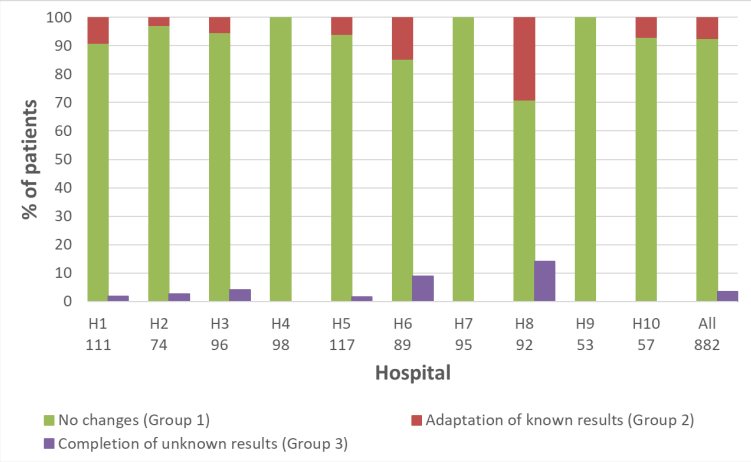



**Figure 19 – Correctness of HER2 receptor status result obtained via immunohistochemical testing, by hospital**

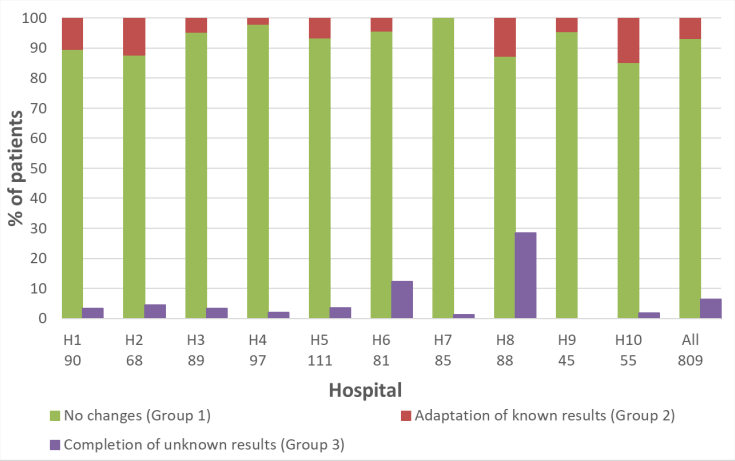
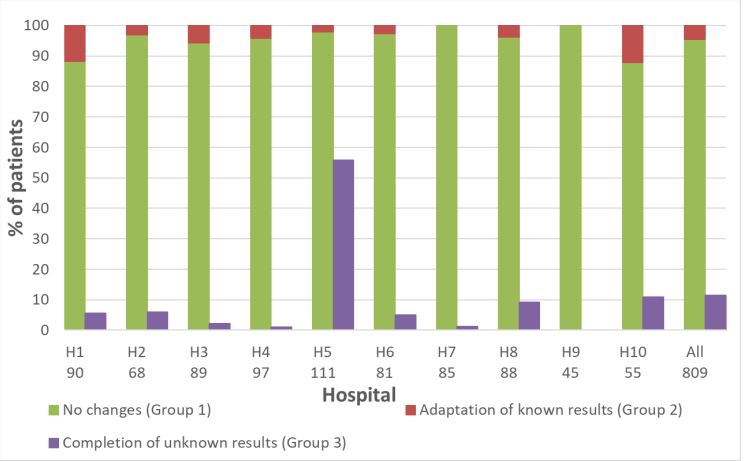



**Figure 20 – Correctness of HER2 receptor status result obtained via gene amplification through in situ hybridization, by hospital**



The overall **oestrogen (ER) receptor status** result was **concordant** with the hospital information for 795 cases (**93%**; group 1), with a range of 86% to 100% over the different hospitals (Figure 17). In total, 63 cases (7%) were considered as discordant (group 2). For a majority of discordant cases (44/63), a positive ER result was changed to negative, followed by 11/63 cases for which the validating hospitals changed the result to unknown, and 8/63 cases for which the result was changed from negative to positive. For 24 cases (3%; group 3), the unknown ER result was completed by the validating hospitals, with a range of 0% to 14%.

For the **progesterone (PR) receptor status**, there was an overall **concordance** for 788 cases (**93%**; group 1), with a range of 71% to 100% (Figure 18). A total of 63 cases (7%) was considered as discordant (group 2), for which the majority (32/63) was changed from a positive to a negative PR result, followed by 23/63 with a change from a negative to a positive result and 8/63 cases for which the validating hospitals indicated that the result was unknown. For 31 cases (4%; group 3), the unknown PR result was completed by the validating hospitals, with a range of 0% to 14%.

The overall **HER2 receptor status** result obtained via immunohistochemical testing (**HER2 IHC**) showed a **concordance** for 706 cases (**93%**) (group 1), with a range of 87% to 100% over the different hospitals (Figure 19). In total, 51 cases (7%) were considered as discordant (group 2). For 19/51 cases, the result was changed from negative to equivocal, followed by 11/51 cases for which the hospital stated that the result was unknown. Other changes were: from positive to negative (7/51 cases), from negative to positive (5/51 cases), from equivocal to positive (5/51 cases), from positive to equivocal (2/51 cases) and from equivocal to negative (2/51 cases). For 52 cases (6%; group 3) the unknown HER2 IHC result was completed by the validating hospitals, with a range of 0% to 28%.

For the **HER2 receptor status** result obtained via gene amplification through in situ hybridization (**HER2 ISH**), there was an overall concordance for 683 cases (**95%**; group 1), with a range of 88% to 100% over the different hospitals (Figure 20). A total of 33 cases (5%) had a discordance between the result retrieved by BCR and the information available to the hospitals (group 2). For 11/33 cases the result was changed to unknown by the validating hospitals, followed by a change from positive to negative (8/33), from negative to positive (8/33), equivocal to negative (3/33), equivocal to positive (2/33) and from negative to equivocal (1/33). For 93 cases (12%; group 3), the unknown HER2 ISH result was completed by the validating hospitals, with a range of 0% to 56%.

### Box 11 – Data flows of pathology reports to the BCR

The BCR receives the following data from the laboratories for anatomical pathology:

For the 'classical registration': Services for pathological anatomy and hospitals with an oncological care programme are legally obliged to cooperate with cancer registration. The anatomical pathologists supply BCR with a structured file containing histological information on all encoded cancer diagnoses and a separate file with the written reports containing the conclusion (i.e. the pathology protocols). Combined with the information provided by the hospitals (i.e. the standard cancer registration form or the follow-up form), these data form the BCR's standard cancer registration database, are used for publications on incidence, prevalence, mortality and survival rate, as well as for different national and international collaborations and studies (often after completion with IMA – AIM data).

For the cytohistopathological (CHP) database: All laboratories for anatomical pathology in Belgium are legally obliged since 2010 to transmit the encoded test results of all breast, cervical and colorectal samples (i.e. for cancer as well as non-cancer cases) to the BCR in order to create a central CHP database. The selection done by the laboratories is based on the organ code. For all Belgian patients for whom a breast specimen, colorectal specimen or cervical smear/biopsy is available, all encoded diagnoses (negative results, benign and [pre]malignant lesions) and pathology reports are transferred to the BCR. More precisely for breast, the structured file with breast samples includes patient data (INSZ/NISS, sex, date of birth, postal code, country code), specimen reference and sampling date, RIZIV-INAMI number of the applicant, organ code/topography, lesion code/morphology/behaviour, and laterality of the breast sample. Differentiation grade, pT, pN, pM is provided for the 'classical registration' but not for the CHP database. After completion with IMA – AIM reimbursement data of medical acts that are relevant for the

detection, monitoring and treatment of breast, colorectal and cervical cancer the data allow BCR to evaluate and help organize the cancer screening programs.

# APPENDIX 10. VALIDATION STUDY

This chapter gives an overview on conclusions made after a validation phase performed in all Belgian hospitals by the Belgian Cancer Registry (BCR). Each hospital received a validation report from the BCR, containing the description of the number of patients included in the study for their hospital/campuses (=volume) together with the hospital's/campuses' results for the selected quality and descriptive indicators for processes of care.

Two different volumes were described in the validation report: 'total volume' and the 'volume of the study population'. 'Total volume' corresponds to the total number of breast tumours (invasive and in situ, regardless of other previous tumours) for patients allocated to their hospital/campus during the incidence period 2014 - 2018. The 'volume of the study population' is a sub-selection of the total volume, where patients having multiple tumours (of the breast or any other organ) during the period 2004-2018, male patients, patients diagnosed with a sarcoma or a Paget's disease were excluded. It corresponds to a homogenous group of patients included in the quality indicators calculation.

As mentioned in the methodological section, different allocation algorithms are used and described in the report: allocation based on diagnosis, on main treatment, on first treatment and on first surgery (see Appendix 8.4). Allocation based on main treatment, first treatment and first surgery were performed at both hospital and campus level. During the validation phase, hospitals were asked to verify whether they agreed with the volumes as described in their report and with the distribution of patients in the different campuses, when applicable.

Next to that, results of 15 different process indicators were described, at hospital or at campus level. Hospitals having issues with their results received a patient list from the BCR to enhance an in depth (qualitative) analysis of the possible problems.

During this validation phase, no benchmarking was provided to the hospitals; the outcome indicators were not assessed.

# Appendix 10.1. Validation of process indicator results

## *Appendix 10.1.1. Proportion of women with IBC who received mammography and breast sonography before any treatment*

**Comments and suggestions:**

The general comment of almost all hospitals was that a mammography and a breast ultrasound is always performed before any treatment. Based on additional investigation for patients where our information did not correspond to what was found in the patient's medical file, billing rules showed to be an important limitation factor for this indicator: (1) only one ultrasound can be billed per day, and (2) as the fee for breast ultrasound is often lower, the more expensive ultrasound is billed and as a result the information on the ultrasound of the breast is missing in the database. For a limited number of cases, an echo-guided biopsy/puncture, which was not taken into account as an ultrasound of the breast, was performed. One hospital also mentioned that the time frame should be enlarged to 6 months before incidence date (instead of 3 months in the current definition). This suggestion was not taken into account, to avoid including imaging not related to the BC.

Finally, some hospitals suggested to exclude cases with cT4b/c (ulceration) as well as cT4d from this analysis as in these cases a mammography is not indicated.

**Decision:**

Patients fulfilled this quality indicator in case the following was invoiced:

- Mammography AND a breast ultrasound (excluding echo-guided biopsy) within three months before incidence and one day before the start of oncological treatment

OR

- Mammography within three months before incidence and one day before the start of oncological treatment AND one of the non-specific nomenclature codes for US Table 53) on the same day as the mammography

OR

- [Breast puncture OR breast biopsy] AND the additional fee when punctures are performed under US or radiological guidance (nomenclature code 355913-355924) were invoiced together with a mammography on the same day; it is considered that these patients had mammography & US (i.e. the US was not billed since the puncture was taken under US guidance)

OR

- [Breast puncture OR breast biopsy] AND additional fee when punctures are performed under US or radiological guidance (nomenclature code 355913-355924) are invoiced together with a breast or non-specific US on the same day; it is considered that these patients had mammography & US (i.e. the mammography was not billed since the puncture was taken under mammography guidance).

Two additional sensitivity analyses are provided, one excluding cT4b/c/d cases, and one, based on the clinical experts' comments, excluding patients younger than 30 years, for whom a mammography is in general not advised.

## *Appendix 10.1.2. Proportion of women with IBC with histological and/or cytological assessment before any treatment*

**Comments and suggestions:**

A suggestion was given to exclude cases for whom the date of incidence is equal to the date of first treatment (especially for surgery), because sometimes the malignancy is discovered during a surgery made for another reason ('accidental finding'). This suggestion was not implemented in order to avoid excluding patients with suspected BC undergoing immediately surgery. To take into account possible accidental findings where no preceding histological or cytological assessment was performed, the target was deliberately set at 90% and not at 100%.

**Decision:**

No change for this QI based on the validation phase.

### *Appendix 10.1.3. Proportion of women with IBC in whom HER2 status and/or oestrogen receptor (ER) and/or progesterone receptor (PR) status were assessed before any systemic treatment*

**Comments and suggestions:**

For one patient, there was no billing of a test in the health insurance data while it actually had been performed according to the hospital (administrative errors).

**Decision:**

No change for this QI based on the validation phase.

### *Appendix 10.1.4. Proportion of women with BC discussed during a multidisciplinary team (MDT) meeting*

**Comments and suggestions:**

The major concern on this quality indicator was that it is not reflecting the process of care, but rather the billing of the MDT. Patients are often discussed multiple times at a MDT, within and after two months after incidence date, but billing rules make it impossible to bill them all. According to some hospitals, the time frame of two months after incidence date is not long enough to capture the date of the MDT that is billed, which may be delayed until the final treatment plan is decided, e.g. the MDT for patients treated with neoadjuvant therapy may be delayed until after surgery, more than 2 months after incidence date. Billing rules should therefore clearly be mentioned in the description of this indicator.

Also, according to some hospitals, calculating this indicator on the centre of diagnosis is not always fair because the diagnostic centre can be the centre where only a biopsy (on demand of an external physician) is performed and the treatment plan has been worked out at another hospital. In that case, diagnostic centre is not responsible for discussion at the MDT. A suggestion given by one hospital was also to remove patients deceased within 2 months after incidence date from the denominator because they are not 'at risk' for 2 months.

**Decision:**

Given the limitations of the data and billing rules, the indicator was elaborated as a 'descriptive indicator'. It means no target and no funnel plot will be given (only a scatter plot).

A sensitivity analysis is provided excluding patients deceased within 2 months after incidence date.

### *Appendix 10.1.5. Proportion of women with BC for whom the cTNM stage is reported to the Belgian Cancer Registry (BCR)*

**Comments and suggestions:**

It was suggested that the definition of the QI should clearly indicate that the reported TNM should be valid (meaning that, e.g. cTxNxMx is invalid). Some hospitals also mentioned that the TNM completeness improved over time and should be better for more recent incidence years.

**Decision:**

The title of this QI clearly indicates that TNM should be 'valid'.

### *Appendix 10.1.6. Proportion of women with BC who had surgery for whom the (y)pTNM stage is reported to the Belgian Cancer Registry (BCR)*

**Comments and suggestions:**

Reporting of ypTNM for the considered incidence years is not always captured in the dataset by BCR, due to the reporting method used by some hospitals in the past. Actually, ypTNM should have been reported via the same field as the pTNM, while some hospitals reported the ypTNM via a general comments field.

**Decision:**

We were unable to retrieve this information during the study time. Registration methods for ypTNM have already been changed by the BCR (separate, specific field for registration of the ypTNM) so that this issue is resolved for future projects.

### *Appendix 10.1.7. Proportion of women with IBC for whom the time interval between the incidence date and the date of first treatment was ≤ 6 weeks*

**Comments and suggestions:**

Endocrine therapy is sometimes found in medical files while we were unable to identify it in the health insurance data. In many of these cases, the therapy was part of a clinical trial and inherently not available in the health insurance data. Also, even if the impact of treatment given in the context of a clinical trial on treatment schemes was estimated to less than 1% during the pre-validation phase, the start date of treatment can be influenced more often by clinical trials.

Some patients had axillary lymph node dissection (ALND) within 6 weeks after incidence date. This procedure was also found in the health insurance database, but it could not be taken into account as a treatment with curative intent for the primary tumour.

Finally, some hospitals had issues with the fact that this QI is calculated on the centre of diagnosis: they don't agree that both centre of diagnosis and centre of first treatment share the responsibility of the time to initiate treatment.

**Decision:**

No change for this QI based on the validation phase.

### *Appendix 10.1.8. Proportion of women with IBC and clinically negative axilla who undergo sentinel lymph-node biopsy (SLNB) only (excluding patients who received neoadjuvant systemic treatment)*

**Comments and suggestions:**

According to the feedback of the hospitals, the result should be nearly 100%. The reason why most hospitals didn't reach 100% is due to the nomenclature codes to define SLNB and ALND which are not specific enough. As an example, the nomenclature code: 227813- 227824 ('*Borstsparende volledige resectie van een bewezen kwaadaardig borstletsel met macroscopisch voldoende veiligheidsmarge, en resectie van schildwachtlymfeklier, die wanneer tumoraal ingenomen bij peroperatoir anatomo-pathologisch onderzoek gevolgd wordt door een okseluitruiming' / '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 tumoral démontré à l'examen anatomo-pathologique peropératoire est suivi d'un évidement ganglionnaire de l'aisselle'*). As mentioned in the description, this code refers to a breast conserving surgery during which a sentinel lymph node biopsy/resection (SLNB) is performed. An axillary lymph node dissection (ALND) is then performed in case the SLNB was positive. As we don't have the result of SLNB (positive or negative), we don't know if the ALND took place or not. In our analyses, we considered that ALND was performed when those nomenclature codes were billed. It means that the proportion of ALND is overestimated in our analyses.

According to some hospitals, we also need to add another inclusion criteria and limit the selection to patients with cN0 and pN0.

Finally, a suggestion is also made to limit the results to incidence years 2017-2018 because of a study published in 2017 (ACOSOG Z0011),[120, 124] not supporting the idea of ALND anymore for women with T1 or T2 invasive primary BC, no palpable axillary adenopathy, and 1 or 2 sentinel lymph nodes containing metastases. This conclusion was made on a population-based study on 10-years outcome.

**Decisions:**

Based on exploratory analyses, it was decided to keep this QI, but elaborate it as a 'descriptive indicator'. It means no target is provided, and a scatter plot is provided, instead of a funnel plot. Indeed, the nomenclature codes used to define ALND is not specific enough and make a correct patient selection impossible.

For the calculation of the indicator all incidence years are included and patient selection is restricted to cN0 patients, but a sensitivity analysis is performed where the indicator is restricted to patients with cN0 and pN0. Changes over the years can be deduced from the sub-analyses that were provided.

### *Appendix 10.1.9. Proportion of women with DCIS who do not undergo axillary lymph node dissection (ALND) as first axillary surgery*

As the same (non-specific) nomenclature codes are used, the same decisions apply.

### *Appendix 10.1.10. Proportion of women with DCIS who received just one operation (excluding reconstruction)*

**Comments and suggestions:**

A distinction should be made between the type of first surgery (breast conserving surgery or mastectomy), and the result for this indicator should be interpreted into the light of the number of patients undergoing breast conserving surgery versus mastectomy.

Surgeries leading to accidental findings should not be considered in the definition of surgery, as, in this case, the likelihood for a follow up surgery is much higher.

Also, if 2 mastectomies are performed, it is possible that the second surgery is a preventive resection of the other breast: laterality is not known in the health insurance data.

**Decisions:**

The main indicator is not changed, i.e. both BCS and mastectomy are considered together, but excluding surgeries leading to accidental finding, because this is the method used in international literature. Separate results will also be provided by type of first surgery.

For patients having a second surgery, the type of this second surgery is also mentioned.

In addition, the ratio BCS/mastectomy is also be provided in a graph, in relation to hospitals' QI result.

### *Appendix 10.1.11. Proportion of women with IBC (M0) who received a single (breast) operation for the primary tumour (excluding reconstruction)*

Comments, suggestions and decisions were the same as for the previous quality indicator.

### *Appendix 10.1.12. Proportion of women < 70 years old with IBC (M0) who started radiotherapy within 9 months after breast conserving surgery*

**Comments and suggestions:**

For some patients the start date of radiotherapy was not correct. As the start date of radiotherapy is estimate at BCR based on an algorithm which takes simulation date and several other parameters into account, we could not improve our methodology in the context of this study.

No further comments were raised on this quality indicator.

**Decision:**

No change for this QI based on the validation phase.

### *Appendix 10.1.13. Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy and/or endocrine therapy*

Hospitals agreed that this indicator was elaborated as a 'descriptive indicator', i.e. without target, and with a scatter plot instead of a funnel plot.

### *Appendix 10.1.14. Proportion of women <70 years old with metastatic BC who received systemic therapy*

Hospitals agreed that this indicator was elaborated as a 'descriptive indicator', i.e. without target, and with a scatter plot instead of a funnel plot.

## Appendix 10.2. Validation of volume and centre allocation

Several comments were received during the validation phase concerning the allocation algorithms for centre of diagnosis, centre of main treatment and centre of first treatment.

**Centre of diagnosis:**

As mentioned in Appendix 8.4.1, the procedures taken into account to define the centre of diagnosis are breast biopsy, breast puncture, lymph node puncture, and some imaging procedures. During the validation phase, we noticed a billing issue for breast biopsy. When a needle is used for the biopsy, there should be a billing record for the procedure and for the needle. For some hospitals the identification of the hospital was only reported in the billing record for the needle, while only the billing record for the procedure itself was taken into account. It was decided to incorporate the identification of the centre from the billing record for the needle when the centre was unknown in the billing record for the procedure, only if both biopsy procedure and material are billed at the same date (see Table 27)

**Centre of main treatment and centre of first treatment:**

Based on comments received from hospitals, it was decided to remove targeted therapy and endocrine therapy from the algorithms centre of main treatment and centre of first treatment. Those treatments can be given during a hospitalisation stay which is not related to the BC, while it was prescribed in another hospital/campus. In this situation, the hospital/campus where targeted or endocrine therapy was administered to the patient would incorrectly be identified as being the centre of main treatment/first treatment.

# APPENDIX 11. DESCRIPTION OF THE STUDY COHORT

## Appendix 11.1. Patient characteristics

**Table 61 – Patient characteristics at diagnosis of patients with DCIS, by recognition status of the campus of main treatment**

| | Total (N=3 973) | | Coordinating breast clinics (N=2 850) | | Satellite breast clinics (N=188) | | Campus not recognised for BC (N=786) | | Campus unknown (N=149) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Age** | | | | | | | | | | |
| Mean, SD (years) | 58.6 (11.6) | | 58.2 (11.4) | | 58.7 (11.4) | | 59.2 (11.5) | | 62.1 (15.8) | |
| Median, Q1-Q3 (years) | 58.0 (50.0-66.0) | | 58.0 (50.0-66.0) | | 58.0 (51.0-66.0) | | 59.0 (51.0-67.0) | | 59.0 (49.0-72.0) | |
| <40 years | 164 | 4.1 | 119 | 4.2 | 7 | 3.7 | 33 | 4.2 | 5 | 3.4 |
| 40-49 years | 716 | 18.0 | 534 | 18.7 | 31 | 16.5 | 118 | 15.0 | 33 | 22.1 |
| 50-59 years | 1 238 | 31.2 | 892 | 31.3 | 64 | 34.0 | 245 | 31.2 | 37 | 24.8 |
| 60-69 years | 1 194 | 30.1 | 857 | 30.1 | 55 | 29.3 | 253 | 32.2 | 29 | 19.5 |
| 70-79 years | 481 | 12.1 | 339 | 11.9 | 23 | 12.2 | 100 | 12.7 | 19 | 12.8 |
| 80+ years | 180 | 4.5 | 109 | 3.8 | 8 | 4.3 | 37 | 4.7 | 26 | 17.4 |
| **Laterality** | | | | | | | | | | |
| Left | 2 093 | 52.7 | 1 516 | 53.2 | 97 | 51.6 | 405 | 51.5 | 75 | 50.3 |
| Right | 1 868 | 47.0 | 1 329 | 46.6 | 91 | 48.4 | 378 | 48.1 | 70 | 47.0 |
| Unknown | 12 | 0.3 | 5 | 0.2 | 0 | 0.0 | 3 | 0.4 | 4 | 2.7 |
| **WHO performance status at time of diagnosis** | | | | | | | | | | |
| 0 – Asymptomatic | 2 809 | 70.7 | 2 097 | 73.6 | 113 | 60.1 | 526 | 66.9 | 73 | 49.0 |
| 1 – Symptomatic but completely ambulatory | 711 | 17.9 | 477 | 16.7 | 55 | 29.3 | 157 | 20.0 | 22 | 14.8 |

| | Total (N=3 973) | | Coordinating breast clinics (N=2 850) | | Satellite breast clinics (N=188) | | Campus not recognised for BC (N=786) | | Campus unknown (N=149) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| 2 – Symptomatic, up and about more than 50% of waking hours | 19 | 0.5 | 9 | 0.3 | 2 | 1.1 | 6 | 0.8 | 2 | 1.3 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 8 | 0.2 | 0 | 0.0 | 0 | 0.0 | 3 | 0.4 | 5 | 3.4 |
| 4 – Completely disabled; totally confined to bed or chair | 9 | 0.2 | 8 | 0.3 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| Missing | 417 | 10.5 | 259 | 9.1 | 18 | 9.6 | 93 | 11.8 | 47 | 31.5 |
| **Number of comorbidities** | | | | | | | | | | |
| 0 | 2 442 | 61.5 | 1 788 | 62.7 | 114 | 60.6 | 463 | 58.9 | 77 | 51.7 |
| 1 | 1 207 | 30.4 | 849 | 29.8 | 58 | 30.9 | 250 | 31.8 | 50 | 33.6 |
| 2 | 301 | 7.6 | 197 | 6.9 | 16 | 8.5 | 67 | 8.5 | 21 | 14.1 |
| 3 | 23 | 0.6 | 16 | 0.6 | 0 | 0.0 | 6 | 0.8 | 1 | 0.7 |
| **Type of comorbidities** | | | | | | | | | | |
| Cardiovascular disease | 1 335 | 33.6 | 929 | 32.6 | 63 | 33.5 | 279 | 35.5 | 64 | 43.0 |
| Respiratory diseases | 263 | 6.6 | 177 | 6.2 | 14 | 7.4 | 51 | 6.5 | 21 | 14.1 |
| Diabetes | 280 | 7.0 | 185 | 6.5 | 13 | 6.9 | 72 | 9.2 | 10 | 6.7 |
| **Number of inpatient bed days in year prior to incidence** | | | | | | | | | | |
| No | 3 005 | 75.6 | 2 155 | 75.6 | 140 | 74.5 | 604 | 76.8 | 106 | 71.1 |
| 1-5 days | 773 | 19.5 | 571 | 20.0 | 38 | 20.2 | 141 | 17.9 | 23 | 15.4 |

| | Total (N=3 973) | | Coordinating breast clinics (N=2 850) | | Satellite breast clinics (N=188) | | Campus not recognised for BC (N=786) | | Campus unknown (N=149) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| 6-15 days | 143 | 3.6 | 96 | 3.4 | 6 | 3.2 | 28 | 3.6 | 13 | 8.7 |
| >15 days | 52 | 1.3 | 28 | 1.0 | 4 | 2.1 | 13 | 1.7 | 7 | 4.7 |

*DCIS: ductal carcinoma in situ; SD: standard deviation; Q1: first quartile; Q3: third quartile; WHO: World Health Organization*
*Source: BCR-IMA-HDD*

**Table 62 – Patient characteristics at diagnosis of patients with IBC, by recognition status of the campus of main treatment**

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown(N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Age** | | | | | | | | | | |
| Mean, SD (years) | 62.6 (14.3) | | 61.08 (13.7) | | 62.4 (13.9) | | 63.1 (13.9) | | 77.1 (13.7) | |
| Median, Q1-Q3 (years) | 62.0 (52.0-73.0) | | 61.0 (51.0-71.0) | | 62.0 (52.0-73.0) | | 63.0 (53.0-73.0) | | 81.0 (69.0-87.0) | |
| <40 years | 2 261 | 4.9 | 1 677 | 5.5 | 121 | 4.9 | 422 | 4.1 | 41 | 1.4 |
| 40-49 years | 6 798 | 14.8 | 4 903 | 16.2 | 360 | 14.7 | 1 416 | 13.8 | 119 | 3.9 |
| 50-59 years | 10 580 | 23.0 | 7 507 | 24.7 | 573 | 23.4 | 2 290 | 22.4 | 210 | 7.0 |
| 60-69 years | 11 611 | 25.2 | 7 875 | 26.0 | 619 | 25.2 | 2 725 | 26.6 | 392 | 13.0 |
| 70-79 years | 8 294 | 18.0 | 5 264 | 17.4 | 477 | 19.4 | 1 978 | 19.3 | 575 | 19.0 |
| 80+ years | 6 491 | 14.1 | 3 106 | 10.2 | 303 | 12.4 | 1 398 | 13.7 | 1 684 | 55.7 |
| **Laterality** | | | | | | | | | | |
| Left | 23 680 | 51.4 | 15 600 | 51.4 | 1 266 | 51.6 | 5 299 | 51.8 | 1 515 | 50.1 |
| Right | 22 123 | 48.1 | 14 659 | 48.3 | 1 179 | 48.1 | 4 891 | 47.8 | 1 394 | 46.1 |
| Unknown | 232 | 0.5 | 73 | 0.2 | 8 | 0.3 | 39 | 0.4 | 112 | 3.7 |
| **WHO performance status at time of diagnosis** | | | | | | | | | | |

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown(N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| 0 – Asymptomatic | 24 975 | 54.3 | 18 091 | 59.6 | 1 078 | 43.9 | 5 095 | 49.8 | 711 | 23.5 |
| 1 – Symptomatic but completely ambulatory | 16 016 | 34.8 | 9 826 | 32.4 | 1 064 | 43.4 | 3 909 | 38.2 | 1 217 | 40.3 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 794 | 1.7 | 290 | 1.0 | 42 | 1.7 | 207 | 2.0 | 255 | 8.4 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 299 | 0.6 | 93 | 0.3 | 14 | 0.6 | 60 | 0.6 | 132 | 4.4 |
| 4 – Completely disabled; totally confined to bed or chair | 103 | 0.2 | 37 | 0.1 | 1 | 0.0 | 13 | 0.1 | 52 | 1.7 |
| Missing | 3 848 | 8.4 | 1 995 | 6.6 | 254 | 10.4 | 945 | 9.2 | 654 | 21.6 |
| **Number of comorbidities** | | | | | | | | | | |
| 0 | 24 330 | 52.9 | 17 111 | 56.4 | 1 263 | 51.5 | 5 076 | 49.6 | 880 | 29.1 |
| 1 | 16 362 | 35.5 | 10 104 | 33.3 | 899 | 36.6 | 3 853 | 37.7 | 1 506 | 49.9 |
| 2 | 4 938 | 10.7 | 2 874 | 9.5 | 269 | 11.0 | 1 221 | 11.9 | 574 | 19.0 |
| 3 | 405 | 0.9 | 243 | 0.8 | 22 | 0.9 | 79 | 0.8 | 61 | 2.0 |
| **Type of comorbidities** | | | | | | | | | | |
| Cardiovascular disease | 19 645 | 42.7 | 11 856 | 39.1 | 1 088 | 44.4 | 4 678 | 45.7 | 2 023 | 67.0 |
| Respiratory disease | 3 174 | 6.9 | 1 983 | 6.5 | 172 | 7.0 | 705 | 6.9 | 314 | 10.4 |
| Diabetes | 4 634 | 10.1 | 2 742 | 9.0 | 243 | 9.9 | 1 149 | 11.2 | 500 | 16.6 |
| **Number of inpatient bed days in year prior to incidence** | | | | | | | | | | |
| No | 34 199 | 74.3 | 23 130 | 76.3 | 1 860 | 75.8 | 7 568 | 74.0 | 1 641 | 54.3 |

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown(N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| 1-5 days | 7 927 | 17.2 | 5 181 | 17.1 | 417 | 17.0 | 1 773 | 17.3 | 556 | 18.4 |
| 6-15 days | 2 379 | 5.2 | 1 291 | 4.3 | 111 | 4.5 | 558 | 5.5 | 419 | 13.9 |
| >15 days | 1 530 | 3.3 | 730 | 2.4 | 65 | 2.6 | 330 | 3.2 | 405 | 13.4 |

*IBC: invasive breast cancer; SD: standard deviation; Q1: first quartile; Q3: third quartile; WHO: World Health Organization*
*Source: BCR-IMA-HDD*

## Appendix 11.2. Tumour characteristics

**Table 63 – Histological subtype and sublocalisation (ICD-O-3) in IBC, by recognition status of the campus of main treatment**

| | IBC (N=46 035) | | Recognised breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown (N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Histological subtype*** | | | | | | | | | | |
| Invasive ductal carcinoma (IDC) | 35 741 | 77.6 | 23 639 | 77.9 | 1 901 | 77.5 | 8 064 | 78.8 | 2 137 | 70.7 |
| Invasive lobular carcinoma (ILC) | 6 838 | 14.9 | 4 450 | 14.7 | 349 | 14.2 | 1 476 | 14.4 | 563 | 18.6 |
| Mixed ductal & lobular | 1 409 | 3.1 | 1 050 | 3.5 | 79 | 3.2 | 257 | 2.5 | 23 | 0.8 |
| Papillary & micropapillary | 527 | 1.1 | 355 | 1.2 | 30 | 1.2 | 115 | 1.1 | 27 | 0.9 |
| Mucineus | 467 | 1.0 | 260 | 0.9 | 29 | 1.2 | 112 | 1.1 | 66 | 2.2 |
| Metaplastic | 254 | 0.6 | 175 | 0.6 | 21 | 0.9 | 50 | 0.5 | 8 | 0.3 |
| Medullary | 171 | 0.4 | 116 | 0.4 | 12 | 0.5 | 43 | 0.4 | 0 | 0.0 |
| Cribriform & tubular | 124 | 0.3 | 83 | 0.3 | 10 | 0.4 | 26 | 0.3 | 5 | 0.2 |
| Inflammatory** | 16 | 0.0 | 9 | 0.0 | 2 | 0.1 | 3 | 0.0 | 2 | 0.1 |
| Neuroendocrine | 70 | 0.2 | 48 | 0.2 | 3 | 0.1 | 13 | 0.1 | 6 | 0.2 |
| Salivary gland type | 32 | 0.1 | 19 | 0.1 | 1 | 0.0 | 10 | 0.1 | 2 | 0.1 |
| Apocrine*** | 14 | 0.0 | 11 | 0.0 | 0 | 0.0 | 2 | 0.0 | 1 | 0.0 |

| | IBC (N=46 035) | | Recognised breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown (N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| Other carcinoma | 12 | 0.0 | 7 | 0.0 | 1 | 0.0 | 3 | 0.0 | 1 | 0.0 |
| Carcinoma. NOS | 360 | 0.8 | 110 | 0.4 | 15 | 0.6 | 55 | 0.5 | 180 | 6.0 |
| **Sublocalisation** | | | | | | | | | | |
| C50.0: Nipple | 425 | 0.9 | 215 | 0.7 | 22 | 0.9 | 152 | 1.5 | 36 | 1.2 |
| C50.1: Central portion of breast | 2 719 | 5.9 | 1 802 | 5.9 | 149 | 6.1 | 525 | 5.1 | 243 | 8.0 |
| C50.2: Upper-inner quadrant of breast | 5 099 | 11.1 | 3 393 | 11.2 | 298 | 12.1 | 1 198 | 11.7 | 210 | 7.0 |
| C50.3: Lower-inner quadrant of breast | 2 467 | 5.4 | 1 627 | 5.4 | 105 | 4.3 | 604 | 5.9 | 131 | 4.3 |
| C50.4: Upper-outer quadrant of breast | 14 960 | 32.5 | 9 925 | 32.7 | 826 | 33.7 | 3 490 | 34.1 | 719 | 23.8 |
| C50.5: Lower-outer quadrant of breast | 3 612 | 7.8 | 2 488 | 8.2 | 173 | 7.1 | 795 | 7.8 | 156 | 5.2 |
| C50.6: Axillary tail of breast | 327 | 0.7 | 202 | 0.7 | 28 | 1.1 | 71 | 0.7 | 26 | 0.9 |
| C50.8: Overlapping lesion of breast | 658 | 1.4 | 431 | 1.4 | 34 | 1.4 | 118 | 1.2 | 75 | 2.5 |
| C50.9: Breast, NOS | 15 768 | 34.3 | 10 249 | 33.8 | 818 | 33.3 | 3 276 | 32.0 | 1 425 | 47.2 |

*IBC: invasive breast cancer; NOS: not otherwise specified; *: Various sources were used to classify the morphology codes: RARECAREnet Information Network on Rare Cancers, List of Rare Cancers (October 2015; retrieved from http://rarecarenet.istitutotumori.mi.it/rarecarenet/index.php/cancerlist), The Surveillance, Epidemiology, and End Results (SEER) Program - Breast Solid Tumor Rules (2018, update July 2019; Retrieved from https://seer.cancer.gov/tools/solidtumor/Breast_STM.pdf), the World Health Organization Classification of Tumours Editorial Board & International Agency for Research on Cancer (2012) and personal communication with clinical experts; **: Inflammatory BC is registered in the BCR database with ICD-O-3 morphology code 8530/3. However, inflammatory BC can also be identified based on TNM, i.e. cT4d cases. For this study there were N=630 cases registered as cT4d: N=492 (78.1%) were registered with a ductal morphology (codes 8500/3, 8523/3), N=85 (13.5%) as lobular (codes 8520/3, 8524/3), N=14 (2.2%) as inflammatory (code 8530/3), N=13 (2.1%) as carcinoma NOS* (codes 8000/3, 8012/3, 8140/3), N=10 (1.6%) as mixed ductal & lobular (code 8522/3), N=6 (0.9%) as (micro)papillary (codes 8503/3, 8507/3), N=5 (0.8%) as mucinous (code 8480/3), N=4 (0.6%) as metaplastic (codes 8573/3, 8575/3), N=1 (0.2%) as neuroendocrine (code 8574/3); ***: Apocrine BC is registered in the BCR database with ICD-O-3 morphology code 8401/3.*
*Source: BCR-IMA-HDD*

**Table 64 – Tumour characteristics in DCIS, by recognition status of the campus of main treatment**

| | Total (N=3 973) | | Coordinating breast clinics (N=2 850) | | Satellite breast clinics (N=188) | | Campus not recognised for BC (N=786) | | Campus unknown (N=149) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Incidence years** | | | | | | | | | | |
| 2014 | 807 | 20.3 | 552 | 19.4 | 16 | 8.5 | 219 | 27.9 | 20 | 13.4 |
| 2015 | 777 | 19.6 | 540 | 18.9 | 25 | 13.3 | 183 | 23.3 | 29 | 19.5 |
| 2016 | 808 | 20.3 | 609 | 21.4 | 37 | 19.7 | 138 | 17.6 | 24 | 16.1 |
| 2017 | 771 | 19.4 | 564 | 19.8 | 53 | 28.2 | 123 | 15.6 | 31 | 20.8 |
| 2018 | 810 | 20.4 | 585 | 20.5 | 57 | 30.3 | 123 | 15.6 | 45 | 30.2 |
| **Clinical stage*** | | | | | | | | | | |
| c0 ˜ | 2 646 | 100.0 | 1 977 | 100.0 | 130 | 100.0 | 463 | 100.0 | 76 | 100.0 |
| Unknown | 1 327 | 33.4 | 873 | 30.6 | 58 | 30.9 | 323 | 41.1 | 73 | 49.0 |
| **Pathological stage* ° ϕ** | | | | | | | | | | |
| **Patients who had surgery** | 3 809 | 95.9 | 2 832 | 99.4 | 188 | 100.0 | 782 | 99.5 | 7 | 4.7 |
| (y)p0 | 3 556 | 100.0 | 2 663 | 100.0 | 174 | 100.0 | 712 | 100.0 | 7 | 100.0 |
| Unknown | 253 | 6.6 | 169 | 6.0 | 14 | 7.4 | 70 | 9.0 | 0 | 0.0 |
| **Combined stage*ϕ** | | | | | | | | | | |
| (y)0 ˜ | 3 774 | 100.0 | 2 747 | 100.0 | 182 | 100.0 | 743 | 100.0 | 102 | 100.0 |
| Unknown | 199 | 5.0 | 103 | 3.6 | 6 | 3.2 | 43 | 5.5 | 47 | 31.5 |
| **Grade** | | | | | | | | | | |
| I | 530 | 13.3 | 366 | 12.8 | 30 | 16.0 | 117 | 14.9 | 17 | 11.4 |
| II | 887 | 22.3 | 625 | 21.9 | 36 | 19.1 | 204 | 26.0 | 22 | 14.8 |
| III | 1 234 | 31.1 | 923 | 32.4 | 33 | 17.6 | 249 | 31.7 | 29 | 19.5 |
| Unknown$ | 1 322 | 33.3 | 936 | 32.8 | 89 | 47.3 | 216 | 27.5 | 81 | 54.4 |

*DCIS: ductal carcinoma in situ; *: percentages for stages 0-IV were calculated excluding the unknown category; °: only includes patients who underwent surgery; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0; ϕ: patients might have had neoadjuvant therapy (NAT), resulting in a ypStage in these cases. Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); the combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage; $: The high proportion of grade unknown is due to the incomplete information BCR received from the oncological care programs and/or laboratories for anatomical pathology.*
*Source: BCR-IMA-HDD*

**Table 65 – Tumour characteristics in IBC, by recognition status of the campus of main treatment**

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown (N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Incidence years** | | | | | | | | | | |
| 2014 | 8 980 | 19.5 | 5 655 | 18.6 | 219 | 8.9 | 2 548 | 24.9 | 558 | 18.5 |
| 2015 | 8 973 | 19.5 | 5 842 | 19.3 | 318 | 13.0 | 2 272 | 22.2 | 541 | 17.9 |
| 2016 | 9 363 | 20.3 | 6 194 | 20.4 | 527 | 21.5 | 2 036 | 19.9 | 606 | 20.1 |
| 2017 | 9 193 | 20.0 | 6 208 | 20.5 | 665 | 27.1 | 1 681 | 16.4 | 639 | 21.2 |
| 2018 | 9 526 | 20.7 | 6 433 | 21.2 | 724 | 29.5 | 1 692 | 16.5 | 677 | 22.4 |
| **Clinical stage*** | | | | | | | | | | |
| c0 ˜ | 569 | 1.4 | 464 | 1.7 | 22 | 1.0 | 81 | 0.9 | 2 | 0.1 |
| cIA | 18 658 | 45.7 | 13 182 | 47.5 | 1 013 | 47.0 | 4 093 | 47.5 | 370 | 15.9 |
| cIIA | 11 500 | 28.1 | 7 898 | 28.5 | 613 | 28.4 | 2 480 | 28.8 | 509 | 21.9 |
| cIIB | 4 197 | 10.3 | 2 904 | 10.5 | 208 | 9.6 | 885 | 10.3 | 200 | 8.6 |
| cIIIA | 1 181 | 2.9 | 809 | 2.9 | 71 | 3.3 | 249 | 2.9 | 52 | 2.2 |
| cIIIB | 1 387 | 3.4 | 766 | 2.8 | 77 | 3.6 | 328 | 3.8 | 216 | 9.3 |
| cIIIC | 455 | 1.1 | 348 | 1.3 | 17 | 0.8 | 69 | 0.8 | 21 | 0.9 |
| cIV | 2 921 | 7.1 | 1 389 | 5.0 | 136 | 6.3 | 439 | 5.1 | 957 | 41.1 |
| Unknown | 5 167 | 11.2 | 2 572 | 8.5 | 296 | 12.1 | 1 605 | 15.7 | 694 | 23.0 |

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown (N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Pathological stage* ° ϕ** | | | | | | | | | | |
| **Patients who had surgery** | 40 233 | 87.4 | 28 383 | 93.6 | 2 279 | 92.9 | 9 511 | 93.0 | 60 | 2.0 |
| (y)p0 | 1 072 | 2.8 | 869 | 3.2 | 39 | 1.8 | 164 | 1.8 | 0 | 0.0 |
| ypis | 343 | 0.9 | 290 | 1.1 | 21 | 1.0 | 32 | 0.3 | 0 | 0.0 |
| (y)pIA | 18 284 | 47.2 | 12 932 | 47.4 | 1 022 | 46.6 | 4 305 | 46.9 | 25 | 45.5 |
| (y)pIB | 1 014 | 2.6 | 724 | 2.7 | 65 | 3.0 | 223 | 2.4 | 2 | 3.6 |
| (y)pIIA | 9 191 | 23.7 | 6 335 | 23.2 | 556 | 25.4 | 2 283 | 24.9 | 17 | 30.9 |
| (y)pIIB | 4 473 | 11.6 | 3 144 | 11.5 | 249 | 11.4 | 1 073 | 11.7 | 7 | 12.7 |
| (y)pIIIA | 2 743 | 7.1 | 1 916 | 7.0 | 162 | 7.4 | 661 | 7.2 | 4 | 7.3 |
| (y)pIIIB | 422 | 1.1 | 238 | 0.9 | 27 | 1.2 | 157 | 1.7 | 0 | 0.0 |
| (y)pIIIC | 1 049 | 2.7 | 769 | 2.8 | 45 | 2.1 | 235 | 2.6 | 0 | 0.0 |
| (y)pIV | 134 | 0.3 | 80 | 0.3 | 7 | 0.3 | 47 | 0.5 | 0 | 0.0 |
| Unknown | 1 508 | 3.7 | 1 086 | 3.8 | 86 | 3.8 | 331 | 3.5 | 5 | 8.3 |
| **Combined stage*ϕ** | | | | | | | | | | |
| (y)0 ˜ | 1 065 | 2.4 | 863 | 2.9 | 37 | 1.5 | 165 | 1.6 | 0 | 0.0 |
| yis | 337 | 0.7 | 286 | 1.0 | 20 | 0.8 | 31 | 0.3 | 0 | 0.0 |
| (y)IA | 19 104 | 42.5 | 13 282 | 44.2 | 1 037 | 42.8 | 4 411 | 43.7 | 374 | 15.7 |
| (y)IB | 1 022 | 2.3 | 728 | 2.4 | 65 | 2.7 | 222 | 2.2 | 7 | 0.3 |
| (y)IIA | 10 470 | 23.3 | 6 883 | 22.9 | 599 | 24.7 | 2 459 | 24.4 | 529 | 22.1 |
| (y)IIB | 5 037 | 11.2 | 3 399 | 11.3 | 261 | 10.8 | 1 165 | 11.6 | 212 | 8.9 |
| (y)IIIA | 2 914 | 6.5 | 1 993 | 6.6 | 174 | 7.2 | 687 | 6.8 | 60 | 2.5 |
| (y)IIIB | 893 | 2.0 | 406 | 1.3 | 41 | 1.7 | 236 | 2.3 | 210 | 8.8 |

| | Total (N=46 035) | | Coordinating breast clinics (N=30 332) | | Satellite breast clinics (N=2 453) | | Campus not recognised for BC (N=10 229) | | Campus unknown (N=3 021) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| (y)IIIC | 1 123 | 2.5 | 808 | 2.7 | 49 | 2.0 | 244 | 2.4 | 22 | 0.9 |
| (y)IV | 3 009 | 6.7 | 1 427 | 4.7 | 142 | 5.9 | 465 | 4.6 | 975 | 40.8 |
| Unknown | 1 061 | 2.3 | 257 | 0.8 | 28 | 1.1 | 144 | 1.4 | 632 | 20.9 |
| **Grade** | | | | | | | | | | |
| I | 6 455 | 14.0 | 4 223 | 13.9 | 306 | 12.5 | 1 551 | 15.2 | 375 | 12.4 |
| II | 20 954 | 45.5 | 13 812 | 45.5 | 1 052 | 42.9 | 4 737 | 46.3 | 1 353 | 44.8 |
| III | 15 259 | 33.1 | 10 655 | 35.1 | 781 | 31.8 | 3 182 | 31.1 | 641 | 21.2 |
| Unknown[$] | 3 367 | 7.3 | 1 642 | 5.4 | 314 | 12.8 | 759 | 7.4 | 652 | 21.6 |

*IBC: invasive breast cancer; HER2: Human epidermal growth factor receptor 2; IHC: Immunohistochemistry; ISH: In situ hybridization; *: percentages for stages 0-IV were calculated excluding the unknown category; °: only includes patients who underwent surgery; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; ϕ: patients might have had neoadjuvant therapy (NAT), resulting in a ypStage in these cases. Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); the combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage, except when the presence of metastasis is specified in the clinical stage[$]: The high proportion of grade unknown is due to the incomplete information BCR received from the oncological care programs and/or laboratories for anatomical pathology.*
*Source: BCR-IMA-HDD*

**Table 66 – Tumour characteristics for operated patients with DCIS, not treated with neoadjuvant therapy, by recognition status of the campus of main treatment**

| | Total (N=3 789) | | Coordinating breast clinics (N=2 817) | | Satellite breast clinics (N=186) | | Campus not recognised for BC (N=779) | | Campus unknown (N=7) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Pathological stage** | | | | | | | | | | |
| p0 | 3 536 | 100.0 | 2 648 | 100.0 | 172 | 100.0 | 709 | 100.0 | 7 | 100.0 |
| Unknown | 253 | 6.7 | 169 | 6.0 | 14 | 7.5 | 70 | 9.0 | 0 | 0.0 |
| **Combined stage** | | | | | | | | | | |
| 0 ˜ | 3 641 | 100.0 | 2 717 | 100.0 | 180 | 100.0 | 737 | 100.0 | 7 | 100.0 |
| Unknown | 148 | 3.9 | 100 | 3.5 | 6 | 3.2 | 42 | 5.4 | 0 | 0.0 |

*DCIS: ductal carcinoma in situ; BC: breast cancer; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0; The combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage.*
*Source: BCR-IMA-HDD*

**Table 67 – Tumour characteristics for operated patients with IBC, not treated with neoadjuvant therapy, by recognition status of the campus of main treatment**

| | Total (N=34 257) | | Coordinating breast clinics (N=23 758) | | Satellite breast clinics (N=1 968) | | Campus not recognised for BC (N=8 476) | | Campus unknown (N=55) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Pathological stage** | | | | | | | | | | |
| pIA | 17 109 | 50.7 | 12 003 | 51.4 | 967 | 49.7 | 4 114 | 49.3 | 25 | 48.1 |
| pIB | 934 | 2.8 | 659 | 2.8 | 58 | 3.0 | 215 | 2.6 | 2 | 3.8 |
| pIIA | 8 258 | 24.5 | 5 616 | 24.0 | 510 | 26.2 | 2 116 | 25.3 | 16 | 30.8 |
| pIIB | 4 009 | 11.9 | 2 800 | 12.0 | 224 | 11.5 | 980 | 11.7 | 5 | 9.6 |
| pIIIA | 2 176 | 6.5 | 1 488 | 6.4 | 128 | 6.6 | 556 | 6.7 | 4 | 7.7 |

| | Total (N=34 257) | | Coordinating breast clinics (N=23 758) | | Satellite breast clinics (N=1 968) | | Campus not recognised for BC (N=8 476) | | Campus unknown (N=55) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| pIIIB | 327 | 1.0 | 185 | 0.8 | 18 | 0.9 | 124 | 1.5 | 0 | 0.0 |
| pIIIC | 837 | 2.5 | 591 | 2.5 | 37 | 1.9 | 209 | 2.5 | 0 | 0.0 |
| pIV | 72 | 0.2 | 32 | 0.1 | 5 | 0.3 | 35 | 0.4 | 0 | 0.0 |
| Unknown | 535 | 1.6 | 384 | 1.6 | 21 | 1.1 | 127 | 1.5 | 3 | 5.5 |
| **Combined stage** | | | | | | | | | | |
| 0 ˜ | 9 | <0.1 | 7 | <0.1 | 0 | 0.0 | 2 | <0.1 | 0 | 0.0 |
| IA | 17 266 | 50.7 | 12 133 | 51.3 | 968 | 49.5 | 4 139 | 49.2 | 26 | 47.3 |
| IB | 932 | 2.7 | 658 | 2.8 | 58 | 3.0 | 214 | 2.5 | 2 | 3.6 |
| IIA | 8 331 | 24.5 | 5 685 | 24.0 | 506 | 25.9 | 2 123 | 25.3 | 17 | 30.9 |
| IIB | 4 012 | 11.8 | 2 808 | 11.9 | 222 | 11.3 | 977 | 11.6 | 5 | 9.1 |
| IIIA | 2 157 | 6.3 | 1 479 | 6.3 | 128 | 6.5 | 546 | 6.5 | 4 | 7.3 |
| IIIB | 313 | 0.9 | 179 | 0.8 | 16 | 0.8 | 118 | 1.4 | 0 | 0.0 |
| IIIC | 811 | 2.4 | 574 | 2.4 | 36 | 1.8 | 201 | 2.4 | 0 | 0.0 |
| IV | 239 | 0.7 | 128 | 0.5 | 23 | 1.2 | 87 | 1.0 | 1 | 1.8 |
| Unknown | 187 | 0.5 | 107 | 0.5 | 11 | 0.6 | 69 | 0.8 | 0 | 0.0 |

*IBC: invasive breast cancer; *: percentages for stages 0-IV were calculated excluding the unknown category; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; The combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage, except when the presence of metastasis is specified in the clinical stage.*
*Source: BCR-IMA-HDD*

**Table 68 – Tumour characteristics for operated patients with IBC, treated with neoadjuvant therapy, by recognition status of the campus of main treatment**

| | Total (N=5 976) | | Coordinating breast clinics (N=4 625) | | Satellite breast clinics (N=311) | | Campus not recognised for BC (N=1 035) | | Unknown status (N=5) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Pathological stage*** | | | | | | | | | | |
| ypT0 | 1 072 | 21.4 | 869 | 22.2 | 39 | 15.9 | 164 | 19.7 | 0 | 0.0 |
| ypTis | 343 | 6.9 | 290 | 7.4 | 21 | 8.5 | 32 | 3.9 | 0 | 0.0 |
| ypTIA | 1 175 | 23.5 | 929 | 23.7 | 55 | 22.4 | 191 | 23.0 | 0 | 0.0 |
| ypTIB | 80 | 1.6 | 65 | 1.7 | 7 | 2.8 | 8 | 1.0 | 0 | 0.0 |
| ypTIIA | 933 | 18.6 | 719 | 18.3 | 46 | 18.7 | 167 | 20.1 | 1 | 33.3 |
| ypTIIB | 464 | 9.3 | 344 | 8.8 | 25 | 10.2 | 93 | 11.2 | 2 | 66.7 |
| ypTIIIA | 567 | 11.3 | 428 | 10.9 | 34 | 13.8 | 105 | 12.6 | 0 | 0.0 |
| ypTIIIB | 95 | 1.9 | 53 | 1.4 | 9 | 3.7 | 33 | 4.0 | 0 | 0.0 |
| ypTIIIC | 212 | 4.2 | 178 | 4.5 | 8 | 3.3 | 26 | 3.1 | 0 | 0.0 |
| ypTIV | 62 | 1.2 | 48 | 1.2 | 2 | 0.8 | 12 | 1.4 | 0 | 0.0 |
| Unknown | 973 | 16.3 | 702 | 15.2 | 65 | 20.9 | 204 | 19.7 | 2 | 40.0 |
| **Combined stage** | | | | | | | | | | |
| (y)T0 | 1 056 | 18.0 | 856 | 18.8 | 37 | 12.3 | 163 | 16.1 | 0 | 0.0 |
| yTis | 337 | 5.7 | 286 | 6.3 | 20 | 6.6 | 31 | 3.1 | 0 | 0.0 |
| (y)TIA | 1 239 | 21.1 | 973 | 21.4 | 58 | 19.2 | 208 | 20.5 | 0 | 0.0 |
| (y)TIB | 79 | 1.3 | 64 | 1.4 | 7 | 2.3 | 8 | 0.8 | 0 | 0.0 |
| (y)TIIA | 1 198 | 20.4 | 911 | 20.0 | 70 | 23.2 | 216 | 21.3 | 1 | 25.0 |
| (y)TIIB | 657 | 11.2 | 482 | 10.6 | 34 | 11.3 | 138 | 13.6 | 3 | 75.0 |
| (y)TIIIA | 610 | 10.4 | 452 | 9.9 | 39 | 12.9 | 119 | 11.7 | 0 | 0.0 |

| | Total (N=5 976) | | Coordinating breast clinics (N=4 625) | | Satellite breast clinics (N=311) | | Campus not recognised for BC (N=1 035) | | Unknown status (N=5) | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| (y)IIIB | 163 | 2.8 | 102 | 2.2 | 8 | 2.6 | 53 | 5.2 | 0 | 0.0 |
| (y)IIIC | 234 | 4.0 | 195 | 4.3 | 9 | 3.0 | 30 | 3.0 | 0 | 0.0 |
| (y)IV | 295 | 5.0 | 228 | 5.0 | 20 | 6.6 | 47 | 4.6 | 0 | 0.0 |
| Unknown | 108 | 1.8 | 76 | 1.6 | 9 | 2.9 | 22 | 2.1 | 1 | 20.0 |

*IBC: invasive breast cancer; *: percentages for stages 0-IV were calculated excluding the unknown category; Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); The combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage, except when the presence of metastasis is specified in the clinical stage.*
*Note: Twenty patients diagnosed with DCIS received neoadjuvant treatment. Further exploration of these cases revealed that twelve of them, only had neoadjuvant endocrine therapy; a treatment strategy that has been suggested in hormone-positive DCIS.[148, 149] For another DCIS case, neoadjuvant chemotherapy and targeted therapy was confirmed. For three cases, additional information indicated that the neoadjuvant treatment was actually administered for the recurrence of a previous tumour and not for the DCIS under study. For the last four cases, it cannot be deduced from the available information provided in the administrative database and the pathology reports whether the neoadjuvant treatment was provided for DCIS or for another indication.*
*Source: BCR-IMA-HDD*

**Consistency between clinical and pathological stage** was evaluated for those patients with IBC who underwent surgery, and for whom both clinical and pathological stage were reported to the BCR. The analyses were done separately for patients who did not (Table 69) and who did receive neoadjuvant treatment (Table 70) .The analyses indicated that the pathological stage was identical to the clinical stage for 21 946 patients (i.e. 73.3% of 29 924 eligible patients) who did not receive neoadjuvant treatment. Of note, 154 patients were staged as clinical stage IV, while the pathological stage was lower. Further analysis (not presented in the table) revealed that for 67.5% of these cases pN+ was recorded and for 24.0% pN0. Similarly, 556 patients were diagnosed as clinical stage 0, while the pathological stage was higher (86% of them pStage I and 12.9% pStage II). Among the 5 976 women who received neoadjuvant therapy the level of consistency was markedly lower (33.6%). As expected, in 59% of these women, pathological stage was lower than clinical stage.

**Table 69 – Consistency between clinical and pathological staging for operated patients diagnosed with IBC, not treated with neoadjuvant therapy**

| Clinical stage | | | | Pathological stage | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | pStage missing | pStage reported | pI | | pII | | pIII | | pIV | |
| | N | N | N | N | % | N | % | N | % | N | % |
| **c0** | 565 | 9 | 556 **(100%)** | 478 | 86.0 | 72 | 12.9 | 6 | 1.1 | 0 | 0.0 |
| **cI** | 17 495 | 173 | 17 322 **(100%)** | 13 756 | 79.4 | 3 218 | 18.6 | 338 | 2.0 | 10 | 0.1 |
| **cII** | 11 112 | 133 | 10 979 **(100%)** | 1 557 | 14.2 | 7 487 | 68.2 | 1 919 | 17.5 | 16 | 0.1 |
| **cIII** | 895 | 20 | 875 **(100%)** | 24 | 2.7 | 185 | 21.1 | 665 | 76.0 | 1 | 0.1 |
| **cIV** | 205 | 13 | 192[$] **(100%)** | 18 | 9.4 | 57 | 29.7 | 79 | 41.1 | 38 | 19.8 |
| **Total known cStage** | 30 272 | 348 (1.1%) | 29 924 (98.9%) | | | | | | | | |
| **Total unknown cStage** | 3 985 | 187 | 3 798 **(100%)** | 2 210 | 58.2 | 1 248 | 32.9 | 333 | 8.8 | 7 | 0.2 |
| **Total** | 34 257 | 535 | | | | | | | | | |

*IBC: invasive breast cancer.*
*Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined; [$]: this number may be higher than expected based on clinical experience, but it is important to note that pStage can also be based on the pN and/or pM category only, without a pT having to be filled out.*
*Source: BCR*



**Table 70 – Consistency between clinical and pathological staging for patients diagnosed with IBC treated with neoadjuvant therapy**

| Clinical stage | | Pathological stage | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | pStage missing | pStage reported | yp0 | | ypis | | ypI | | ypII | | ypIII | | ypIV | |
| | N | N | N | N | % | N | % | N | % | N | % | N | % | N | % |
| **c0** | 1 | 1 | 0 **(100%)** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **cI** | 578 | 87 | 491 **(100%)** | 145 | 29.5 | 28 | 5.7 | 245 | 49.9 | 60 | 12.2 | 11 | 2.2 | 2 | 0.4 |
| **cII** | 3 302 | 515 | 2 787 **(100%)** | 674 | 24.2 | 222 | 8.0 | 771 | 27.7 | 845 | 30.3 | 270 | 9.7 | 5 | 0.2 |
| **cIII** | 1 500 | 204 | 1 296 **(100%)** | 212 | 16.4 | 74 | 5.7 | 167 | 12.9 | 363 | 28.0 | 474 | 36.6 | 6 | 0.5 |
| **cIV** | 279 | 58 | 221 **(100%)** | 17 | 7.7 | 6 | 2.7 | 24 | 10.9 | 57 | 25.8 | 71 | 32.1 | 46 | 20.8 |
| **Total known cStage** | 5 660 | 865 (15.3%) | 4795 (84.7%) | | | | | | | | | | | | |
| **Total unknown cStage** | 316 | 108 | 208 **(100%)** | 24 | 11.5 | 13 | 6.3 | 48 | 23.1 | 72 | 34.6 | 48 | 23.1 | 3 | 1.4 |
| **Total** | 5 976 | 973 | | | | | | | | | | | | | |

*IBC: invasive breast cancer.*
*Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined.*
*Source: BCR*

## Appendix 11.3. Main diagnostic and staging procedures

**Table 71 – Diagnostic and staging procedures performed within 3 months around the incidence date, unless otherwise specified**

| Category | DCIS | | IBC | |
|---|---|---|---|---|
| | N | % | N | % |
| **Puncture and/or biopsy** | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 46 035 | |
| **Overall*** | 3 731 | 93.9 | 43 984 | 95.5 |
| Breast biopsy[$] | 3 575 | 90.0 | 39 688 | 86.2 |
| Incision biopsy | 17 | 0.4 | 485 | 1.1 |
| Core biopsy | 1 566 | 39.4 | 37 671 | 81.8 |
| Vacuum assisted biopsy | 2 347 | 59.1 | 3 087 | 6.7 |
| Breast puncture[$] | 1 222 | 30.8 | 18 852 | 41.0 |
| Lymph node puncture[$] | 12 | 0.3 | 712 | 1.5 |
| ***Comparison period 2009 - 2013*** | 3 830 | | 43 507 | |
| ***Overall*** | 3 548 | 92.6 | 39 837 | 91.6 |
| **Cytohistopathological examination** | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 46 035 | |
| **Overall*** | 3 958 | 99.6 | 45 787 | 99.5 |
| Cytological examination | 943 | 23.7 | 20 491 | 44.5 |
| Anatomical-pathological examinations | 3 954 | 99.5 | 45 639 | 99.1 |
| Biopsy specimens | 3 398 | 85.5 | 43 285 | 94.0 |
| Resection specimens | 3 744 | 94.2 | 36 650 | 79.6 |
| Frozen section | 1 110 | 27.9 | 19 002 | 41.3 |
| Immunohistochemical examination (general)[#] | 3 827 | 96.3 | 45 577 | 99.0 |
| HER2 in situ hybridization** | 78 | 2.0 | 30 989 | 67.3 |

| Category | DCIS | | IBC | |
|---|---|---|---|---|
| | N | % | N | % |
| ***Comparison period 2009 - 2013*** | 3 830 | | 43 507 | |
| ***Overall*** | 3 813 | 99.6 | 43 181 | 99.3 |
| **Genetic testing** | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 46 035 | |
| BRCA (within -3 to +3 months of incidence) | 148 | 3.7 | 3 560 | 7.7 |
| BRCA (within -1 to +1 years of incidence) | 370 | 9.3 | 7 082 | 15.4 |
| BRCA (within -1 to +5 years of incidence) | 483 | 12.2 | 8 820 | 19.2 |
| ***Comparison period 2009 - 2013*** | 3 830 | | 43 507 | |
| BRCA (within -3 to +3 months of incidence) | 12 | 0.3 | 433 | 1.0 |
| BRCA (within -1 to +1 years of incidence) | 67 | 1.8 | 1 333 | 3.1 |
| BRCA (within -1 to +5 years of incidence) | 176 | 4.6 | 3 090 | 7.1 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; HER2: Human epidermal growth factor receptor 2; BRCA: breast cancer gene; for nomenclature codes based on which diagnostic procedures were defined, please see Appendix 8.1; *: for several diagnostic procedures the numbers of the subcategories do not add up as for some patients more than one type of staging/diagnostic procedure was billed. $: the interpretation of these results should be performed with caution since the pre-validation study indicated that codes for breast biopsy, breast puncture and lymph node puncture are used interchangeably in some Belgian hospitals (e.g. a FNAC of the axillary glands being coded as 'breast puncture' instead of 'lymph node puncture'); #: no specific code exists for immunohistochemical testing of HER2. An IHC HER2 testing could only be billed as part of the general immunohistochemical examination. Note that separate nomenclature codes do exist for testing the oestrogen and progesterone receptors (see Appendix 15.1), but since these codes didn't occur in the health insurance data of our study population, they could not be reported separately; **according to the protocols prevailing in 2014 - 2018, an ISH test was only to be performed when the HER2 IHC test result was equivocal (score 2+) or 3+.*
*Source: BCR-IMA*

**Table 72 – Imaging procedures performed within 3 months around incidence date, excluding all imaging as from start of treatment and additionally for CT those as from 14 days before start date of radiotherapy**

| Category | DCIS | | IBC | |
|---|---|---|---|---|
| | N | % | N | % |
| **Imaging exclusively for breast** | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 46 035 | |
| **Overall*** | 3 818 | 96.1 | 45 121 | 98.0 |
| Mammography and/or breast ultrasound | 3 751 | 94.4 | 44 880 | 97.5 |
| Mammography | 3 546 | 89.3 | 42 417 | 92.1 |
| Diagnostic mammography only | 2 674 | 67.3 | 37 194 | 80.8 |
| Screening mammography only | 150 | 3.8 | 2 369 | 5.1 |
| Diagnostic AND screening mammography | 788 | 19.8 | 3 117 | 6.8 |
| Breast ultrasound[$] | 3 382 | 85.1 | 43 099 | 93.6 |
| MRI breast | 1 898 | 47.8 | 23 019 | 50.0 |
| Mammography and/or breast ultrasound combined with MRI breast | 1 831 | 46.1 | 22 778 | 49.5 |
| ***Comparison period 2009 - 2013*** | 3 830 | | 43 507 | |
| ***Overall*** | 3 650 | 95.3 | 42 157 | 96.9 |
| **Imaging - other** | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 46 035 | |
| **Overall** | 2 206 | 55.5 | 41 976 | 91.2 |
| X-ray thorax | 1 541 | 38.8 | 31 782 | 69.0 |
| Abdominal ultrasound | 896 | 22.6 | 29 802 | 64.7 |
| X-ray thorax and abdominal ultrasound | 667 | 16.8 | 26 942 | 58.5 |
| SPECT and/or SPECT-CT and/or scintigraphy | 1180 | 29.7 | 36 216 | 78.7 |
| SPECT | 625 | 15.7 | 26 633 | 57.9 |
| SPECT-CT | 203 | 5.1 | 8 251 | 17.9 |
| Scintigraphy | 654 | 16.5 | 14 640 | 31.8 |
| CT body[£] | 431 | 10.8 | 14 553 | 31.6 |
| PET-CT | 32 | 0.8 | 4 296 | 9.3 |

| Category | DCIS | | IBC | |
|---|---|---|---|---|
| | N | % | N | % |
| CT and/or MRI brain | 101 | 2.5 | 2 558 | 5.6 |
| MRI body | 41 | 1.0 | 1 178 | 2.6 |
| ***Comparison period 2009 - 2013*** | 3 830 | | 43 507 | |
| ***Overall*** | 2 307 | 60.2 | 39 970 | 91.9 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: for several diagnostic procedures the numbers of the subcategories do not add up as for some patients more than one type of staging/diagnostic procedure was billed. £: CT body performed within 14 days before the start of a radiotherapy series was excluded; $: non-breast-specific US nomenclature codes as well as echo-guided breast biopsies were not considered.*
*Source: BCR-IMA*

### Table 73 – Imaging procedures[$] for staging in patients diagnosed with IBC, per clinical stage

| Imaging procedure | Clinical stage | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | cStage 0 (N=569) | | cStage I-II (N=34 355) | | cStage III-IV (N=5 944) | | Unknown (N=5 167) | |
| | N | % | N | % | N | % | N | % |
| **X-ray thorax** | 258 | 45.3 | 24 864 | 72.4 | 3 340 | 56.2 | 3 320 | 64.3 |
| **Abdominal ultrasound** | 179 | 31.5 | 23 787 | 69.2 | 2 934 | 49.4 | 2 902 | 56.2 |
| **X-ray thorax and abdominal ultrasound** | 148 | 26.0 | 21 910 | 63.8 | 2 226 | 37.5 | 2 658 | 51.4 |
| **SPECT and/or SPECT-CT and/or scintigraphy** | 259 | 45.5 | 27 979 | 81.4 | 4 334 | 72.9 | 3 644 | 70.5 |
| **SPECT** | 133 | 23.4 | 20 567 | 59.9 | 3 329 | 56.0 | 2 604 | 50.4 |
| **SPECT-CT** | 37 | 6.5 | 6 919 | 20.1 | 850 | 14.3 | 445 | 8.6 |
| **scintigraphy** | 151 | 26.5 | 11 682 | 34.0 | 1 259 | 21.2 | 1 548 | 30.0 |
| **CT body** | 87 | 15.3 | 9 236 | 26.9 | 3 602 | 60.6 | 1 628 | 31.5 |
| **PET-CT** | 5 | 0.9 | 2 242 | 6.5 | 1 743 | 29.3 | 306 | 5.9 |
| **CT and/or MRI brain** | 13 | 2.3 | 1 338 | 3.9 | 866 | 14.6 | 341 | 6.6 |
| **MRI body** | 6 | 1.1 | 770 | 2.2 | 301 | 5.1 | 101 | 2.0 |

*IBC: invasive breast cancer; [$]Time frame: within 3 months around incidence date, excluding all imaging as from start of treatment and additionally for CT those as from 14 days before start date of radiotherapy.*
*Source: BCR-IMA*

### Table 74 – Diagnostic and staging procedures[$] for which the hospital is not known

| Category | Total DCIS (N=3 973) | | | Total IBC (N=46 035) | | |
|---|---|---|---|---|---|---|
| | Number of procedures (1 per patient) | Number of procedures with unknown hospital' | % | Number of procedures (1 per patient) | Number of procedures with unknown hospital' | % |
| **Puncture and/or biopsy** | | | | | | |
| Breast biopsy* | 3 575 | 206 | 5.8 | 39 688 | 3 331 | 8.4 |
| Incision biopsy | 17 | 2 | 11.8 | 485 | 122 | 25.2 |
| Core biopsy | 1 566 | 137 | 8.8 | 37 671 | 3 165 | 8.4 |
| Vacuum assisted biopsy | 2 347 | 79 | 3.4 | 3 087 | 89 | 2.9 |
| Breast puncture | 1 222 | 165 | 13.5 | 18 852 | 4 069 | 21.6 |
| Lymph node puncture | 12 | 0 | 0.0 | 712 | 7 | 1.0 |
| **Cytohistopathological examination** | | | | | | |
| Cytological examination | 943 | 106 | 11.2 | 20 491 | 2 723 | 13.3 |
| Anatomical-pathological examinations | 3 954 | 507 | 12.8 | 45 639 | 7 182 | 15.7 |
| Biopsy specimens | 3 398 | 509 | 15.0 | 43 285 | 7 042 | 16.3 |
| Resection specimens | 3 744 | 98 | 2.6 | 36 650 | 789 | 2.2 |
| Frozen section | 1 110 | 1 | 0.1 | 19 002 | 98 | 0.5 |
| Immunohistochemical examination (general) | 3 827 | 452 | 11.8 | 45 577 | 7 195 | 15.8 |
| HER2 in situ hybridization** | 78 | 8 | 10.3 | 30 989 | 5 462 | 17.6 |

| Category | Total DCIS (N=3 973) | | | Total IBC (N=46 035) | | |
|---|---|---|---|---|---|---|
| | Number of procedures (1 per patient) | Number of procedures with unknown hospital' | % | Number of procedures (1 per patient) | Number of procedures with unknown hospital' | % |
| **Genetic testing** | | | | | | |
| BRCA (within -3 to +3 months of incidence) | 148 | 20 | 13.5 | 3 560 | 635 | 17.8 |
| BRCA (within -1 to +1 years of incidence) | 370 | 62 | 16.8 | 7 082 | 1 227 | 17.3 |
| BRCA (within -1 to +5 years of incidence) | 483 | 79 | 16.4 | 8 820 | 1 575 | 17.9 |
| **Imaging exclusively for breast** | | | | | | |
| Mammography* | 3 546 | 519 | 14.6 | 42 417 | 12 306 | 29.0 |
| Diagnostic mammography | 3 462 | 448 | 12.9 | 40 311 | 10 702 | 26.6 |
| Screening mammography | 938 | 695 | 74.1 | 5 486 | 4 010 | 73.1 |
| Breast ultrasound | 3 382 | 568 | 16.8 | 43 099 | 7 325 | 17.0 |
| **Imaging - other** | | | | | | |
| X-ray thorax | 1 541 | 118 | 7.7 | 31 782 | 1 831 | 5.8 |
| Abdominal ultrasound | 896 | 64 | 7.1 | 29 802 | 2 213 | 7.4 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; HER2: Human epidermal growth factor receptor 2; BRCA: breast cancer gene; for nomenclature codes based on which diagnostic procedures were defined, please see Appendix 8.1; for several diagnostic procedures the numbers of the subcategories do not add up as for some patients more than one type of staging/diagnostic procedure was billed; $: time frames for punctures, biopsies, cytohistological examinations and genetic testing: 3 months around incidence date; imaging: 3 months around incidence with exclusion of imaging procedures as from start of treatment, and additionally for CT body exclusion of those within 14 days before start RT; *: the summary category 'breast biopsy' comprises incision biopsy, core biopsy and vacuum assisted biopsy; whether it is categorized as 'centre known' or 'centre unknown' depends on the biopsy procedure closest to incidence date. For instance, if for the procedure closest to incidence date (e.g. core biopsy) no information on the hospital is provided in the database, the summary category 'breast biopsy' is classified as 'unknown', even though the subsequent incision biopsy was performed in a hospital which name is provided in the database. The same reasoning applies to summary category 'mammography' (where both diagnostic and screening mammographies were considered); **: according to the protocols prevailing in 2014 - 2018, an ISH test was only to be performed when the HER2 immunohistochemical test result was equivocal (score 2+) or 3+. An immunohistochemical HER2 testing could only be billed as part of the general immunohistochemical examination.*
*Source: BCR-IMA*

## Appendix 11.4. Main therapeutic procedures

**Table 75 – Main treatment schemes in DCIS, by recognition status of the campus of main treatment**

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Surgery < adjuvant RT** | 1 216 | 30.6 | 906 | 31.8 | 69 | 36.7 | 238 | 30.3 | 3 | 2.0 |
| **Surgery < adjuvant systemic Tx** | 411 | 10.3 | 301 | 10.6 | 27 | 14.4 | 83 | 10.6 | 0 | 0.0 |
| Surgery < TT a/o ET | 403 | 10.1 | 295 | 10.4 | 27 | 14.4 | 81 | 10.3 | 0 | 0.0 |
| Surgery < chemo (+ TT a/o ET) | 8 | 0.2 | 6 | 0.2 | 0 | 0.0 | 2 | 0.3 | 0 | 0.0 |
| **Surgery < adjuvant RT + systemic Tx** | 1 015 | 25.5 | 766 | 26.9 | 32 | 17.0 | 216 | 27.5 | 1 | 0.7 |
| Surgery < RT + TT a/o ET | 1 010 | 25.4 | 763 | 26.8 | 32 | 17.0 | 214 | 27.2 | 1 | 0.7 |
| Surgery < chemo/RT + TT a/o ET | 3 | 0.1 | 2 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| Surgery < chemo/RT | 2 | 0.1 | 1 | <0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| **Neoadjuvant Tx < Surgery (< adjuvant Tx)** | 20 | 0.5 | 15 | 0.5 | 2 | 1.1 | 3 | 0.4 | 0 | 0.0 |
| **Chemo a/o RT + TT a/o ET < Surgery < RT or chemo/RT (+ TT a/o ET)** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Chemo a/o RT < Surgery < RT or chemo/RT + TT a/o ET** | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Chemo a/o RT < Surgery < RT or chemo/RT** | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **TT a/o ET < Surgery < chemo a/o RT (+ TT a/o ET)** | 6 | 0.2 | 2 | 0.1 | 1 | 0.5 | 3 | 0.4 | 0 | 0.0 |
| **Chemo a/o RT (+ TT a/o ET) < Surgery (< TT a/o ET)** | 3 | 0.1 | 3 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **TT a/o ET < Surgery (< TT a/o ET)** | 8 | 0.2 | 7 | 0.2 | 1 | 0.5 | 0 | 0.0 | 0 | 0.0 |
| **Chemo a/o RT (+ TT a/o ET) < Surgery < chemo (+ TT a/o ET)** | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Surgery only** | 1 147 | 28.9 | 844 | 29.6 | 58 | 30.9 | 242 | 30.8 | 3 | 2.0 |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Primary systemic and/or radiotherapy (no surgery)** | 55 | 1.4 | 18 | 0.6 | 0 | 0.0 | 4 | 0.5 | 33 | 22.1 |
| ET a/o TT | 27 | 0.7 | 10 | 0.4 | 0 | 0.0 | 3 | 0.4 | 14 | 9.4 |
| Chemo (+ TT a/o ET) | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| RT (+ TT a/o ET) | 27 | 0.7 | 7 | 0.2 | 0 | 0.0 | 1 | 0.1 | 19 | 12.8 |
| Chemo/RT (+ TT a/o ET) | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **No oncological treatment** | 109 | 2.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 109 | 73.2 |
| **Comparison period 2009 - 2013** | 3 830 | | - | | - | | - | | - | |
| **Surgery < adjuvant RT** | 1 099 | 28.7 | - | - | - | - | - | - | - | - |
| **Surgery < adjuvant systemic Tx** | 430 | 11.2 | - | - | - | - | - | - | - | - |
| **Surgery < adjuvant RT + systemic Tx** | 933 | 24.4 | - | - | - | - | - | - | - | - |
| **Neoadjuvant Tx < Surgery (< adjuvant Tx)** | 15 | 0.4 | - | - | - | - | - | - | - | - |
| **Surgery only** | 1 231 | 32.1 | - | - | - | - | - | - | - | - |
| **Primary systemic and/or radiotherapy (no surgery)** | 41 | 1.1 | - | - | - | - | - | - | - | - |
| **No oncological treatment** | 81 | 2.1 | - | - | - | - | - | - | - | - |

*IBC: invasive breast cancer; RT: radiotherapy; TT: targeted therapy; ET: endocrine therapy; Tx: treatment; a/o: and/or; <: followed by.*
*Source: BCR-IMA-HDD*

### Table 76 – Main treatment schemes in IBC, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Surgery < adjuvant RT (no systemic Tx)** | 899 | 2.0 | 634 | 2.1 | 45 | 1.8 | 218 | 2.1 | 2 | 0.1 |
| **Surgery < adjuvant systemic Tx** | 5 176 | 11.2 | 3 505 | 11.6 | 298 | 12.1 | 1 367 | 13.4 | 6 | 0.2 |
| Surgery < TT a/o ET | 3 749 | 8.1 | 2 525 | 8.3 | 225 | 9.2 | 994 | 9.7 | 5 | 0.2 |
| Surgery < chemo (+ TT a/o ET) | 1 427 | 3.1 | 980 | 3.2 | 73 | 3.0 | 373 | 3.6 | 1 | <0.1 |
| **Surgery < adjuvant RT + systemic Tx** | 27 374 | 59.5 | 19 090 | 62.9 | 1 590 | 64.8 | 6 653 | 65.0 | 41 | 1.4 |
| Surgery < RT + TT a/o ET | 17 477 | 38.0 | 12 209 | 40.3 | 1 012 | 41.3 | 4 223 | 41.3 | 33 | 1.1 |
| Surgery < chemo/RT + TT a/o ET | 8 105 | 17.6 | 5 695 | 18.8 | 465 | 19.0 | 1 939 | 19.0 | 6 | 0.2 |
| Surgery < chemo/RT | 1 792 | 3.9 | 1 186 | 3.9 | 113 | 4.6 | 491 | 4.8 | 2 | 0.1 |
| **Neoadjuvant Tx < Surgery (< adjuvant Tx)** | 5 976 | 13.0 | 4 625 | 15.2 | 311 | 12.7 | 1 035 | 10.1 | 5 | 0.2 |
| Chemo a/o RT + TT a/o ET < Surgery < RT or chemo/RT (+ TT a/o ET) | 1 798 | 3.9 | 1 413 | 4.7 | 104 | 4.2 | 281 | 2.7 | 0 | 0.0 |
| Chemo a/o RT < Surgery < RT or chemo/RT + TT a/o ET | 1 590 | 3.5 | 1 206 | 4.0 | 90 | 3.7 | 294 | 2.9 | 0 | 0.0 |
| Chemo a/o RT < Surgery < RT or chemo/RT | 1 534 | 3.3 | 1 188 | 3.9 | 80 | 3.3 | 264 | 2.6 | 2 | 0.1 |
| TT a/o ET < Surgery < chemo a/o RT (+ TT a/o ET) | 427 | 0.9 | 351 | 1.2 | 18 | 0.7 | 56 | 0.5 | 2 | 0.1 |
| Chemo a/o RT (+ TT a/o ET) < Surgery (< TT a/o ET) | 415 | 0.9 | 324 | 1.1 | 12 | 0.5 | 79 | 0.8 | 0 | 0.0 |
| TT a/o ET < Surgery (< TT a/o ET) | 161 | 0.3 | 110 | 0.4 | 4 | 0.2 | 46 | 0.4 | 1 | <0.1 |
| Chemo a/o RT (+ TT a/o ET) < Surgery < chemo (+ TT a/o ET) | 51 | 0.1 | 33 | 0.1 | 3 | 0.1 | 15 | 0.1 | 0 | 0.0 |
| **Surgery only** | 808 | 1.8 | 529 | 1.7 | 35 | 1.4 | 238 | 2.3 | 6 | 0.2 |
| **Primary systemic and/or radiotherapy (no surgery)** | 4 861 | 10.6 | 1 949 | 6.4 | 174 | 7.1 | 718 | 7.0 | 2 020 | 66.9 |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ET a/o TT | 2 818 | 6.1 | 799 | 2.6 | 71 | 2.9 | 363 | 3.5 | 1 585 | 52.5 |
| Chemo (+ TT a/o ET) | 962 | 2.1 | 633 | 2.1 | 73 | 3.0 | 241 | 2.4 | 15 | 0.5 |
| RT (+ TT a/o ET) | 618 | 1.3 | 187 | 0.6 | 0 | 0.0 | 15 | 0.1 | 416 | 13.8 |
| Chemo/RT (+ TT a/o ET) | 463 | 1.0 | 330 | 1.1 | 30 | 1.2 | 99 | 1.0 | 4 | 0.1 |
| **No oncological treatment** | 941 | 2.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 941 | 31.1 |
| **Comparison period 2009 - 2013** | 43 507 | | - | | - | | - | | - | |
| **Surgery < adjuvant RT** | 988 | 2.3 | - | - | - | - | - | - | - | - |
| **Surgery < adjuvant systemic Tx** | 5 281 | 12.1 | - | - | - | - | - | - | - | - |
| **Surgery < adjuvant RT + systemic Tx** | 27 344 | 62.8 | - | - | - | - | - | - | - | - |
| **Neoadjuvant Tx < Surgery (< adjuvant Tx)** | 3 828 | 8.8 | - | - | - | - | - | - | - | - |
| **Surgery only** | 999 | 2.3 | - | - | - | - | - | - | - | - |
| **Primary systemic and/or radiotherapy (no surgery)** | 4 149 | 9.5 | - | - | - | - | - | - | - | - |
| **No oncological treatment** | 918 | 2.1 | - | - | - | - | - | - | - | - |

*IBC: invasive breast cancer; RT: radiotherapy; TT: targeted therapy; ET: endocrine therapy; Tx: treatment; a/o: and/or; <: followed by.*
*Source: BCR-IMA-HDD*

### Table 77 – Surgical procedures in DCIS, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown status | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Breast surgery** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 3 809 | 95.9 | 2 832 | 99.4 | 188 | 100.0 | 782 | 99.5 | 7 | 4.7 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| **Overall** | 3 708 | 96.8 | - | - | - | - | - | - | - | - |
| **Breast conserving surgery (BCS)*** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 2 972 | 74.8 | 2 193 | 76.9 | 143 | 76.1 | 631 | 80.3 | 5 | 3.4 |
| BCS for benign breast lesion | 477 | 12.0 | 347 | 12.2 | 21 | 11.2 | 108 | 13.7 | 1 | 0.7 |
| BCS without SLNB or ALND | 1 521 | 38.3 | 1 139 | 40.0 | 81 | 43.1 | 298 | 37.9 | 3 | 2.0 |
| BCS with SLNB, without ALND | 1 161 | 29.2 | 848 | 29.8 | 58 | 30.9 | 254 | 32.3 | 1 | 0.7 |
| BCS with SLNB and possibly ALND | 32 | 0.8 | 21 | 0.7 | 2 | 1.1 | 9 | 1.1 | 0 | 0.0 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| **Overall** | 2 945 | 76.9 | - | - | - | - | - | - | - | - |
| **Mastectomy*** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 1 078 | 27.1 | 802 | 28.1 | 57 | 30.3 | 216 | 27.5 | 3 | 2.0 |
| Mastectomy without SLNB or ALND | 352 | 8.9 | 257 | 9.0 | 18 | 9.6 | 76 | 9.7 | 1 | 0.7 |
| Mastectomy with SLNB, without ALND | 707 | 17.8 | 549 | 19.3 | 38 | 20.2 | 119 | 15.1 | 1 | 0.7 |
| Mastectomy with SLNB and possibly ALND | 89 | 2.2 | 56 | 2.0 | 2 | 1.1 | 30 | 3.8 | 1 | 0.7 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| **Overall** | 1 218 | 31.8 | - | - | - | - | - | - | - | - |
| **First surgery** | | | | | | | | | | |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown status | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Study period 2014 - 2018*** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| BCS | 2 993 | 78.6 | 2 203 | 77.8 | 145 | 77.1 | 640 | 81.8 | 5 | 71.4 |
| BCS (*stricto sensu*[ss]) | 2 539 | 66.7 | 1 883 | 66.5 | 127 | 67.6 | 525 | 67.1 | 4 | 57.1 |
| Surgery for benign breast lesions | 409 | 10.7 | 290 | 10.2 | 15 | 8.0 | 103 | 13.2 | 1 | 14.3 |
| Excision biopsy | 15 | 0.4 | 15 | 0.5 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Surgery leading to accidental findings | 30 | 0.8 | 15 | 0.5 | 3 | 1.6 | 12 | 1.5 | 0 | 0.0 |
| Mastectomy | 816 | 21.4 | 629 | 22.2 | 43 | 22.9 | 142 | 18.2 | 2 | 28.6 |
| ***Comparison period 2009 - 2013*** | 3 708 | | - | | - | | - | | - | |
| BCS | 2 967 | 80.0 | - | - | - | - | - | - | - | - |
| BCS (*stricto sensu*[ss]) | 2 406 | 64.9 | - | - | - | - | - | - | - | - |
| Surgery for benign breast lesions | 520 | 14.0 | - | - | - | - | - | - | - | - |
| Excision biopsy | 23 | 0.6 | - | - | - | - | - | - | - | - |
| Surgery leading to accidental findings | 18 | 0.5 | - | - | - | - | - | - | - | - |
| Mastectomy | 741 | 20.0 | - | - | - | - | - | - | - | - |
| **Lymph node surgery (separate nomenclature codes)** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 838 | | 190 | | 788 | | 157 | |
| SLNB | 55 | 1.4 | 31 | 1.1 | 11 | 5.9 | 9 | 1.1 | 4 | 2.7 |
| ALND | 3 | 0.1 | 2 | 0.1 | 0 | 0.0 | 0 | 0.0 | 1 | 0.7 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| SLNB | 29 | 0.8 | - | - | - | - | - | - | - | - |
| ALND | 7 | 0.2 | - | - | - | - | - | - | - | - |

*DCIS: ductal carcinoma in situ; BCS: breast conserving surgery; SLN**B**: sentinel lymph node biopsy; ALND: axillary lymph node dissection; *: note that the subchapter 'Total' in the chapters 'BCS' and 'Mastectomy' are not the sum of the other subchapters as for some patients more than one type of breast conserving surgery or mastectomy was billed. The subchapter 'Total' will thus contain as many or less patients than the sum of the other subchapters.*
*Source: BCR-IMA-HDD*

**Table 78 – Surgical procedures in IBC, by recognition status of the campus of main treatment**

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Breast surgery** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 40 233 | 87.4 | 28 383 | 93.6 | 2 279 | 92.9 | 9 511 | 93.0 | 60 | 2.0 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| **Overall** | 38 440 | 88.4 | - | - | - | - | - | - | - | - |
| **Breast conserving surgery (BCS)*** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 28 145 | 61.1 | 19 732 | 65.1 | 1 699 | 69.3 | 6 671 | 65.2 | 43 | 1.4 |
| BCS for benign breast lesion | 966 | 2.1 | 691 | 2.3 | 55 | 2.2 | 210 | 2.1 | 10 | 0.3 |
| BCS without SLNB or ALND | 2 620 | 5.7 | 1 645 | 5.4 | 431 | 17.6 | 531 | 5.2 | 13 | 0.4 |
| BCS with SLNB, without ALND | 20 755 | 45.1 | 14 775 | 48.7 | 1 036 | 42.2 | 4 916 | 48.1 | 28 | 0.9 |
| BCS with SLNB and possibly ALND | 5 590 | 12.1 | 3 898 | 12.9 | 290 | 11.8 | 1 399 | 13.7 | 3 | 0.1 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| **Overall** | 25 951 | 59.7 | - | - | - | - | - | - | - | - |
| **Mastectomy*** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 13 645 | 29.6 | 9 717 | 32.0 | 678 | 27.6 | 3 228 | 31.6 | 22 | 0.7 |
| Mastectomy without SLNB or ALND | 1 923 | 4.2 | 1 395 | 4.6 | 93 | 3.8 | 434 | 4.2 | 1 | 0.0 |
| Mastectomy with SLNB, without ALND | 4 395 | 9.5 | 3 301 | 10.9 | 227 | 9.3 | 860 | 8.4 | 7 | 0.2 |
| Mastectomy with SLNB and possibly ALND | 7 794 | 16.9 | 5 384 | 17.8 | 369 | 15.0 | 2 027 | 19.8 | 14 | 0.5 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| **Overall** | 14 528 | 33.4 | - | - | - | - | - | - | - | - |
| **First surgery** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| BCS | 27 892 | 69.3 | 19 534 | 68.8 | 1 681 | 73.8 | 6 634 | 69.8 | 43 | 71.7 |
| BCS (*stricto sensu*[ss]) | 27 366 | 68.0 | 19 184 | 67.6 | 1 652 | 72.5 | 6 496 | 68.3 | 34 | 56.7 |
| Surgery for benign breast lesions | 516 | 1.3 | 345 | 1.2 | 29 | 1.3 | 133 | 1.4 | 9 | 15.0 |
| Excision biopsy | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Surgery leading to accidental findings | 9 | <0.1 | 4 | <0.1 | 0 | 0.0 | 5 | 0.1 | 0 | 0.0 |
| Mastectomy | 12 341 | 30.7 | 8 849 | 31.2 | 598 | 26.2 | 2 877 | 30.3 | 17 | 28.3 |
| ***Comparison period 2009 - 2013*** | 38 440 | | - | | - | | - | | - | |
| BCS | 25 708 | 66.9 | - | - | - | - | - | - | - | - |
| BCS (*stricto sensu*[ss]) | 24 908 | 64.8 | - | - | - | - | - | - | - | - |
| Surgery for benign breast lesions | 787 | 2.1 | - | - | - | - | - | - | - | - |
| Excision biopsy | 3 | <0.1 | - | - | - | - | - | - | - | - |
| Surgery leading to accidental findings | 10 | <0.1 | - | - | - | - | - | - | - | - |
| Mastectomy | 12 732 | 33.1 | - | - | - | - | - | - | - | - |
| **Lymph node surgery (separate nomenclature codes)** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| SLNB | 1 452 | 3.2 | 901 | 3.0 | 320 | 13.0 | 220 | 2.2 | 11 | 0.4 |
| ALND | 1 387 | 3.0 | 879 | 2.9 | 116 | 4.7 | 373 | 3.6 | 19 | 0.6 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| SLNB | 578 | 1.3 | - | - | - | - | - | - | - | - |
| ALND | 1 951 | 4.5 | - | - | - | - | - | - | - | - |

*IBC: invasive breast cancer; BCS: breast conserving surgery; SLNB: sentinel lymph node biopsy; ALND: axillary lymph node dissection; *: note that the subchapter 'Total' in the chapters 'BCS' and 'Mastectomy' are not the sum of the other subchapters as for some patients more than one type of breast conserving surgery or mastectomy was billed. The subchapter 'Total' will thus contain as many or less patients than the sum of the other subchapters.*
*Source: BCR-IMA-HDD*

### Table 79 – Radiotherapy in DCIS, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 2 267 | 57.1 | 1 684 | 59.1 | 102 | 54.3 | 458 | 58.3 | 23 | 15.4 |
| **Operated patients** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| Before surgery | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Adjuvant | 2 239 | 58.8 | 1 676 | 59.2 | 102 | 54.3 | 457 | 58.4 | 4 | 57.1 |
| **Non-operated patients** | 164 | | 18 | | 0 | | 4 | | 142 | |
| In non-operated patients | 27 | 16.5 | 7 | 38.9 | 0 | 0.0 | 1 | 25.0 | 19 | 13.4 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| ***Overall*** | 2 057 | 53.7 | - | - | - | - | - | - | - | - |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; percentages of adjuvant radiotherapy and radiotherapy given before surgery are calculated on the total number of operated patients; percentages 'In non-operated patients' are calculated on the total number of non-operated patients.*
*Source: BCR-IMA-HDD*

### Table 80 – Radiotherapy in IBC, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 34 699 | 75.4 | 24 393 | 80.4 | 1 956 | 79.7 | 7 883 | 77.1 | 467 | 15.5 |
| **Operated patients** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |
| Before surgery | 26 | 0.1 | 19 | 0.1 | 1 | <0.1 | 6 | 0.1 | 0 | 0.0 |
| Adjuvant | 33 610 | 83.5 | 23 872 | 84.1 | 1 926 | 84.5 | 7 765 | 81.6 | 47 | 78.3 |
| **Non-operated patients** | 5 802 | | 1 949 | | 174 | | 718 | | 2 961 | |
| In non-operated patients | 1 081 | 18.6 | 517 | 26.5 | 30 | 17.2 | 114 | 15.9 | 420 | 14.2 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| ***Overall*** | 32 712 | 75.2 | - | - | - | - | - | - | - | - |

*IBC: invasive breast cancer; percentages of adjuvant radiotherapy and radiotherapy given before surgery are calculated on the total number of operated patients. Percentages 'In non-operated patients' are calculated on the total number of non-operated patients.*
*Source: BCR-IMA-HDD*

### Table 81 – Systemic treatment in DCIS, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Targeted therapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** (anti-HER2 and other) | 4 | 0.1 | 3 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| **Operated patients** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| Neoadjuvant only | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Adjuvant only | 2 | 0.1 | 1 | <0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| Both neoadjuvant and adjuvant | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Non-operated patients** | 164 | | 18 | | 0 | | 4 | | 142 | |
| In non-operated patients | 1 | 0.6 | 1 | 5.6 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Anti-HER2 only** | 3 | 0.1 | 2 | 0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| **Operated patients** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| Neoadjuvant only | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Adjuvant only | 2 | 0.1 | 1 | <0.1 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| Both neoadjuvant and adjuvant | 1 | <0.1 | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Non-operated patients** | 164 | | 18 | | 0 | | 4 | | 142 | |
| In non-operated patients | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| ***Overall*** | 5 | 0.1 | - | - | - | - | - | - | - | - |
| **Chemotherapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 19 | 0.5 | 15 | 0.5 | 0 | 0.0 | 4 | 0.5 | 0 | 0.0 |
| **Operated patients** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| Neoadjuvant only | 3 | 0.1 | 3 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| Adjuvant only | 13 | 0.3 | 9 | 0.3 | 0 | 0.0 | 4 | 0.5 | 0 | 0.0 |
| Both neoadjuvant and adjuvant | 2 | 0.1 | 2 | 0.1 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Non-operated patients** | 164 | | 18 | | 0 | | 4 | | 142 | |
| In non-operated patients | 1 | 0.6 | 1 | 5.6 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| ***Overall*** | 19 | 0.5 | - | - | - | - | - | - | - | - |
| **Endocrine therapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 3 973 | | 2 850 | | 188 | | 786 | | 149 | |
| **Overall** | 1 476 | 37.2 | 1 086 | 38.1 | 61 | 32.5 | 304 | 38.7 | 25 | 16.8 |
| **Operated patients** | 3 809 | | 2 832 | | 188 | | 782 | | 7 | |
| Neoadjuvant only | 1 | <0.1 | 0 | 0.0 | 0 | 0.0 | 1 | 0.1 | 0 | 0.0 |
| Adjuvant only | 1 423 | 37.4 | 1 066 | 37.6 | 59 | 31.4 | 297 | 38.0 | 1 | 14.3 |
| Both neoadjuvant and adjuvant | 13 | 0.3 | 9 | 0.3 | 2 | 1.1 | 2 | 0.3 | 0 | 0.0 |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Non-operated patients** | 164 | | 18 | | 0 | | 4 | | 142 | |
| In non-operated patients | 39 | 23.8 | 11 | 61.1 | 0 | 0.0 | 4 | 100.0 | 24 | 16.9 |
| ***Comparison period 2009 - 2013*** | 3 830 | | - | | - | | - | | - | |
| ***Overall*** | 1 401 | 36.6 | - | - | - | - | - | - | - | - |

*DCIS: ductal carcinoma in situ; BC: breast cancer; HER2: Human epidermal growth factor receptor 2; percentages of (neo-)adjuvant treatment are calculated on the total number of operated patients. Percentages 'In non-operated patients' are calculated on the total number of non-operated patients.*
*Source: BCR-IMA-HDD*

### Table 82 – Systemic treatment in IBC, by recognition status of the campus of main treatment

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Targeted therapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** (anti-HER2 and other) | 6 166 | 13.4 | 4 252 | 14.0 | 349 | 14.2 | 1 364 | 13.3 | 201 | 6.7 |
| **Operated patients** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |
| Neoadjuvant only | 58 | 0.1 | 47 | 0.2 | 0 | 0.0 | 11 | 0.1 | 0 | 0.0 |
| Adjuvant only | 3 355 | 8.3 | 2 293 | 8.1 | 200 | 8.8 | 861 | 9.1 | 1 | 1.7 |
| Both neoadjuvant and adjuvant | 1 737 | 4.3 | 1 350 | 4.8 | 96 | 4.2 | 291 | 3.1 | 0 | 0.0 |
| **Non-operated patients** | 5 802 | | 1 949 | | 174 | | 718 | | 2 961 | |
| In non-operated patients | 1 016 | 17.5 | 562 | 28.8 | 53 | 30.5 | 201 | 28.0 | 200 | 6.8 |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Anti-HER2 only** | 5 625 | 12.2 | 4 005 | 13.2 | 323 | 13.2 | 1 281 | 12.5 | 16 | 0.5 |
| **Operated patients** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |
| Neoadjuvant only | 46 | 0.1 | 36 | 0.1 | 0 | 0.0 | 10 | 0.1 | 0 | 0.0 |
| Adjuvant only | 3 278 | 8.2 | 2 245 | 7.9 | 192 | 8.4 | 840 | 8.8 | 1 | 1.7 |
| Both neoadjuvant and adjuvant | 1 726 | 4.3 | 1 343 | 4.7 | 94 | 4.1 | 289 | 3.0 | 0 | 0.0 |
| **Non-operated patients** | 5 802 | | 1 949 | | 174 | | 718 | | 2 961 | |
| In non-operated patients | 575 | 9.9 | 381 | 19.6 | 37 | 21.3 | 142 | 19.83 | 15 | 0.5 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| ***Overall*** | 4 678 | 10.8 | - | - | - | - | - | - | - | - |
| **Chemotherapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 18 214 | 39.6 | 13 055 | 43.0 | 1 045 | 42.6 | 4 084 | 39.9 | 30 | 1.0 |
| **Operated patients** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |
| Neoadjuvant only | 4 872 | 12.1 | 3 761 | 13.3 | 269 | 11.8 | 842 | 8.9 | 0 | 0.0 |
| Adjuvant only | 11 416 | 28.4 | 7 938 | 28.0 | 653 | 28.7 | 2 816 | 29.6 | 9 | 15.0 |
| Both neoadjuvant and adjuvant | 501 | 1.3 | 393 | 1.4 | 20 | 0.9 | 86 | 0.9 | 2 | 3.3 |
| **Non-operated patients** | 5 802 | | 1 949 | | 174 | | 718 | | 2 961 | |
| In non-operated patients | 1 425 | 24.6 | 963 | 49.4 | 103 | 59.2 | 340 | 47.4 | 19 | 0.6 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| ***Overall*** | 17 720 | 40.7 | - | - | - | - | - | - | - | - |

| Category | Total | | Coordinating breast clinics | | Satellite breast clinics | | Campus not recognised for BC | | Campus unknown | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | % | N | % | N | % | N | % | N | % |
| **Endocrine therapy** | | | | | | | | | | |
| ***Study period 2014 - 2018*** | 46 035 | | 30 332 | | 2 453 | | 10 229 | | 3 021 | |
| **Overall** | 36 762 | 79.9 | 24 510 | 80.8 | 1 982 | 80.8 | 8 280 | 81.0 | 1 990 | 65.9 |
| **Operated patients** | 40 233 | | 28 383 | | 2 279 | | 9 511 | | 60 | |
| Neoadjuvant only | 93 | 0.2 | 81 | 0.3 | 6 | 0.3 | 5 | 0.1 | 1 | 1.7 |
| Adjuvant only | 31 934 | 79.4 | 22 444 | 79.1 | 1 829 | 80.3 | 7 618 | 80.1 | 43 | 71.7 |
| Both neoadjuvant and adjuvant | 793 | 2.0 | 628 | 2.2 | 35 | 1.5 | 128 | 1.4 | 2 | 3.3 |
| **Non-operated patients** | 5 802 | | 1 949 | | 174 | | 718 | | 2 961 | |
| In non-operated patients | 3 942 | 67.9 | 1 357 | 69.6 | 112 | 64.4 | 529 | 73.7 | 1 944 | 65.7 |
| ***Comparison period 2009 - 2013*** | 43 507 | | - | | - | | - | | - | |
| ***Overall*** | 34 385 | 79.0 | - | - | - | - | - | - | - | - |

*IBC: invasive breast cancer; HER2: human epidermal growth factor receptor 2; percentages of (neo-)adjuvant treatment are calculated on the total number of operated patients. Percentages 'In non-operated patients' are calculated on the total number of non-operated patients.*
*Source: BCR-IMA-HDD*

Table 83 provides an **overview of systemic treatment**[ggg] that was provided to **patients with non-metastatic** (i.e. combined stage 0, I, II, III) IBC. These data are further explored in Table 84 where the various classes of systemic therapy are provided[hhh]. Overall, 83.3% of non-operated patients (N=2 134/2 561) with M0 IBC received any type of systemic therapy (Table 83**), i**n most of them this was endocrine therapy (73.4%, Table 84), more precisely aromatase inhibitors (35.0%) and oestrogen receptor blockers (33.7%). Chemotherapy was recorded for 14.9% of non-operated patients, either alone or in combination with targeted and/or endocrine therapy; the combination of an anthracycline agent with cyclophosphamide and taxane (TAC/AC-T) was most frequently offered (6.1%). A minority of non-operated patients received any targeted therapy (6.1%), mostly anti-HER2 therapy (4.9%).

Among the 39 404 women with M0 IBC who had surgery, 14.1% received any type of systemic therapy in the neoadjuvant setting (Table 83); for most of them this was chemotherapy (12.8%, Table 84), more precisely the combination of an anthracycline agent with cyclophosphamide and taxane (7.9%). In the neoadjuvant setting also targeted therapy (4.2%), mostly anti-HER2 therapy (4.1%) and to a minimal extend endocrine therapy (2.0%) was provided. In the adjuvant setting, 81.7% of patients with M0 IBC received any type of systemic therapy. Endocrine therapy was offered to 73.6% of these patients; most often oestrogen receptor blockers (40.2%) or aromatase inhibitors (29.0%) were prescribed. Chemotherapy was recorded for 28.5% of patients with M0 IBC; they received the combination of an anthracycline agent with cyclophosphamide and taxane (17.3%), the combination of fluorouracil, anthracycline, cyclophosphamide and taxane (FAC + taxane, 4.0%) or another (combination of) product(s). Targeted therapy, almost always anti-HER2 therapy, was recorded for 8.0% of patients in the adjuvant setting.

**Table 83 – Systemic treatment modalities in patients with invasive, non-metastatic (i.e. combined stage 0, I, II, III) BC**

| | Non-operated patients N=2 561 | | Operated patients N=39 404 | | | |
|---|---|---|---|---|---|---|
| | | | Neoadjuvant setting~ | | Adjuvant setting~ | |
| | N | %** | N | %*** | N | %*** |
| **Systemic therapy*** | **2 134** | **83.3** | **5 573** | **14.1** | **32 197** | **81.7** |
| **Endocrine therapy only** | 1 721 | 67.2 | 528 | 1.3 | 20 936 | 53.1 |
| **Chemotherapy only** | 166 | 6.5 | 3 236 | 8.2 | 2 172 | 5.5 |
| **Targeted therapy only** | 6 | 0.2 | 1 | <0.1 | 13 | < 0.1 |

ggg A certain type of systemic therapy is reported when a corresponding Anatomical Therapeutic Chemical (ATC) code is charged at least once within one month before until nine months after incidence for patients who did not undergo surgery, between one month before incidence until the date of surgery for the neoadjuvant setting, and within nine months after surgery for the adjuvant setting.

hhh In this table combinations of systemic therapy were not analysed to the detail of the number of cycles or whether the individual products in combinations are administered sequentially or concomitantly. Per category, (combinations of) active agents are shown when they represent >20% of the corresponding category (with all patients with invasive non-metastatic breast cancer who received this category as the denominator); that is the reason why the various subtotals do not (always) add up to the bold total above.

| | Non-operated patients N=2 561 | | Operated patients N=39 404 | | | |
|---|---|---|---|---|---|---|
| | | | Neoadjuvant setting~ | | Adjuvant setting~ | |
| | N | %** | N | %*** | N | %*** |
| **Chemotherapy + endocrine therapy** | 90 | 3.5 | 166 | 0.4 | 5 930 | 15.1 |
| **Chemotherapy + targeted therapy** | 81 | 3.2 | 1 562 | 4.0 | 1 000 | 2.5 |
| **Endocrine therapy + targeted therapy** | 25 | 1.0 | 10 | <0.1 | 35 | 0.1 |
| **Chemotherapy + targeted therapy + endocrine therapy** | 45 | 1.8 | 70 | 0.2 | 2 111 | 5.4 |

*BC: breast cancer; * A certain type of systemic therapy is reported when a corresponding ATC-code is charged at least once within one month before incidence until nine months after incidence for patients without surgery, between one month before surgery until the date of surgery for the neoadjuvant setting and within nine months after surgery for the adjuvant setting. All ATC codes for chemotherapy, targeted therapy and endocrine therapy can be consulted in Appendix 8.1.2; ~ 4 099 patients received neoadjuvant and adjuvant systemic therapy and are only included in the category neoadjuvant systemic therapy; 1 634 operated patients received no neoadjuvant or adjuvant systemic treatment ;** non-operated patients as the denominator; *** operated patients as the denominator.*
*Source: BCR-IMA*

### Table 84 – Systemic treatment products in patients with invasive, non-metastatic (i.e. combined stage 0, I, II, III) BC

| | Non-operated patients (N=2 561) | | Operated patients (N=39 404) | | | |
|---|---|---|---|---|---|---|
| | Systemic therapy* N=2 134 | | Neoadjuvant systemic therapy*~ N=5 573 | | Adjuvant systemic therapy*~ N=32 197 | |
| | N | %** | N | %*** | N | %*** |
| **Chemotherapy** | | | | | | |
| Any chemotherapy | 382 | 14.9 | 5 034 | 12.8 | 11 213 | 28.5 |
| **Anthracycline agent + cyclophosphamide + taxane (TAC/AC-T)° ϕ** | **156** | **6.1** | **3 097** | **7.9** | **6 827** | **17.3** |
| Epirubicin + paclitaxel + cyclophosphamide | 135 | 5.3 | 2 459 | 6.2 | 5 778 | 14.7 |
| **Anthracycline agent + cyclophosphamide + taxane + platinum derivative (TAC/AC-T + platinum derivative)° ϕ** | **34** | **1.3** | **889** | **2.3** | **263** | **0.7** |
| Epirubicin + paclitaxel + cyclophosphamide + carboplatin | 30 | 1.2 | 817 | 2.1 | 219 | 0.6 |
| **Fluorouracil + anthracycline + cyclophosphamide (FAC)° ϕ** | **9** | **0.4** | **9** | **< 0.1** | **115** | **0.3** |

| | Non-operated patients (N=2 561) | | Operated patients (N=39 404) | | | |
|---|---|---|---|---|---|---|
| | Systemic therapy* N=2 134 | | Neoadjuvant systemic therapy*~ N=5 573 | | Adjuvant systemic therapy*~ N=32 197 | |
| | N | %** | N | %*** | N | %*** |
| Fluorouracil + epirubicin + cyclophospamide (FEC) | 8 | 0.3 | 9 | < 0.1 | 113 | 0.3 |
| **Fluorouracil + anthracycline + cyclophosphamide + taxane (FAC + taxane)° ϕ** | **25** | **1.0** | **472** | **1.2** | **1 580** | **4.0** |
| Fluorouracil + epirubicin + cyclophosphamide + docetaxel | 19 | 0.7 | 362 | 0.9 | 1 162 | 3.0 |
| Fluorouracil + epirubicin + cyclophosphamide + paclitaxel | 4 | 0.2 | 87 | 0.2 | 343 | 0.9 |
| **Anthracycline + cyclophosphamide (AC)° ϕ** | **29** | **1.1** | **63** | **0.2** | **224** | **0.6** |
| Epirubicin + cyclophosphamide (EC) | 27 | 1.1 | 52 | 0.1 | 197 | 0.5 |
| **Anthracycline + taxane° ϕ** | **2** | **0.1** | **4** | **< 0.1** | **14** | **< 0.1** |
| Epirubicin + paclitaxel | 1 | < 0.1 | 1 | < 0.1 | 12 | < 0.1 |
| Epirubicin + docetaxel | 0 | < 0.1 | 3 | < 0.1 | 2 | < 0.1 |
| **Taxane + platinum derivative° ϕ** | **23** | **0.9** | **96** | **0.2** | **72** | **0.2** |
| Paclitaxel + carboplatin | 19 | 0.7 | 72 | 0.2 | 36 | 0.1 |
| Docetaxel + carboplatin | 4 | 0.2 | 17 | < 0.1 | 31 | 0.1 |
| **Taxane + cyclophosphamide° ϕ** | **16** | **0.6** | **122** | **0.3** | **1 099** | **2.8** |
| Docetaxel + cyclophosphamide | 13 | 0.5 | 106 | 0.3 | 1 031 | 2.6 |
| **Cyclophosphamide + methotrexate + fluorouracil (CMF)° ϕ** | **1** | **< 0.1** | **4** | **< 0.1** | **8** | **< 0.1** |
| **Single agent°** | **75** | **2.9** | **207** | **0.5** | **935** | **3.1** |
| Paclitaxel | 42 | 1.6 | 140 | 0.4 | 852 | 2.2 |
| **Other combinations° ϕ** | **12** | **0.5** | **71** | **0.2** | **76** | **0.4** |
| **Targeted therapy** | | | | | | |
| Any targeted therapy | 157 | 6.1 | 1 643 | 4.2 | 3 159 | 8.0 |
| **Anti-HER2- therapy°** | **125** | **4.9** | **1 634** | **4.1** | **3 138** | **8.0** |
| Trastuzumab | 88 | 3.4 | 1 499 | 3.8 | 3 098 | 7.9 |
| **Other targeted therapy° £** | **32** | **1.2** | **9** | **< 0.1** | **20** | **0.1** |
| Palbociclib | 27 | 1.1 | 5 | < 0.1 | 12 | 0.0 |

| | Non-operated patients (N=2 561) | | Operated patients (N=39 404) | | | |
|---|---|---|---|---|---|---|
| | Systemic therapy* N=2 134 | | Neoadjuvant systemic therapy*~ N=5 573 | | Adjuvant systemic therapy*~ N=32 197 | |
| | N | %** | N | %*** | N | %*** |
| Bevacizumab | 4 | 0.2 | 2 | < 0.1 | 8 | < 0.1 |
| **Anti-HER2 + other targeted therapy°** | / | / | / | / | **1** | **< 0.1** |
| | | | | | | |
| Any endocrine therapy | 1 881 | 73.4 | 774 | 2.0 | 29 012 | 73.6 |
| **Aromatase inhibitors°** | **897** | **35.0** | **329** | **0.8** | **11 426** | **29.0** |
| Letrozol | 699 | 27.3 | 271 | 0.7 | 8 867 | 22.5 |
| Anastrazol | 186 | 7.3 | 53 | 0.1 | 2 317 | 5.9 |
| **Oestrogen receptor blockers°** | **864** | **33.7** | **286** | **0.7** | **15 842** | **40.2** |
| Tamoxifen | 862 | 33.7 | 251 | 0.6 | 15 826 | 40.2 |
| **Ovarian suppression°** | **5** | **0.2** | **122** | **0.3** | **67** | **0.2** |
| Goserelin | 5 | 0.2 | 110 | 0.3 | 60 | 0.2 |
| **Ovarian suppression + aromatase inhibitor°** | **5** | **0.2** | **19** | **< 0.1** | **384** | **1.0** |
| Goserelin + letrozol | 4 | 0.2 | 15 | < 0.1 | 215 | 0.6 |
| **Ovarian suppression + oestrogen receptor blockers°** | **6** | **0.2** | **4** | **< 0.1** | **335** | **0.9** |
| Goserelin + tamoxifen | 6 | 0.2 | 4 | < 0.1 | 327 | 0.8 |
| **Aromatase inhibitor + oestrogen receptor blocker°** | **101** | **3.9** | **13** | **< 0.1** | **901** | **2.3** |
| Letrozol + tamoxifen | 69 | 2.7 | 10 | < 0.1 | 602 | 1.5 |
| Anastrozol + tamoxifen | 19 | 0.7 | 2 | < 0.1 | 249 | 0.6 |
| **Ovarian suppression + aromatase inhibitor + oestrogen receptor blocker°** | **3** | **0.1** | **1** | **< 0.1** | **56** | **0.1** |
| Letrozol + tamoxifen + goserelin | 3 | 0.1 | 1 | < 0.1 | 31 | 0.1 |

*BC: breast cancer; HER2: Human epidermal growth factor receptor 2; *: a certain type of systemic therapy is reported when a corresponding ATC-code is charged at least once within one month before incidence until nine months after incidence for patients without surgery, between one month before surgery until the date of surgery for the neoadjuvant setting, and within nine months after surgery for the adjuvant setting; all ATC codes for chemotherapy, targeted therapy and endocrine therapy can be consulted in Appendix 8.1.2; ~: 4 099 patients received neoadjuvant and adjuvant systemic therapy and are only included in the category neoadjuvant systemic therapy; 1 634 operated patients received no neoadjuvant or adjuvant systemic treatment; °: therapy combinations are not analysed to the detail of the number of cycles or whether the individual products in combinations are administered sequentially or concomitantly; per category, (combinations of) active agents are shown when they represent >20% of the corresponding category (all patients*

*with invasive non-metastatic BC who received this category as the denominator); ϕ: patients who received this combination of chemotherapy may have also received vinorelbine, capecitabine, gemcitabine, or eribulin within the corresponding time frame; £: drugs included in this category are CDK-inhibitors (Palbociclib, ribociclib, abemaciclib), everolimus, and bevacizumab; all ATC-codes for other targeted therapy can be consulted in Appendix 8.1.2; $: 4 patients who received a certain type/combination of endocrine therapy have also received megestrol within the corresponding time frame; **: non-operated patients as the denominator; ***: operated patients as the denominator.*
*Source: BCR-IMA*

Table 85 provides an overview of some patient and tumour characteristics of **patients from whom no oncological treatment was identified** in the administrative database. The mean age of this patient subgroup was 12.3 years higher than the overall group of patients with IBC; for the patients with DCIS this difference was less pronounced (61.5 years vs. 58.6 years). While in the overall group of patients with DCIS and IBC 70.7% and 54.3% had an asymptomatic WHO performance status at the time of diagnosis, the respective proportions in the subgroup who did not receive oncological treatment was much lower (45.0% and 17.5%, respectively). In line with this finding, for 51.4% and 36.2% of patients with DCIS and IBC who did not receive oncological treatment, no comorbidities were recorded, while in the overall group of patients with DCIS and IBC the respective proportions were higher (i.e. 61.5% and 52.9%. respectively). As said before, the majority of patients with IBC with known clinical stage was diagnosed with an early stage of the tumour (cIA: 45.7%. cIIA: 28.1%. cIIB: 10.3%) and only 7.1% with cStage IV. In the subgroup of patients with IBC who did not undergo oncological treatment, 39.5% was diagnosed with cStage IV and for 34.4% no clinical stage information was sent to the BCR. Last, based on follow-up data up to 1 March 2022, one in two patients with IBC who did not undergo oncological treatment had died within six months after diagnosis; in the DCIS subgroup the respective proportion was 31.6%.

**Table 85 – Characteristics of patients diagnosed with DCIS or IBC who received no oncological treatment**

| Category | DCIS (N=109) | | IBC (N=941) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Age at diagnosis** | | | | |
| Mean, SD (years) | 61.5 (15.5) | | 74.9 (15.2) | |
| Median. Q1-Q3 (years) | 59.0 (49.0-70.0) | | 80.0 (64.0-87.0) | |
| <40 years | 5 | 4.6 | 22 | 2.3 |
| 40-49 years | 23 | 21.1 | 57 | 6.1 |
| 50-59 years | 27 | 24.8 | 83 | 8.8 |
| 60-69 years | 24 | 22.0 | 138 | 14.7 |
| 70-79 years | 12 | 11.0 | 167 | 17.7 |
| 80+ years | 18 | 16.5 | 474 | 50.4 |

| Category | DCIS (N=109) | | IBC (N=941) | |
|---|---|---|---|---|
| | N | % | N | % |
| **WHO performance status at time of diagnosis** | | | | |
| 0 – Asymptomatic | 49 | 45.0 | 165 | 17.5 |
| 1 – Symptomatic but completely ambulatory | 13 | 11.9 | 303 | 32.2 |
| 2 – Symptomatic. <50% in bed during the day | 2 | 1.8 | 72 | 7.7 |
| 3 – Symptomatic. >50% in bed. but not bedbound | 3 | 2.8 | 50 | 5.3 |
| 4 – Bedbound | 0 | 0.0 | 26 | 2.8 |
| Missing | 42 | 38.5 | 325 | 34.5 |
| **Total comorbidities** | | | | |
| 0 | 56 | 51.4 | 341 | 36.2 |
| 1 | 37 | 33.9 | 416 | 44.2 |
| 2 | 16 | 14.7 | 167 | 17.7 |
| 3 | 0 | 0.0 | 17 | 1.8 |
| **Comorbidities** | | | | |
| Cardiac disease | 46 | 42.2 | 565 | 60.0 |
| Respiratory diseases | 15 | 13.8 | 91 | 9.7 |
| Diabetes | 8 | 7.3 | 145 | 15.4 |
| **Number of inpatient bed days in year prior to incidence** | | | | |
| 0 days | 78 | 71.6 | 472 | 50.2 |
| 1-5 days | 16 | 14.7 | 167 | 17.7 |
| 6-15 days | 10 | 9.2 | 151 | 16.0 |
| >15 days | 5 | 4.6 | 151 | 16.0 |
| **Clinical stage*** | | | | |

| Category | DCIS (N=109) | | IBC (N=941) | |
|---|---|---|---|---|
| | N | % | N | % |
| 0 | 49 | 100.0 | 1 | 0.2 |
| IA | 0 | 0.0 | 110 | 17.8 |
| IB | 0 | 0.0 | 0 | 0.0 |
| IIA | 0 | 0.0 | 138 | 22.4 |
| IIB | 0 | 0.0 | 52 | 8.4 |
| IIIA | 0 | 0.0 | 15 | 2.4 |
| IIIB | 0 | 0.0 | 53 | 8.6 |
| IIIC | 0 | 0.0 | 4 | 0.6 |
| IV | 0 | 0.0 | 244 | 39.5 |
| Unknown | 60 | 55.0 | 324 | 34.4 |
| **Grade** | | | | |
| I | 12 | 11.0 | 96 | 10.2 |
| II | 17 | 15.6 | 332 | 35.3 |
| III | 20 | 18.3 | 238 | 25.3 |
| Unknown | 60 | 55.0 | 275 | 29.2 |
| **Vital status (Follow-up until 01/03/2022)** | | | | |
| Alive | 84 | 77.1 | 241 | 25.6 |
| Dead | 19 | 17.4 | 694 | 73.8 |
| Lost to follow-up | 6 | 5.5 | 6 | 0.6 |
| **Survival length of those who died in days (Follow-up until 01/03/2022)** | | | | |
| 0 – 90 days | 4 | 21.1 | 303 | 43.7 |
| 91 – 180 days | 2 | 10.5 | 55 | 7.9 |

| Category | DCIS (N=109) | | IBC (N=941) | |
|---|---|---|---|---|
| | N | % | N | % |
| 181 – 270 days | 0 | 0.0 | 34 | 4.9 |
| 271 – 360 days | 1 | 5.3 | 26 | 3.8 |
| > 360 days | 12 | 63.2 | 276 | 39.8 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; SD: standard deviation; IQ: inter-quartile; *: percentages for stages 0-IV were calculated excluding the unknown category*
*Source: BCR-IMA*

## Appendix 11.5. Referral between hospitals

Overall, 75.0% of patients with DCIS and 78.4% of patients with IBC, were diagnosed and treated in the same hospital[iii] (Table 86). For 19.2% of patients with DCIS and 15.1% of patients with IBC, diagnostic and therapeutic procedures were performed in more than one hospital. For the remaining patients the centre of diagnosis and/or the centre of main treatment was unknown. The data for 2009 - 2013 were comparable (Table 87).

**Table 86 – Referral patterns for patients with DCIS and IBC, 2014 - 2018**

| Referral pattern | DCIS (n=3 973; %) | IBC (n=46 035; %) | Total |
|---|---|---|---|
| **Both centres are different** | 762 (19.2) | 6 948 (15.1) | 7 710 |
| **Both centres are the same** | 2 978 (75.0) | 36 099 (78.4) | 39 077 |
| **Both centres unknown** | 18 (0.5) | 175 (0.4) | 193 |
| **Only centre of diagnosis known** | 95 (2.4) | 1129 (2.5) | 1 224 |
| **Only centre of main treatment known** | 120 (3.0) | 1 684 (3.7) | 1 804 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer.*
*Source: BCR-IMA*

[iii] As most diagnostic procedures are performed when patients are not admitted in hospital, the exact campus of diagnostic procedures could not be revealed because campus identification is based on hospital discharge data. Consequently, we could not perform these analysis at campus level.

**Table 87 – Referral patterns for patients with DCIS and IBC, 2009 – 2013**

| Referral pattern | DCIS (n=3 830; %) | IBC (n=43 507; %) | Total |
|---|---|---|---|
| **Both centres are different** | 765 (20.0) | 5 966 (13.7) | 6 731 |
| **Both centres are the same** | 2 754 (71.9) | 32 997 (75.8) | 35 751 |
| **Both centres unknown** | 13 (0.3) | 231 (0.5) | 244 |
| **Only centre of diagnosis known** | 75 (2.0) | 1 114 (2.6) | 1 189 |
| **Only centre of main treatment known** | 223 (5.8) | 3 199 (7.4) | 3 422 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer.*
*Source: BCR-IMA*

# Appendix 11.6. Observed and relative survival

## *Appendix 11.6.1. Documentation sheet*

| Title | The 5-year observed and relative survival after a diagnosis of IBC |
|---|---|
| **Rationale** | Treatment of any cancer aims to prolong survival and improve quality of life of the involved patient.<br>Observed survival reflects the probability of a patient to be still alive at some specified time after the diagnosis of cancer. It considers deaths from all causes, cancer related and non-cancer related. Relative survival, on the contrary, is specific to the cancer under study and evaluates the impact of the cancer on survival. In other words, relative survival estimates survival excluding mortality due to background causes.<br>This indicator reflects the effectiveness of a country's healthcare system to screen, early detect and treat patients with cancer. |
| **Type of QI** | Outcome |
| **Calculation** | a) The **5-year observed survival** probability is computed using the Kaplan Meier survival method; also median observed survival is provided (if feasible/available)<br>• Cohort to be taken into account:<br>i. All patients with IBC diagnosed in 2014 - 2018 (including patients who did not receive any oncological treatment)<br>ii. All patients with IBC diagnosed in 2014 - 2018 who had breast surgery (BCS or mastectomy), excluding M1 and Mx patients<br>• Stratification variables: cf. subgroup analysis<br>b) The **5-year relative survival** is computed as the ratio of the 5-year observed survival for the female population diagnosed with BC (= probability to be alive at 5 years after the diagnosis) and the 5-year expected survival for a comparable group from the general female population residing in Belgium (matched on age, residence and calendar year).<br>The relative survival is expressed as a percentage, and is related to the excess mortality that can be attributed to the cancer under study. For instance, a relative survival proportion of 50% indicates that the all-cause survival probability for patients who were diagnosed with cancer is only half of the probability in a comparable group sampled from the general population with the same characteristics (e.g. age, residence and calendar year).<br>• Cohort to be taken into account:<br>i. All patients with IBC diagnosed in 2014 - 2018 (including patients who did not receive any oncological treatment)<br>ii. All patients with IBC diagnosed in 2014 - 2018 who had breast surgery (BCS or mastectomy), excluding M1 and Mx patients<br>• Stratification variables: Stage & age at diagnosis, and if possible the presence of comorbidities<br>• Excess hazard ratios: The term 'excess' refers to the fact that there is also a certain risk of death in the general population, and only the additional risk of death in BC patients (i.e. the risk due to BC alone) is represented here. This |

| Title | The 5-year observed and relative survival after a diagnosis of IBC |
|---|---|
| | indicator shows how much greater the risk of dying from BC within five years of diagnosis is in a particular hospital compared with the average for all Belgian hospitals. This adjusted indicator therefore shows the opposite of what one would expect in a survival analysis, namely the risk of death instead of the chance of survival. |
| **Target** | No target |
| **Data source** | Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>Kruispuntbank - Banque Carrefour for mortality data (vital status of patients diagnosed with cancer): up to 1/3/2022<br>IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definition** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26) |
| **Risk adjustment** | • **Observed survival**:<br>Case-mix: patient characteristics (age at diagnosis, WHO performance status, the number of inpatient bed days the year preceding the incidence year, comorbidities (cardiac and respiratory diseases, and diabetes)) and tumour characteristics (combined stage, tumour differentiation grade). Missing observations for a covariate were assigned to an extra-category 'missing'.<br>• **Relative survival**:<br>Case-mix: age and combined stage |
| **Limitations** | There are expected residual confounding factors (e.g. socio-economic background, receptor status) for which no adjustments could be made due to a lack of relevant information in the consulted databases.<br>The database does not allow the calculation of the 10-year observed and relative survival for the due to insufficient length of follow-up. |
| **Subgroup analyses** | - Age at diagnosis<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Year of incidence<br>- Combined stage<br>- Treatment modality<br>- Tumour differentiation grade |
| **Benchmarking** | For the 2014 - 2018 cohort: main treatment campus |
| **Level of benchmarking** | For the 2014 - 2018 cohort: campus level |

## *Appendix 11.6.2. Patients diagnosed in 2014 - 2018 with IBC*

**Table 88 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with IBC, by patient and tumour characteristics and treatment modality**

| | | Unadjusted observed survival (%, 95% CI) | | | p-value[$] | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| **Overall** | 46 035 | 95.9 [95.7, 96.1] | 89.4 [89.1, 89.7] | 83.4 [83.1, 83.8] | | 97.9 [97.8, 98.1] | 95.4 [95.1, 95.7] | 93.3 [92.9, 93.7] |
| **Age at diagnosis (years)** | | | | | <0.0001 | | | |
| <40 | 2 261 | 98.8 [98.3, 99.2] | 95.3 [94.4, 96.1] | 92.1 [90.8, 93.2] | | 98.9 [98.4, 99.3] | 95.5 [94.5, 96.3] | 92.4 [91.1, 93.5] |
| 40-49 | 6 798 | 99.0 [98.7, 99.2] | 96.6 [96.1, 97.0] | 94.3 [93.7, 94.8] | | 99.1 [98.9, 99.3] | 97.1 [96.6, 97.5] | 95.1 [94.5, 95.7] |
| 50-59 | 10 580 | 98.9 [98.7, 99.1] | 96.1 [95.7, 96.5] | 93.5 [93.0, 94.0] | | 99.3 [99.0, 99.4] | 97.2 [96.8, 97.6] | 95.5 [95.0, 96.0] |
| 60-69 | 11 611 | 97.7 [97.4, 97.9] | 94.0 [93.6, 94.4] | 90.3 [89.7, 90.9] | | 98.5 [98.2, 98.8] | 96.7 [96.2, 97.1] | 95.1 [94.5, 95.7] |
| 70-79 | 8 294 | 94.6 [94.1, 95.1] | 87.1 [86.4, 87.8] | 79.1 [78.1, 80.0] | | 96.8 [96.3, 97.3] | 94.3 [93.5, 95.1] | 92.3 [91.2, 93.3] |
| 80 + | 6 491 | 85.4 [84.5, 86.2] | 63.4 [62.2, 64.6] | 45.7 [44.4, 47.0] | | 94.3 [93.3, 95.2] | 88.4 [86.8, 90.0] | 84.3 [81.9, 86.7] |
| **WHO performance status at time of diagnosis** | | | | | <0.0001 | | | |
| 0 – Asymptomatic | 24 975 | 98.6 [98.4, 98.7] | 95.0 [94.7, 95.2] | 90.8 [90.4, 91.1] | | 100.0 [99.8, 100.1] | 99.4 [99.2, 99.7] | 98.6 [98.2, 99.0] |
| 1 – Symptomatic but completely ambulatory | 16 016 | 94.9 [94.6, 95.3] | 85.8 [85.3, 86.4] | 78.1 [77.5, 78.8] | | 97.4 [97.0, 97.7] | 93.1 [92.5, 93.6] | 89.8 [89.1, 90.6] |
| 2 – Symptomatic, up and about more than 50% of waking hours | 794 | 72.2 [68.9, 75.1] | 46.9 [43.3, 50.3] | 31.1 [27.7, 34.6] | | 76.0 [72.4, 79.2] | 57.4 [53.1, 61.7] | 44.6 [39.6, 49.6] |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 299 | 59.2 [53.4, 64.5] | 34.1 [28.8, 39.5] | 20.4 [15.7, 25.4] | | 60.0 [53.6, 66.0] | 41.3 [34.7, 48.1] | 29.0 [22.3, 36.3] |
| 4 – Completely disabled; totally confined to bed or chair | 103 | 49.5 [39.5, 58.7] | 29.1 [20.7, 38.1] | 21.8 [14.3, 30.3] | | 44.9 [34.3, 55.1] | 30.4 [21.1, 40.5] | 26.7 [17.3, 37.7] |

| | | Unadjusted observed survival (%, 95% CI) | | | p-value[$] | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| Missing | 3 848 | 92.0 [91.1, 92.9] | 82.7 [81.5, 83.9] | 75.1 [73.6, 76.5] | | 94.7 [93.8, 95.6] | 90.4 [89.1, 91.7] | 87.2 [85.5, 88.8] |
| **Cardiovascular disease** | | | | | <0.0001 | | | |
| Absent | 26 390 | 97.8 [97.6, 98.0] | 94.0 [93.7, 94.3] | 90.5 [90.1, 90.9] | | 98.8 [98.6, 98.9] | 96.9 [96.6, 97.2] | 95.6 [95.2, 95.9] |
| Present | 19 645 | 93.4 [93.0, 93.7] | 83.2 [82.6, 83.7] | 73.9 [73.3, 74.6] | | 96.8 [96.4, 97.2] | 93.2 [92.6, 93.8] | 90.1 [89.3, 90.9] |
| **Diabetes** | | | | | | | | |
| Absent | 41 401 | 96.3 [96.1, 96.5] | 90.3 [90.0, 90.6] | 84.9 [84.5, 85.2] | | 98.2 [98.0, 98.4] | 96.0 [95.7, 96.3] | 94.3 [93.9, 94.7] |
| Present | 4 634 | 92.4 [91.6, 93.2] | 80.9 [79.7, 82.0] | 70.5 [69.1, 71.9] | | 95.4 [94.6, 96.2] | 89.5 [88.2, 90.7] | 84.1 [82.4, 85.7] |
| **Respiratory disease** | | | | | <0.0001 | | | |
| Absent | 42 861 | 96.2 [96.0, 96.4] | 90.0 [89.7, 90.2] | 84.2 [83.8, 84.5] | | 98.2 [98.0, 98.4] | 95.9 [95.6, 96.2] | 94.0 [93.6, 94.4] |
| Present | 3 174 | 92.1 [91.1, 93.0] | 81.6 [80.3, 83.0] | 73.1 [71.4, 74.7] | | 94.6 [93.6, 95.5] | 88.7 [87.2, 90.1] | 84.1 [82.2, 85.9] |
| **Number of comorbidities** | | | | | <0.0001 | | | |
| 0 | 24 330 | 97.9 [97.7, 98.1] | 94.2 [93.9, 94.5] | 90.8 [90.4, 91.2] | | 98.9 [98.7, 99.0] | 97.1 [96.8, 97.4] | 95.8 [95.3, 96.1] |
| 1 | 16 362 | 94.6 [94.2, 94.9] | 85.8 [85.3, 86.3] | 77.8 [77.1, 78.5] | | 97.7 [97.3, 98.1] | 95.2 [94.6, 95.8] | 93.3 [92.5, 94.1] |
| 2 | 4 938 | 91.3 [90.4, 92.0] | 79.0 [77.9, 80.1] | 67.7 [66.4, 69.1] | | 94.6 [93.8, 95.4] | 88.6 [87.3, 89.8] | 82.6 [80.9, 84.2] |
| 3 | 405 | 87.9 [84.3, 90.7] | 68.4 [63.6, 72.7] | 56.8 [51.6, 61.7] | | 91.1 [87.4, 94.0] | 76.4 [71.1, 81.2] | 68.6 [62.3, 74.5] |
| **Number of inpatient bed days in year prior to incidence** | | | | | <0.0001 | | | |
| 0 days | 34 199 | 97.5 [97.3, 97.7] | 92.2 [91.9, 92.5] | 86.9 [86.5, 87.3] | | 99.3 [99.1, 99.5] | 97.6 [97.3, 97.9] | 96.0 [95.6, 96.5] |
| 1-5 days | 7 927 | 94.9 | 88.6 | 82.5 | | 96.7 | 94.2 | 92.2 |

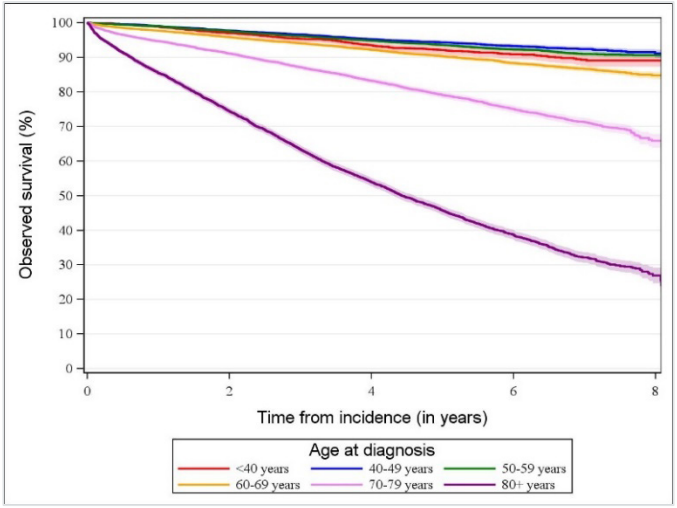
| | | Unadjusted observed survival (%, 95% CI) | | | p-value$ | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| | | [94.4, 95.3] | [87.9, 89.3] | [81.6, 83.4] | | [96.2, 97.2] | [93.5, 95.0] | [91.2, 93.1] |
| 6-15 days | 2 379 | 86.8 [85.3, 88.1] | 72.0 [70.1, 73.7] | 61.2 [59.1, 63.2] | | 90.3 [88.8, 91.7] | 81.8 [79.7, 83.8] | 75.8 [73.2, 78.3] |
| >15 days | 1 530 | 80.1 [78.0, 82.0] | 57.9 [55.4, 60.3] | 45.0 [42.4, 47.6] | | 84.6 [82.3, 86.6] | 69.2 [66.2, 72.1] | 60.8 [57.2, 64.3] |
| **Incidence year** | | | | | 0.702 | | | |
| 2014 | 8 980 | 95.8 [95.3, 96.2] | 89.2 [88.6, 89.9] | 83.4 [82.7, 84.2] | | 97.7 [97.3, 98.1] | 94.8 [94.1, 95.5] | 92.8 [91.9, 93.6] |
| 2015 | 8 973 | 96.3 [95.9, 96.7] | 89.3 [88.6, 89.9] | 83.5 [82.7, 84.3] | | 98.3 [97.9, 98.7] | 95.0 [94.3, 95.7] | 93.1 [92.2, 93.9] |
| 2016 | 9 363 | 96.0 [95.6, 96.4] | 89.5 [88.9, 90.1] | 83.3 [82.5, 84.0] | | 98.0 [97.6, 98.4] | 95.5 [94.8, 96.1] | 93.2 [92.3, 94.0] |
| 2017 | 9 193 | 95.7 [95.2, 96.1] | 89.7 [89.1, 90.3] | 83.7 [82.8, 84.5] | | 97.7 [97.3, 98.1] | 95.9 [95.2, 96.5] | 94.1 [93.2, 94.9] |
| 2018 | 9 526 | 95.8 [95.4, 96.2] | 89.1 [88.5, 89.7] | NA | | 98.0 [97.6, 98.4] | 95.6 [94.9, 96.3] | NA |
| **Combined stage$\phi$** | | | | | <0.0001 | | | |
| (y)0˜ | 1 065 | 99.8 [99.3, 100.0] | 97.8 [96.8, 98.6] | 96.4 [95.1, 97.4] | | 100.3 [99.8, 100.5] | 99.5 [98.4, 100.2] | 99.5 [98.1, 100.5] |
| yis | 337 | 99.4 [97.6, 99.9] | 96.7 [94.2, 98.2] | 93.8 [90.5, 96.1] | | 99.9 [98.1, 100.3] | 98.3 [95.7, 99.8] | 96.6 [93.0, 98.9] |
| (y)I | 20 126 | 99.3 [99.2, 99.4] | 97.1 [96.9, 97.4] | 94.6 [94.2, 94.9] | | 100.7 [100.5, 100.8] | 101.6 [101.4, 101.8] | 102.6 [102.2, 103.0] |
| (y)II | 15 507 | 97.4 [97.1, 97.6] | 90.9 [90.5, 91.4] | 84.2 [83.6, 84.8] | | 99.9 [99.6, 100.1] | 98.5 [98.0, 99.0] | 96.8 [96.1, 97.5] |
| (y)III | 4 930 | 93.3 [92.6, 94.0] | 80.3 [79.2, 81.4] | 70.0 [68.7, 71.3] | | 96.1 [95.3, 96.7] | 87.5 [86.3, 88.7] | 80.8 [79.2, 82.3] |
| (y)IV | 3 009 | 74.8 [73.2, 76.3] | 51.2 [49.4, 52.9] | 34.3 [32.4, 36.1] | | 76.2 [74.6, 77.8] | 55.0 [53.0, 56.9] | 39.2 [37.2, 41.3] |
| Unknown | 1 061 | 78.0 [75.4, 80.4] | 59.1 [56.0, 62.0] | 44.7 [41.6, 47.8] | | 81.8 [79.0, 84.5] | 70.2 [66.6, 73.7] | 59.4 [55.1, 63.6] |

| | | Unadjusted observed survival (%, 95% CI) | | | p-value[$] | Unadjusted relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| **Tumour differentiation grade** | | | | | <0.0001 | | | |
| Well-differentiated | 6 455 | 97.8 [97.4, 98.1] | 93.9 [93.3, 94.4] | 90.4 [89.6, 91.1] | | 99.7 [99.3, 100.0] | 99.8 [99.2, 100.4] | 100.7 [99.8, 101.5] |
| Moderately differentiated | 20 954 | 96.8 [96.5, 97.0] | 91.2 [90.8, 91.6] | 85.4 [84.9, 85.9] | | 98.8 [98.6, 99.1] | 97.5 [97.1, 97.9] | 96.0 [95.5, 96.6] |
| Poorly or undifferentiated | 15 259 | 95.4 [95.0, 95.7] | 87.1 [86.6, 87.6] | 80.5 [79.8, 81.1] | | 97.1 [96.8, 97.4] | 92.2 [91.6, 92.7] | 88.7 [87.9, 89.4] |
| Unknown | 3367 | 89.8 [88.7, 90.9] | 79.7 [78.4, 81.1] | 71.1 [69.4, 72.6] | | 92.6 [91.5, 93.6] | 87.5 [86.0, 89.0] | 83.0 [81.1, 84.9] |
| **Treatment modality** | | | | | <0.0001 | | | |
| Surgery < adjuvant RT | 899 | 96.5 [95.1, 97.6] | 84.5 [81.9, 86.7] | 77.0 [74.0, 79.7] | | 99.8 [98.4, 100.9] | 94.2 [91.4, 96.7] | 93.4 [89.8, 96.7] |
| Surgery < adjuvant systemic Tx | 5 176 | 97.1 [96.6, 97.6] | 91.5 [90.7, 92.2] | 84.1 [83.0, 85.1] | | 99.7 [99.2, 100.2] | 99.8 [98.9, 100.6] | 98.4 [97.2, 99.6] |
| Surgery < adjuvant RT + systemic Tx | 27 374 | 99.6 [99.5, 99.6] | 97.3 [97.1, 97.5] | 94.0 [93.7, 94.3] | | 100.8 [100.7, 100.9] | 101.5 [101.3, 101.7] | 101.7 [101.4, 102.1] |
| Neoadjuvant Tx < Surgery (< adjuvant Tx) | 5 976 | 98.8 [98.5, 99.0] | 91.4 [90.6, 92.0] | 85.6 [84.6, 86.5] | | 99.7 [99.4, 99.9] | 94.2 [93.4, 94.9] | 90.4 [89.4, 91.4] |
| Surgery only | 808 | 87.9 [85.5, 90.0] | 71.7 [68.4, 74.6] | 59.8 [56.1, 63.2] | | 92.9 [90.2, 95.1] | 85.6 [81.7, 89.1] | 79.9 [75.0, 84.6] |
| Primary systemic and/or radiotherapy (no surgery) | 4 861 | 79.8 [78.6, 80.9] | 53.8 [52.4, 55.2] | 35.4 [33.9, 36.9] | | 84.5 [83.2, 85.6] | 65.2 [63.5, 66.9] | 49.7 [47.6, 51.7] |
| No oncological treatment | 941 | 55.4 [52.1, 58.5] | 38.9 [35.8, 42.0] | 28.1 [25.1, 31.1] | | 53.8 [50.2, 57.3] | 43.5 [39.7, 47.2] | 34.9 [31.1, 38.8] |

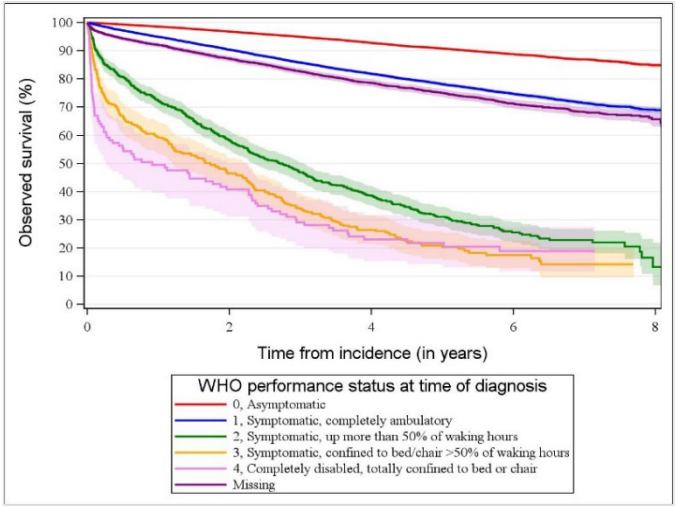
*[$]: p-value from the log rank test; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; ϕ: patients might have had neoadjuvant therapy (NAT), resulting in a ypStage in these cases. Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); the combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage, except when the presence of metastasis is specified in the clinical stage; RT: radiotherapy; Tx: treatment.*
*Source: BCR-IMA*

**Figure 21 – Unadjusted observed survival of patients with IBC, by age at diagnosis (A), WHO performance status (B), combined stage (C) and year of diagnosis (D)**

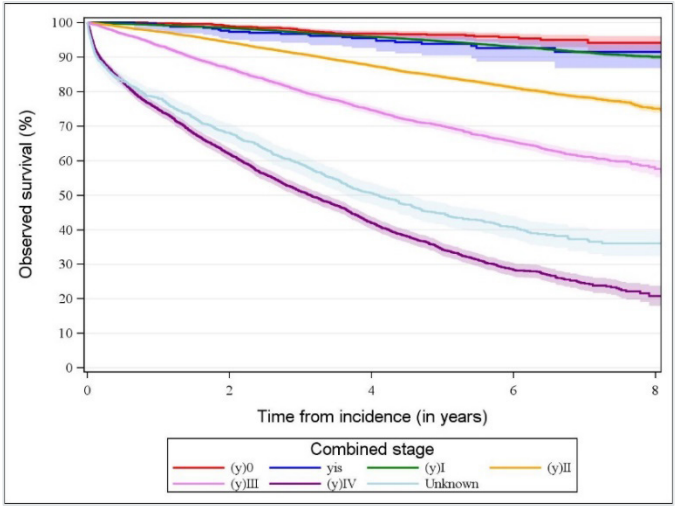
A




B




C




D

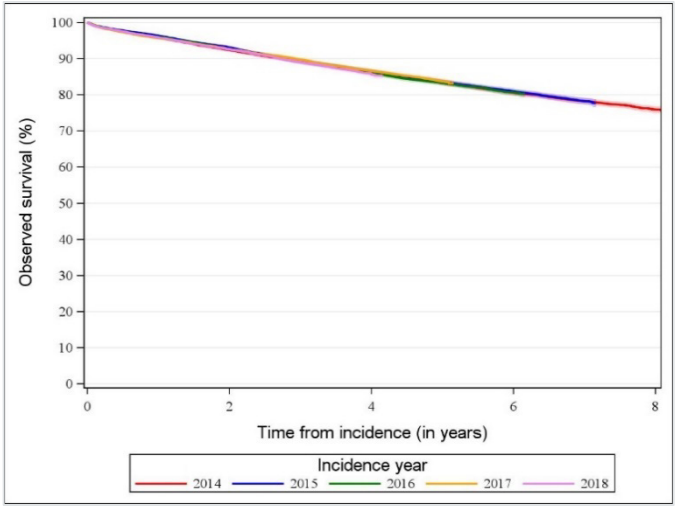
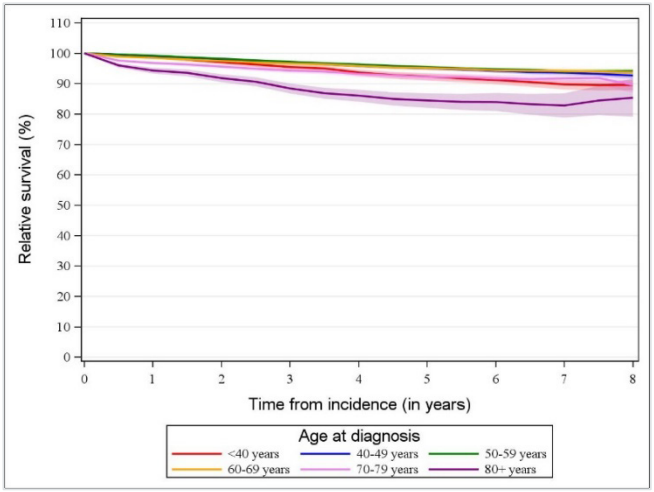
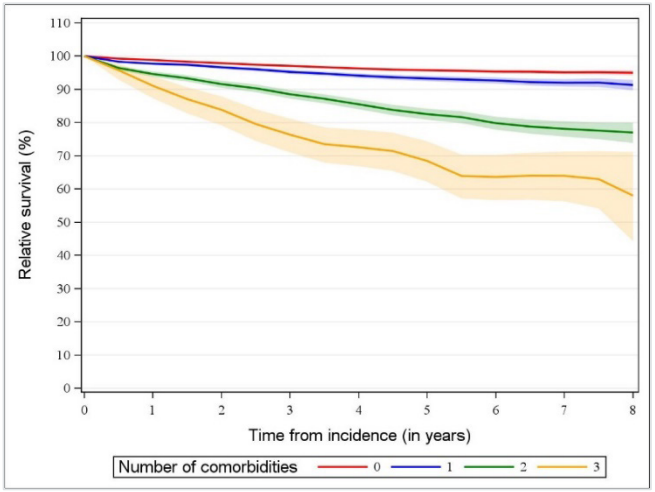


**Figure 22 – Unadjusted relative survival of patients with IBC, by age at diagnosis (A), number of comorbidities (B), combined stage (C) and treatment modality (D)**

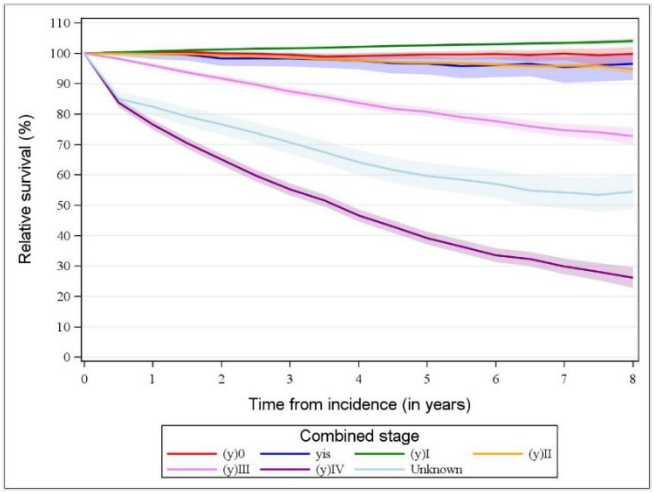
A




B




C




D

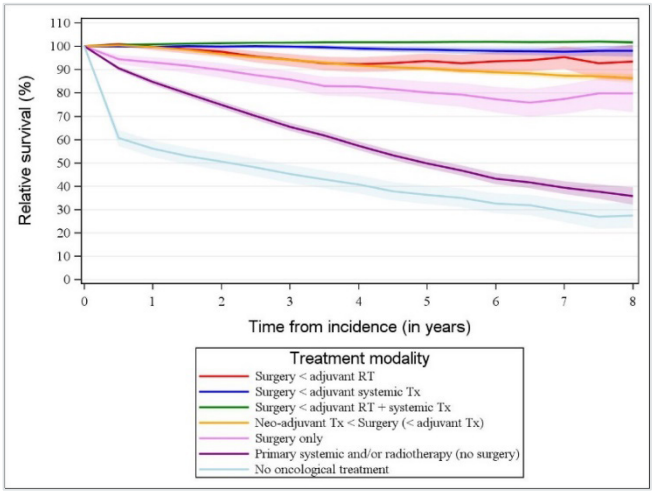
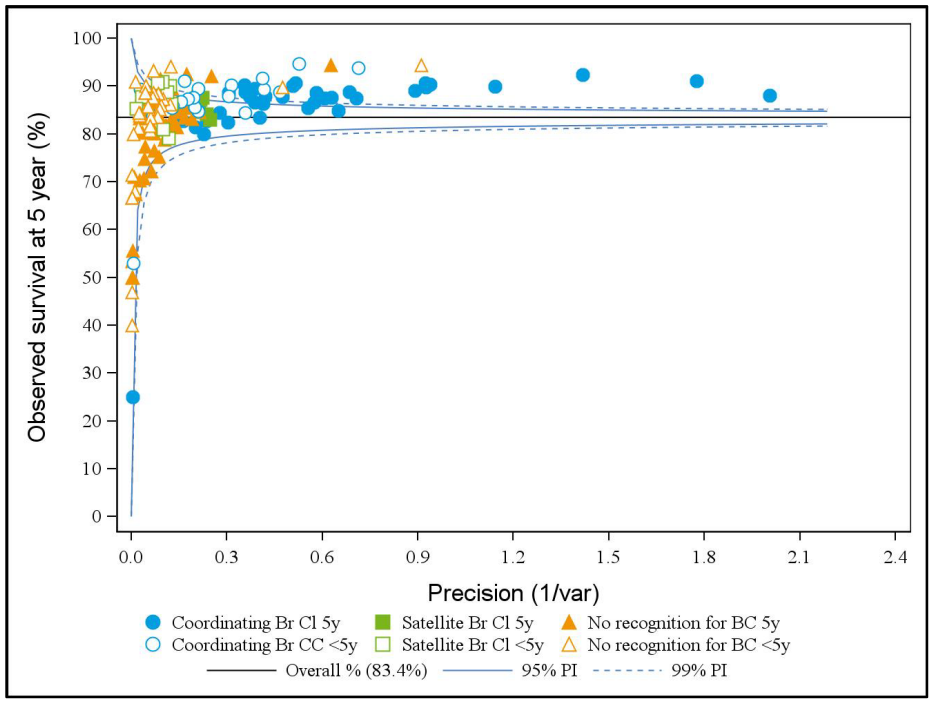
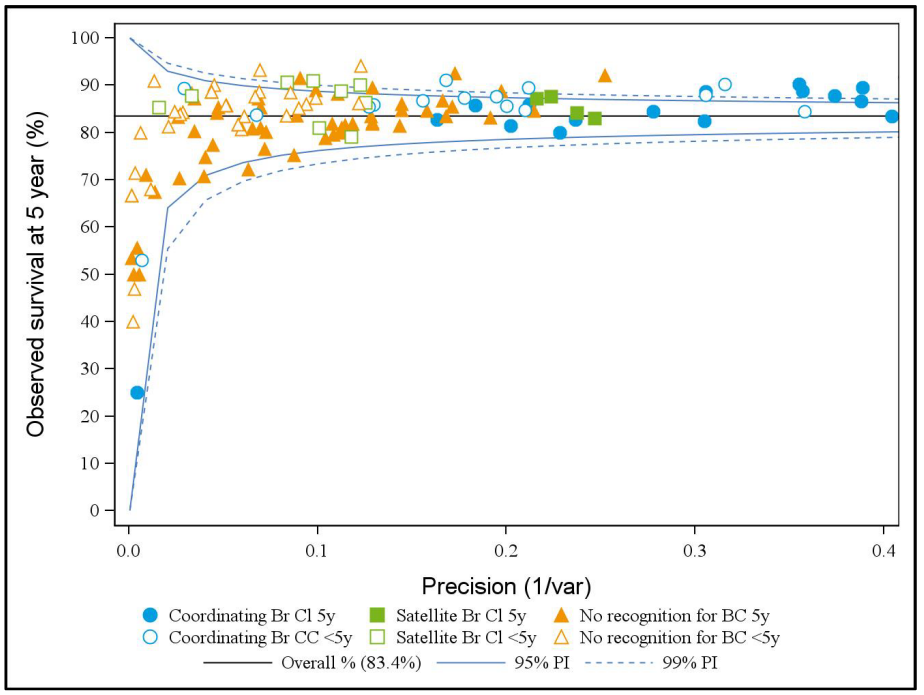


**Figure 23 – Funnel plot of the 5-year unadjusted observed survival for patients with IBC (left) and zoom on the low precision range (right), by main treatment campus**



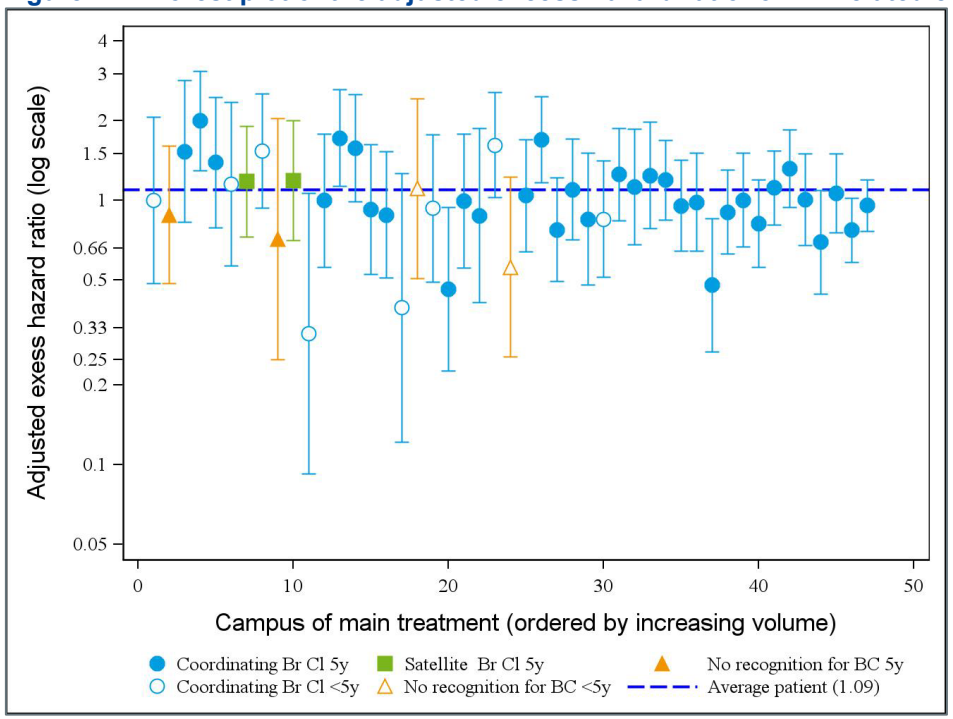




*To quantify the degree of heterogeneity among campuses, the reciprocal of the estimated effect variance (i.e. precision) was used instead of the volume (as was done for the other QIs; see section 4.7); 155 units of analysis presented on the funnel plot; 16 units of analysis which did not achieve a follow-up of 5 years, are not presented on the funnel plot; 11 units of analysis with an observed survival of 0 or 100%, for which the precision does not exist, are not presented on the funnel plot.*

*Note: The funnel plot, which illustrates the variability between the campuses, should be interpreted with caution. First, these results do not take the differences in case-mix between campuses into account. Secondly, the funnel is drawn around the national results of the whole 2014 - 2018 cohort of patients with IBC, which also includes a subgroup of patients who could not be assigned to a campus of main treatment. This subgroup, which represents six percent of the study cohort, had an overall survival of only 35% and thus 'pulled down' the reference line of the funnel, which is based on the national average. This gives the false impression that the funnel itself is positioned 'too low'.*

*Source: BCR-IMA-HDD*

**Figure 24 – Forest plot of the adjusted excess hazard ratio for BC-related excess death in patients with IBC, by main treatment campus**




*Excess hazard ratios (HER) were determined over the [0,5] year survival time interval. A minimum campus size of 300 assigned patients was applied, with size referring to the number of patients available for the analysis. For only 47 campuses the adjusted EHR could be obtained. The excess hazard ratios were adjusted for age at diagnosis and combined tumour stage.*

*Value 1.0 represents the average campus and the dashed blue line is the EHR for the average patient (which equals the weighted sum of all campus EHR, with the number of patients per campus divided by the total number of patients as weight). The campuses are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). An EHR which is lower than 1.0, indicates a lower excess hazard (or instantaneous risk to die of BC), and thus a higher net survival. When the vertical lines, which represent the 95% CI on the campus HR, include value 1.0 (dashed line), the EHR of that campus is not statistically significantly different from the average campus (average patient). Three campuses have their 95%CI above the reference line (performing worse) and five campuses have their 95%CI below the reference line (performing better).*

*Source: BCR-IMA-HDD*

## *Appendix 11.6.3. Patients diagnosed in 2014 - 2018 with non-metastatic IBC, who had surgery*

**Table 89 – 1-, 3-, and 5-year unadjusted observed and relative survival for patients diagnosed with non-metastatic* IBC who had surgery, by patient and tumour characteristics and treatment modality**

| | | Observed survival (%, 95% CI) | | | p-value[$] | Relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| **Overall** | 33 000 | 99.0 [98.9, 99.1] | 95.3 [95.1, 95.5] | 91.1 [90.7, 91.4] | | 100.4 [100.3, 100.5] | 100.0 [99.8, 100.3] | 99.5 [99.1, 99.8] |
| **Age at diagnosis (years)** | | | | | <0.0001 | | | |
| <40 | 1 814 | 99.6 [99.2, 99.8] | 97.1 [96.2, 97.7] | 94.7 [93.5, 95.7] | | 99.7 [99.2, 99.9] | 97.2 [96.3, 97.9] | 95.0 [93.8, 96.0] |
| 40-49 | 5 364 | 99.6 [99.4, 99.7] | 97.9 [97.5, 98.2] | 96.1 [95.5, 96.6] | | 99.8 [99.5, 99.9] | 98.4 [97.9, 98.7] | 96.9 [96.4, 97.5] |
| 50-59 | 8 311 | 99.7 [99.6, 99.8] | 98.1 [97.8, 98.4] | 96.3 [95.9, 96.7] | | 100.1 [99.9, 100.2] | 99.2 [98.9, 99.5] | 98.3 [97.8, 98.7] |
| 60-69 | 8 723 | 99.6 [99.4, 99.7] | 97.5 [97.1, 97.8] | 94.7 [94.1, 95.1] | | 100.4 [100.2, 100.5] | 100.2 [99.8, 100.5] | 99.7 [99.1, 100.2] |
| 70-79 | 5 711 | 98.4 [98.0, 98.7] | 93.1 [92.4, 93.7] | 86.9 [85.9, 87.8] | | 100.6 [100.3, 100.9] | 100.6 [99.9, 101.3] | 101.2 [100.0, 102.2] |
| 80 + | 3 077 | 94.9 [94.1, 95.6] | 80.1 [78.6, 81.4] | 63.3 [61.5, 65.2] | | 103.1 [102.2, 103.8] | 106.2 [104.3, 108.0] | 108.3 [105.2, 111.4] |
| **WHO performance status at time of diagnosis** | | | | | <0.0001 | | | |
| 0 – Asymptomatic | 19 888 | 99.4 [99.3, 99.5] | 96.9 [96.6, 97.1] | 93.5 [93.1, 93.9] | | 100.5 [100.4, 100.6] | 100.8 [100.5, 101.0] | 100.5 [100.1, 100.9] |
| 1 – Symptomatic but completely ambulatory | 10 983 | 98.5 [98.2, 98.7] | 93.1 [92.6, 93.5] | 87.9 [87.2, 88.5] | | 100.3 [100.1, 100.5] | 99.0 [98.5, 99.5] | 98.1 [97.4, 98.8] |
| 2 – Symptomatic, up and about more than 50% of waking hours | 247 | 93.5 [89.6, 96.0] | 76.1 [70.3, 81.0] | 55.1 [48.0, 61.6] | | 98.7 [94.6, 101.3] | 91.6 [84.6, 97.4] | 77.5 [67.5, 86.6] |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 67 | 88.1 [77.5, 93.8] | 67.2 [54.5, 77.0] | 52.4 [39.4, 63.9] | | 93.4 [82.2, 99.5] | 80.8 [65.6, 92.6] | 72.5 [54.6, 88.3] |
| 4 – Completely disabled; totally confined to bed or chair | 19 | 89.5 [64.1, 97.3] | 68.4 [42.8, 84.4] | 63.2 [37.9, 80.4] | | 91.5 [65.6, 99.4] | 72.8 [45.9, 89.5] | 71.2 [43.0, 90.4] |

| | | Observed survival (%, 95% CI) | | | p-value[$] | Relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| Missing | 1 796 | 99.1 [98.5, 99.5] | 95.1 [94.0, 96.0] | 90.3 [88.7, 91.7] | | 100.7 [100.2, 101.1] | 100.4 [99.2, 101.3] | 99.6 [97.8, 101.1] |
| **Cardiovascular disease** | | | | | <0.0001 | | | |
| Absent | 20 053 | 99.5 [99.4, 99.6] | 97.3 [97.1, 97.6] | 95.0 [94.7, 95.3] | | 100.3 [100.1, 100.3] | 99.8 [99.6, 100.0] | 99.5 [99.1, 99.8] |
| Present | 12 947 | 98.2 [97.9, 98.4] | 92.1 [91.7, 92.6] | 85.0 [84.3, 85.6] | | 100.7 [100.5, 101.0] | 100.4 [99.9, 100.9] | 99.4 [98.7, 100.2] |
| **Respiratory disease** | | | | | <0.0001 | | | |
| Absent | 30 915 | 99.1 [99.0, 99.2] | 95.6 [95.3, 95.8] | 91.6 [91.2, 91.9] | | 100.5 [100.4, 100.6] | 100.3 [100.0, 100.5] | 99.9 [99.5, 100.2] |
| Present | 2 085 | 97.7 [97.0, 98.3] | 91.2 [89.9, 92.4] | 83.8 [82.0, 85.4] | | 99.5 [98.7, 100.1] | 96.8 [95.4, 98.0] | 93.2 [91.3, 95.0] |
| **Diabetes** | | | | | <0.0001 | | | |
| Absent | 29 996 | 99.1 [99.0, 99.2] | 95.8 [95.6, 96.0] | 92.1 [91.7, 92.4] | | 100.5 [100.4, 100.6] | 100.3 [100.0, 100.5] | 100.0 [99.6, 100.4] |
| Present | 3 004 | 97.7 [97.1, 98.2] | 90.2 [89.1, 91.3] | 81.2 [79.6, 82.6] | | 100.1 [99.5, 100.6] | 97.8 [96.6, 98.9] | 94.0 [92.2, 95.6] |
| **Number of comorbidities** | | | | | <0.0001 | | | |
| 0 | 18 574 | 99.5 [99.4, 99.6] | 97.4 [97.2, 97.6] | 95.2 [94.8, 95.5] | | 100.3 [100.1, 100.3] | 99.8 [99.6, 100.0] | 99.5 [99.2, 99.9] |
| 1 | 11 063 | 98.6 [98.4, 98.8] | 93.7 [93.3, 94.2] | 88.0 [87.4, 88.6] | | 101.0 [100.7, 101.2] | 101.4 [100.9, 101.9] | 101.6 [100.8, 102.3] |
| 2 | 3 116 | 97.4 [96.7, 97.9] | 89.4 [88.3, 90.4] | 79.3 [77.8, 80.8] | | 100.0 [99.3, 100.5] | 97.6 [96.3, 98.7] | 93.1 [91.2, 94.8] |
| 3 | 247 | 95.1 [91.6, 97.2] | 81.0 [75.5, 85.3] | 68.3 [61.6, 74.1] | | 97.9 [94.2, 100.0] | 88.8 [82.8, 93.6] | 80.7 [72.9, 87.5] |
| **Number of inpatient bed days in year prior to incidence** | | | | | <0.0001 | | | |
| 0 days | 25 318 | 99.2 [99.0, 99.3] | 96.1 [95.8, 96.3] | 92.3 [92.0, 92.7] | | 100.5 [100.4, 100.6] | 100.4 [100.2, 100.7] | 100.1 [99.7, 100.5] |
| 1-5 days | 5 598 | 99.1 [ 98.8, 99.3] | 95.4 [94.9, 96.0] | 91.3 [90.5, 92.1] | | 100.5 [100.2, 100.8] | 100.3 [99.7, 100.8] | 100.0 [99.1, 100.9] |

| | | Observed survival (%, 95% CI) | | | p-value[$] | Relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| 6-15 days | 1 339 | 97.7 [96.7, 98.4] | 89.5 [87.8, 91.1] | 80.7 [78.4, 82.9] | | 100.3 [99.3, 101.0] | 97.9 [95.9, 99.5] | 94.8 [92.1, 97.3] |
| >15 days | 745 | 94.5 [92.6, 95.9] | 77.8 [74.7, 80.7] | 65.2 [61.5, 68.7] | | 98.3 [96.3, 99.7] | 88.2 [84.6, 91.4] | 81.3 [76.7, 85.6] |
| **Incidence year** | | | | | 0.517 | | | |
| 2014 | 5 987 | 99.0 [98.7, 99.2] | 95.3 [94.7, 95.8] | 91.4 [90.7, 92.1] | | 100.4 [100.1, 100.6] | 99.7 [99.1, 100.2] | 99.3 [98.5, 100.1] |
| 2015 | 6 319 | 99.2 [98.9, 99.4] | 95.1 [94.5, 95.6] | 90.9 [90.1, 91.5] | | 100.6 [100.3, 100.8] | 99.7 [99.1, 100.2] | 99.1 [98.3, 99.9] |
| 2016 | 6 506 | 98.9 [98.7, 99.2] | 95.2 [94.6, 95.7] | 90.6 [89.9, 91.3] | | 100.4 [100.1, 100.6] | 99.9 [99.3, 100.4] | 99.0 [98.2, 99.7] |
| 2017 | 7 065 | 98.9 [98.6, 99.1] | 95.5 [95.0, 96.0] | 91.3 [90.5, 92.0] | | 100.3 [100.0, 100.5] | 100.3 [99.8, 100.8] | 99.9 [99.1, 100.7] |
| 2018 | 7 123 | 99.0 [98.7, 99.2] | 95.4 [94.9, 95.8] | NA | | 100.6 [100.3, 100.8] | 100.5 [99.9, 101.0] | NA |
| **Combined stage[ϕ]** | | | | | <0.0001 | | | |
| (y)0~ | 994 | 99.8 [99.2, 99.9] | 97.7 [96.5, 98.4] | 96.4 [95.0, 97.5] | | 100.3 [99.7, 100.5] | 99.4 [98.2, 100.1] | 99.5 [98.1, 100.6] |
| yis | 307 | 99.7 [97.7, 100.0] | 97.4 [94.8, 98.7] | 95.1 [91.8, 97.1] | | 100.1 [98.2, 100.4] | 99.0 [96.4, 100.3] | 97.8 [94.2, 99.9] |
| (y)I | 15 981 | 99.7 [99.6, 99.8] | 98.0 [97.7, 98.2] | 95.8 [95.5, 96.1] | | 100.8 [100.7, 100.9] | 101.8 [101.6, 102.1] | 103.0 [102.6, 103.3] |
| (y)II | 12 091 | 98.8 [98.6, 99.0] | 94.3 [93.9, 94.7] | 88.7 [88.1, 89.3] | | 100.6 [100.4, 100.8] | 100.3 [99.8, 100.7] | 99.1 [98.4, 99.7] |
| (y)III | 3 627 | 96.3 [95.6, 96.8] | 85.9 [84.7, 87.0] | 76.5 [75.0, 77.9] | | 98.2 [97.5, 98.8] | 91.5 [90.2, 92.6] | 85.4 [83.7, 87.0] |
| **Tumour differentiation grade** | | | | | <0.0001 | | | |
| Well-differentiated | 4 708 | 99.4 [99.2, 99.6] | 97.3 [96.8, 97.7] | 95.0 [94.3, 95.6] | | 100.8 [100.5, 101.0] | 101.8 [101.2, 102.2] | 103.1 [102.3, 103.8] |
| Moderately differentiated | 15 537 | 99.2 [99.1, 99.4] | 96.5 [96.2, 96.8] | 92.7 [92.3, 93.1] | | 100.8 [100.6, 100.9] | 101.5 [101.2, 101.8] | 101.7 [101.2, 102.2] |
| Poorly or undifferentiated | 11 332 | 98.4 [98.2, 98.7] | 92.8 [92.3, 93.3] | 87.2 [86.5, 87.8] | | 99.9 [99.6, 100.1] | 97.3 [96.8, 97.8] | 94.8 [94.1, 95.5] |

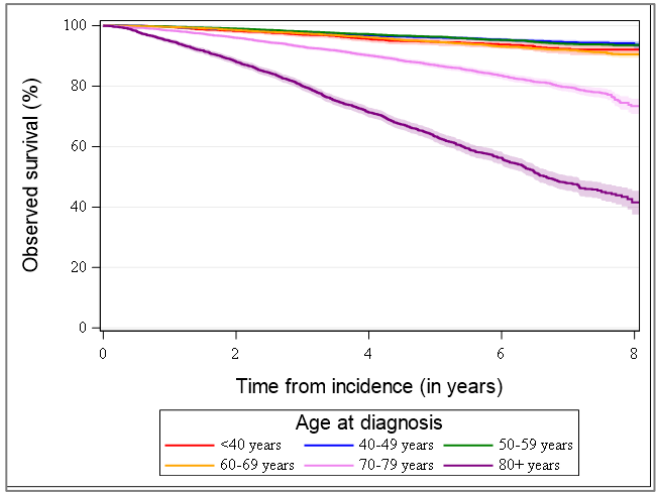
| | | Observed survival (%, 95% CI) | | | p-value[$] | Relative survival (%, 95% CI) | | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **N at risk** | **1-year** | **3-year** | **5-year** | | **1-year** | **3-year** | **5-year** |
| Unknown | 1 43 | 98.9 [98.3, 99.4] | 95.3 [94.1, 96.3] | 91.0 [89.3, 92.5] | | 100.6 [99.9, 101.0] | 100.6 [99.3, 101.6] | 100.3 [98.4, 102.0] |
| **Treatment modality** | | | | | <0.0001 | | | |
| Surgery < adjuvant RT | 707 | 96.3 [94.6, 97.5] | 83.9 [80.9, 86.4] | 76.5 [73.0, 79.5] | | 99.6 [97.9, 100.8] | 93.7 [90.5, 96.5] | 93.2 [89.0, 97.0] |
| Surgery < adjuvant systemic Tx | 4 097 | 97.4 [96.9, 97.9] | 92.2 [91.3, 92.9] | 85.1 [83.9, 86.2] | | 100.0 [99.4, 100.4] | 100.3 [99.3, 101.1] | 99.2 [97.8, 100.5] |
| Surgery < adjuvant RT + systemic Tx | 22 779 | 99.6 [99.5, 99.7] | 97.4 [97.2, 97.6] | 94.1 [93.8, 94.4] | | 100.9 [100.8, 100.9] | 101.6 [101.3, 101.8] | 101.8 [101.4, 102.1] |
| Neoadjuvant Tx < Surgery (< adjuvant Tx) | 4 860 | 99.0 [98.6, 99.2] | 92.5 [91.7, 93.2] | 87.3 [86.3, 88.3] | | 99.8 [99.5, 100.1] | 95.1 [94.3, 95.8] | 91.8 [90.7, 92.8] |
| Surgery only | 557 | 88.3 [85.3, 90.7] | 72.5 [68.6, 76.1] | 60.5 [56.0, 64.6] | | 93.2 [90.0, 95.8] | 86.3 [81.6, 90.5] | 81.1 [75.1, 86.7] |

**Non-metastatic: defined as cM=0, no pM=1 and no unknown combined stage; [$]: p-value from the log rank test; ˜: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; ϕ: patients might have had neoadjuvant therapy (NAT), resulting in a ypStage in these cases. Note that a distinction was made between ypStage 0, i.e. complete pathological response after NAT (ypT0 ypN0,x ypM0,x) and ypStage is, i.e. in situ component remains after NAT (ypTis, ypN0,x ypM0,x); the combined stage is a summary of the information included in the clinical stage and the pathological stage and is defined as follows: a known pathological stage takes priority over a known clinical stage, except when the presence of metastasis is specified in the clinical stage; RT: radiotherapy; Tx: treatment.*

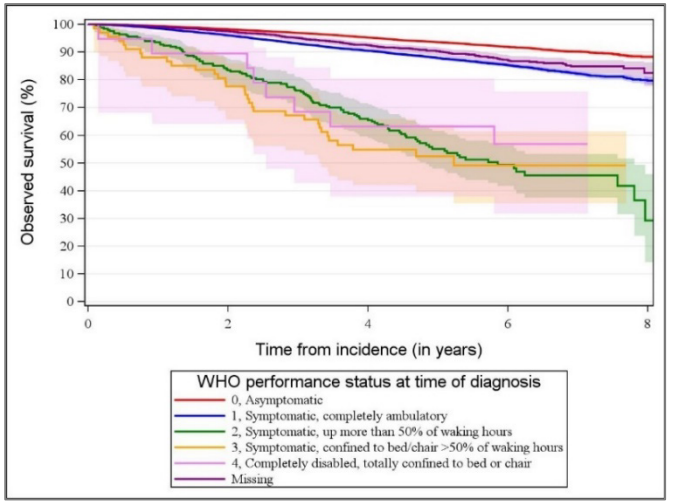
*Source: BCR-IMA*

**Figure 25 – Unadjusted observed survival of patients with non-metastatic IBC who had surgery, by age at diagnosis (A), WHO performance status (B), combined stage (C) and year of diagnosis (D)**

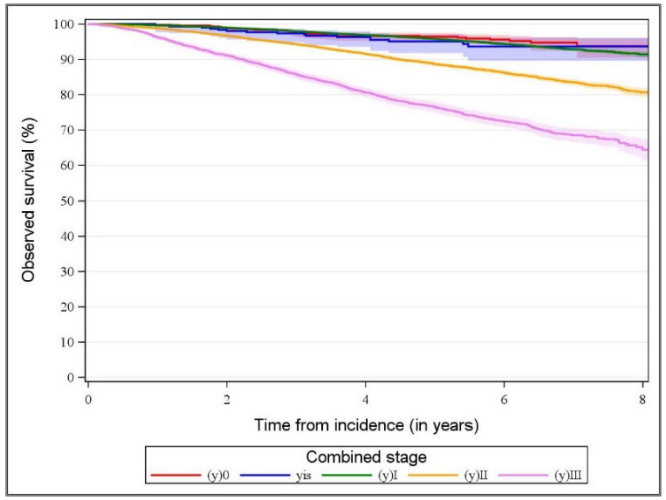
A.




B.




C.




D.

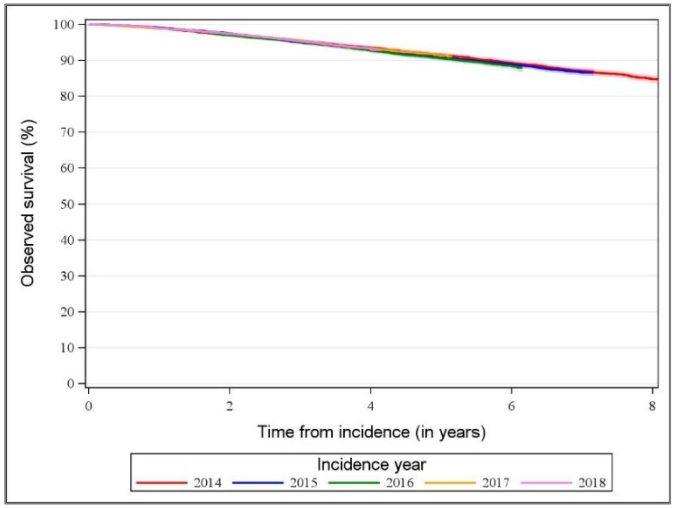
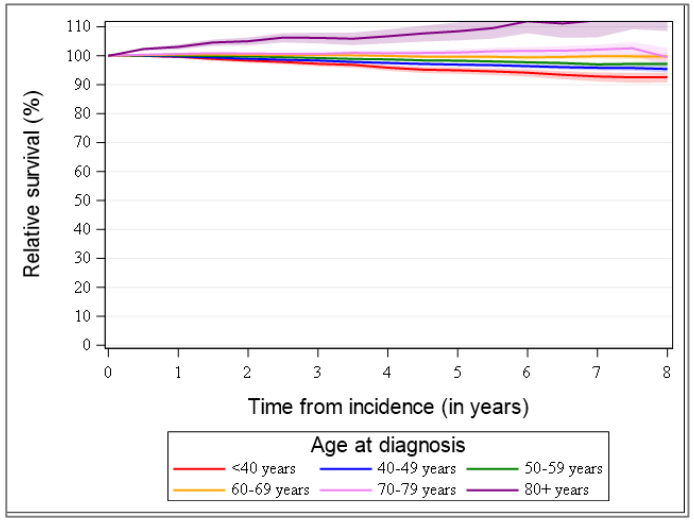
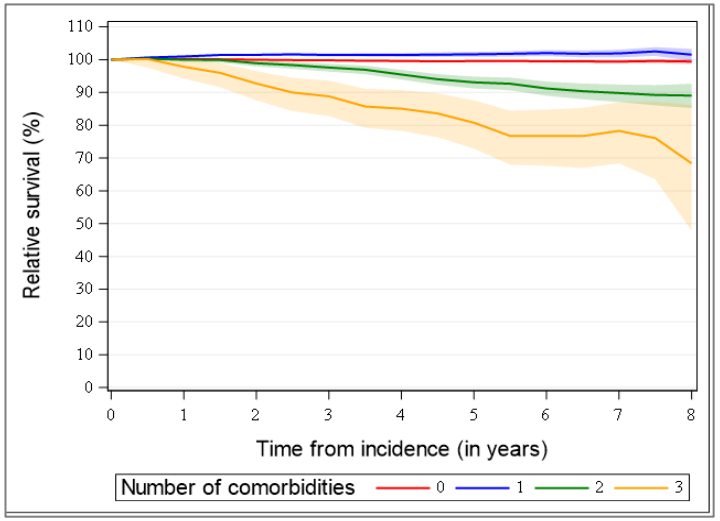


**Figure 26 – Unadjusted relative survival of patients with non-metastatic IBC who had surgery, by age at diagnosis (A), number of comorbidities (B), combined stage (C) and treatment modality (D)**

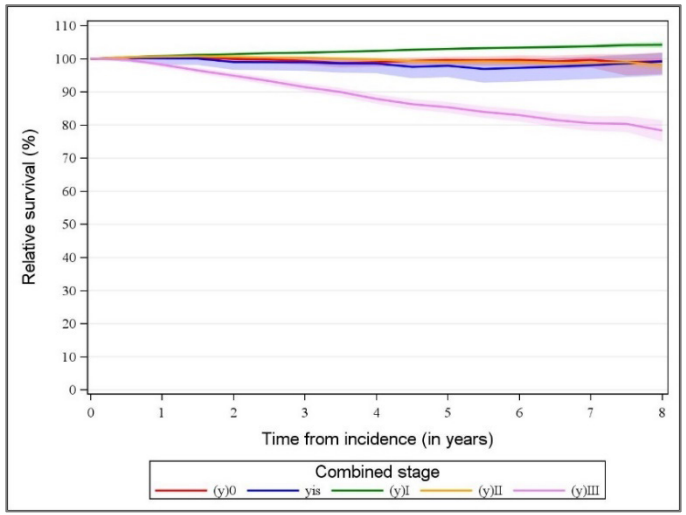
A.



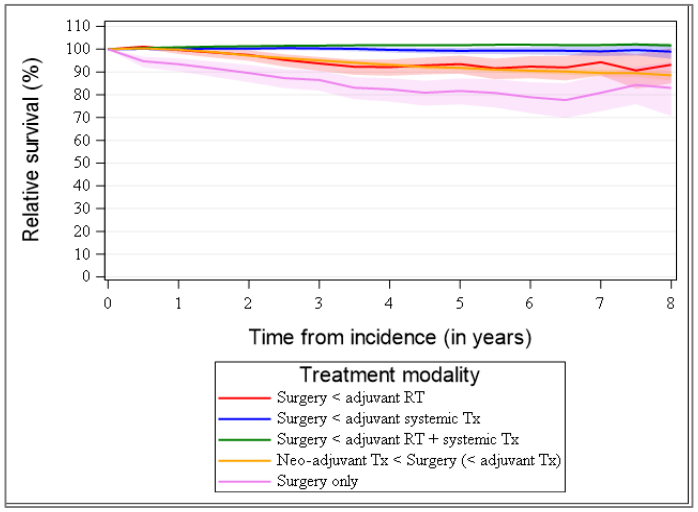

B.




C.

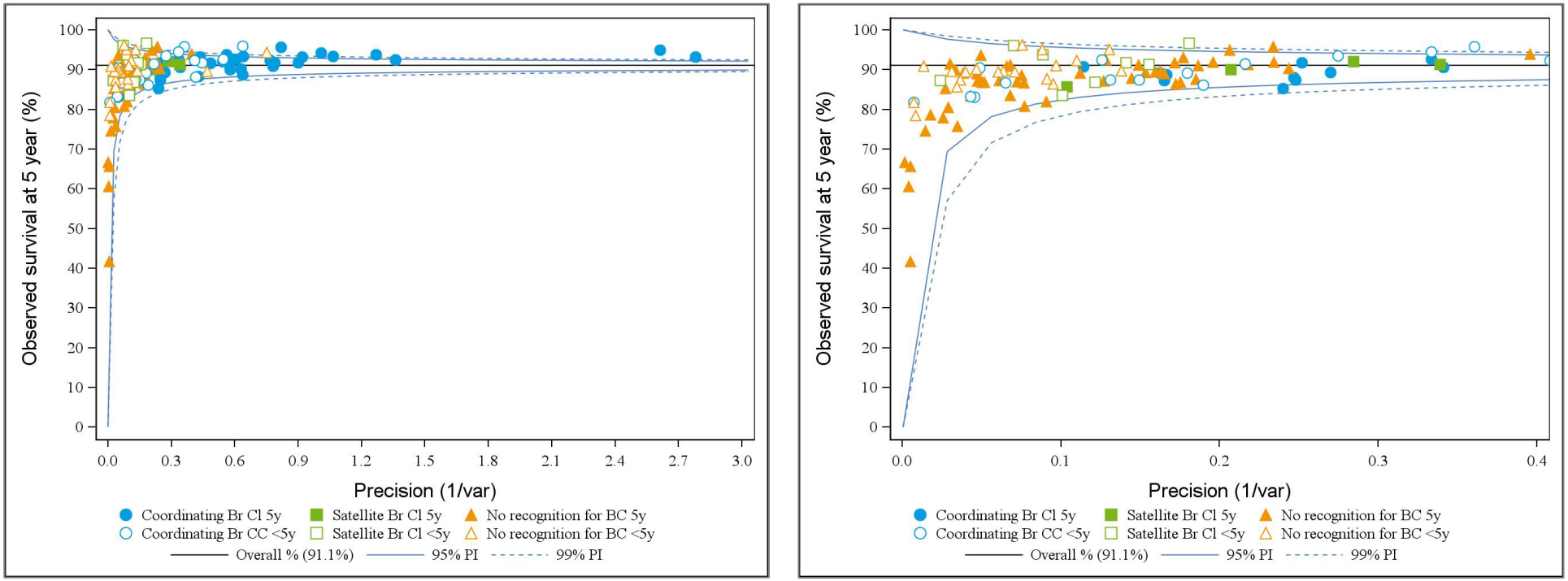



D.



The funnel plot illustrates that the variability between the units of analysis was limited to what can be expected from random variability (Figure 27).

**Figure 27 – Funnel plot of the 5-year unadjusted observed survival for patients with non-metastatic IBC who had surgery (left) and zoom on the low precision range (right), by main treatment campus**




*To quantify the degree of heterogeneity among campuses, the reciprocal of the estimated effect variance (i.e. precision) was used instead of the volume (as was done for the other QIs; see also section 4.7); 139 units of analysis presented on the funnel plot; 12 units of analysis did not achieve a follow-up of 5 years, and are not presented on the funnel plot; 18 units of analysis with an observed survival of 0 or 100%, for which the precision does not exist, are not presented on the funnel plot.*

*Source: BCR-IMA-HDD*

# APPENDIX 12. ASSOCIATION BETWEEN THE RECOGNITION STATUS/VOLUME OF A HOSPITAL CAMPUS AND SURVIVAL

## Appendix 12.1. Documentation sheet

| Title | Association between<br>• Campus recognition status and survival in women diagnosed with IBC<br>• Campus volume and survival in women diagnosed with IBC |
|---|---|
| **Rationale** | In previous KCE reports the relation between volume and outcome was evaluated for several cancer types.[10, 12-14, 150] The effect of hospital volume on 5-year observed survival after BC (diagnosed between 2004 and 2006) has been demonstrated: patients treated in very low and low volume hospitals had a significantly higher hazard ratio for death than their peers treated in high volume hospitals.[137] These results were consistent with previous studies performed in other countries which demonstrated better survival in high volume hospitals (see Discussion section).<br>Since January 2014, hospital campuses can be recognised as 'coordinating breast clinics' ('coördinerend gespecialiseerd oncologisch zorgprogramma voor borstkanker', 'le programme de soins oncologiques spécialisé coordonné pour le cancer du sein') or 'satellite breast clinics' ('het gespecialiseerd oncologisch zorgprogramma voor borstkanker', 'le programme de soins oncologiques spécialisé pour le cancer du sein'), requiring – among others - a minimal level of activity of 125 and 60 new BC diagnoses a year, respectively. Despite the legislator's initial intention to offer specialised BC care in dedicated breast clinics, BC treatment is still be offered outside the recognised centres.<br>The aim of these analyses is two-fold:<br>1. evaluate whether there is an association between the **recognition status** of a hospital campus and observed/relative survival in women diagnosed with IBC, adjusted for a range of patient and tumour characteristics<br>2. evaluate whether there is an association between **campus volume** and observed survival in women diagnosed with IBC, adjusted for a range of patient and tumour characteristics. |
| **Type of QI** | Structure/outcome |
| **Calculation** | Cox proportional hazard models to assess the relation between:<br>1. the recognition status of a hospital campus and 5-year observed survival since diagnosis (2014 - 2018 cohort)<br>2. campus volume and 5-year observed survival since diagnosis (2014 - 2018 cohort)<br>3. the recognition status of a hospital campus and 5-year relative survival since diagnosis (2014 - 2018 cohort)<br>4. campus volume and 5-year relative survival since diagnosis (2014 - 2018 cohort)<br>5. hospital volume and 10-year observed survival since diagnosis (2009 - 2013 cohort)<br>Log-rank tests were used to compare the unadjusted survival curves between categories.<br>In order to account for the clustering of patients into hospitals/campuses, hospital/campus was added as a random term to the Cox regression models that estimated observed survival. As the RS and the EH estimation is performed on grouped datasets (meaning aggregated to volume or recognition level), the clustering of patients into campuses could not be taken into account.<br>The analyses were adjusted for potential confounders by adding them as covariates in the models (see risk adjustment). When there was a statistically significant interaction with volume in the model, stratified analyses were performed and stratum-specific Hazard Ratio (HR) for recognition status/volume were presented. |

| Title | Association between<br>• Campus recognition status and survival in women diagnosed with IBC<br>• Campus volume and survival in women diagnosed with IBC |
|---|---|
| **Target** | No target |
| **Data source** | Belgian Cancer Registry (BCR): incidence years 2014 - 2018 and 2009 - 2013<br>IMA – AIM data: 2008 – 2020 (Q2)<br>Kruispuntbank - Banque Carrefour for mortality data (vital status of patients diagnosed with cancer): up to 1/3/2022 |
| **Technical definition** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Oncological treatment includes:<br>- Surgery, for nomenclature codes, see Table 44, Table 45, Table 46, Table 47<br>- Radiotherapy, for nomenclature codes, see Table 49<br>- Chemotherapy, for ATC codes, see Table 50<br>- Endocrine therapy, for ATC codes, see Table 52<br>- Targeted therapy, for ATC codes, see Table 51<br>Main treatment algorithm: see Appendix 8.4.2<br>Recognition status of the campus at the time the main treatment was performed<br>Cohorts: N=46 035 in 2014 - 2018, N=43 507 in 2009 - 2013 (before exclusions were applied, cf. infra)<br>Volume: comprises ALL patients with BC treated in a campus, also patients excluded for the calculation of the other QIs (e.g. Paget's disease, Phyllodes tumours, other sarcomas (other than Phyllodes tumours), LCIS, or multiple invasive tumours (breast and non-breast) or multiple breast tumours (invasive or in situ), as well as men with BC)<br>Volume categories (for 5-year and 10-year survival): <60, 60-124, ≥125 (cf. thresholds for recognition as coordinating breast/satellite clinic) |
| **Risk adjustment** | Case-mix: patient characteristics (age at diagnosis, WHO performance status at diagnosis, the number of inpatient bed days the year preceding the incidence date, comorbidities (cardiac and respiratory diseases, and diabetes)) and tumour characteristics (combined stage, tumour differentiation grade). Missing observations for a covariate were assigned to an extra-category 'missing'. |
| **Limitations** | For the 2014 - 2018 cohort: women for whom the main treatment campus was not known, were excluded from the analyses.<br>For the 2009 - 2013 cohort: women for whom the main treatment hospital was not known, were excluded from the analyses.<br>There are residual confounding factors (e.g. SES background) for which no adjustments can be made due to a lack of relevant information. |
| **Benchmarking** | For the 2014 - 2018 cohort: main treatment campus<br>For the 2009 - 2013 cohort: main treatment hospital |
| **Level of benchmarking** | For the 2014 - 2018 cohort: campus level<br>For the 2009 - 2013 cohort: hospital level |

## Appendix 12.2. Distribution of BC care in 2014 - 2018

### Table 90 – Number of campuses in 2014 by recognition status and average annual volume

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 25 928 (78.1) | 7104 (21.4) | 150 (0.5) | **33 182** (70.8) |
| **Satellite breast clinic** | 0 | 2 271 (86.0) | 370 (14.0) | **2 641** (5.6) |
| **No recognition for BC** | 1 192 (10.8) | 2 904 (26.4) | 6 919 (62.8) | **11 015** (23.5) |
| **Total** | **27 120 (57.9)** | **12 279 (26.2)** | **7 439 (15.9)** | **46 838** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

### Table 91 – Number of campuses in 2015 by recognition status and average annual volume

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 4 915 (77.0) | 1 428 (22.4) | 39 (0.6) | **6 382** (69.5) |
| **Satellite breast clinic** | 0 (0.0) | 341 (99.4) | 2 (0.6) | **343** (3.7) |
| **No recognition for BC** | 287 (11.7) | 690 (28.1) | 1 478 (60.2) | **2 455** (26.7) |
| **Total** | **5 202 (56.7)** | **2 459 (26.8)** | **1 519 (16.6)** | **9 180** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

### Table 92 – Number of campuses in 2016 by recognition status and average annual volume

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 5 251 (77.2) | 1 518 (22.3) | 34 (0.5) | **6 803** (71.3) |
| **Satellite breast clinic** | 0 (0.0) | 453 (80.3) | 111 (19.7) | **564** (5.9) |
| **No recognition for BC** | 309 (14.2) | 479 (22.0) | 1 386 (63.8) | **2 174** (22.8) |
| **Total** | **5 560 (58.3)** | **2 450 (25.7)** | **1 531 (16.1)** | **9 541** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

### Table 93 – Number of campuses in 2017 by recognition status and average annual volume

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC£** | | | | |
| **Coordinating breast clinic** | 5 253 (77.6) | 1 490 (22.0) | 29 (0.4) | **6 772** (72.9) |
| **Satellite breast clinic** | 0 (0.0) | 587 (81.8) | 131 (18.3) | **718** (7.7) |
| **No recognition for BC** | 150 (8.3) | 432 (24.0) | 1 222 (67.7) | **1 804** (19.4) |
| **Total** | **5 403 (58.1)** | **2 509 (27.0)** | **1 382 (14.9)** | **9 294** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

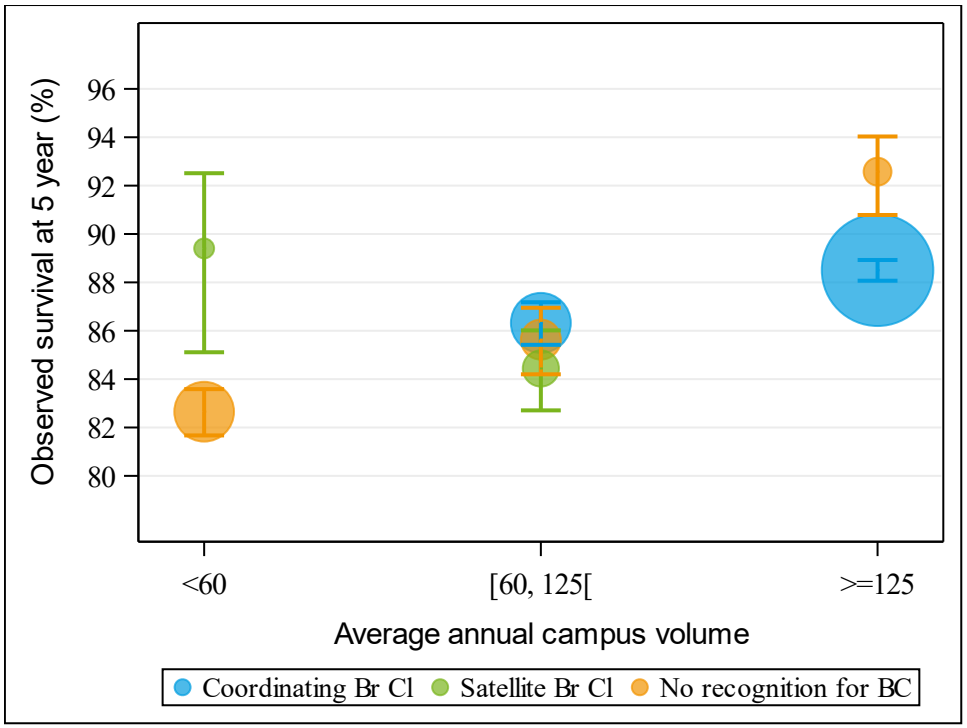
**Table 94 – Number of campuses in 2018 by recognition status and average annual volume**

| | Average annual campus volume* | | | |
|---|---|---|---|---|
| | ≥125 (n, row %) | [60, 125[ (n, row %) | <60 (n, row %) | Total (n, column %) |
| **Recognition status for BC** | | | | |
| **Coordinating breast clinic** | 5 518 (78.6) | 1 482 (21.1) | 18 (0.3) | **7 018** (73.0) |
| **Satellite breast clinic** | 0 (0.0) | 655 (83.9) | 126 (16.1) | **781** (8.1) |
| **No recognition for BC** | 150 (8.3) | 411 (22.6) | 1 254 (69.1) | **1 815** (18.9) |
| **Total** | **5 668 (59.0)** | **2 548 (26.5)** | **1 398 (14.5)** | **9 614** |

**: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients (see section 4.5).*
*Source: BCR-IMA-HDD*

## Appendix 12.3. Unadjusted association between recognition status and campus volume, and 1-, 3- and 5-year observed survival since diagnosis

**Figure 28 – Observed survival probability at 5 year after diagnosis by campus recognition status and average annual campus volume, bubble plot**




*The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients*
*Source: BCR-IMA-HDD*

**Table 95 – 1-, 3-, and 5-year unadjusted observed survival for patients with IBC, by recognition status and campus volume**

| | | Observed survival (%, 95% CI) | | | | | | p-value$ |
|---|---|---|---|---|---|---|---|---|
| | N patients | 1-year | | 3-year | | 5-year | | |
| **Overall** | 42 872 | 97.5 | [97.4, 97.7] | 92.2 | [91.9, 92.4] | 87.0 | [86.7, 87.3] | |
| **Recognition status for BC** | | | | | | | | <0.0001 |
| Coordinating breast clinic | 30 190 | 97.8 | [97.7, 98.0] | 92.9 | [92.6, 93.2] | 88.0 | [87.6, 88.4] | |
| Satellite breast clinic | 2 453 | 96.5 | [95.7, 97.2] | 91.0 | [89.8, 92.1] | 85.1 | [83.6, 86.6] | |
| No recognition for BC | 10 229 | 96.9 | [96.6, 97.2] | 90.3 | [89.7, 90.9] | 84.5 | [83.8, 85.2] | |
| **Average annual campus volume*** | | | | | | | | <0.0001 |
| ≥125 | 24 744 | 98.0 | [97.9, 98.2] | 93.3 | [93.0, 93.6] | 88.7 | [88.3, 89.1] | |
| [60, 125[ | 11 306 | 97.2 | [96.9, 97.5] | 91.5 | [91.0, 92.0] | 85.8 | [85.1, 86.5] | |
| <60 | 6 822 | 96.4 | [95.9, 96.8] | 89.1 | [88.4, 89.8] | 83.0 | [82.0, 83.9] | |
| **Volume groups per recognition status** | | | | | | | | |
| ***Coordinating breast clinics*** | | | | | | | | <0.0001 |
| ≥125 | 23 665 | 98.0 | [97.8, 98.2] | 93.2 | [92.9, 93.5] | 88.5 | [88.1, 88.9] | |
| [60, 125[ | 6 525 | 97.4 | [97.0, 97.7] | 91.9 | [91.2, 92.5] | 86.3 | [85.4, 87.2] | |
| ***Satellite breast clinics*** | | | | | | | | 0.014 |
| [60, 125[ | 2 109 | 96.2 | [95.2, 96.9] | 90.3 | [89.0, 91.5] | 84.4 | [82.7, 86.0] | |
| <60 | 344 | 98.8 | [96.9, 99.6] | 95.3 | [92.5, 97.1] | 89.4 | [85.1, 92.5] | |
| ***No recognition for BC*** | | | | | | | | <0.0001 |
| ≥125 | 1 079 | 99.4 | [98.8, 99.7] | 96.6 | [95.3, 97.5] | 92.6 | [90.8, 94.0] | |
| [60, 125[ | 2 672 | 97.5 | [96.8, 98.0] | 91.5 | [90.3, 92.5] | 85.6 | [84.2, 87.0] | |
| <60 | 6 478 | 96.2 | [95.8, 96.7] | 88.8 | [88.0, 89.5] | 82.7 | [81.7, 83.6] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from log rank test; 3 021 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with low volume were excluded.*
*Source: BCR-IMA-HDD*

**Table 96 – Observed survival, unadjusted HR for patients with IBC, by recognition status and campus volume**

| | Unadjusted HR | 95% CI | p-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | <0.0001 |
| Coordinating breast clinic | 1 | [Reference] | |
| Satellite breast clinic | 1.22 | [0.98, 1.52] | |
| No recognition for BC | 1.40 | [1.24, 1.59] | |
| **Average annual campus volume*** | | | <0.0001 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.30 | [1.14, 1.49] | |
| <60 | 1.65 | [1.45, 1.88] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.014 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.20 | [1.04, 1.38] | |
| ***Satellite breast clinics*** | | | 0.037 |
| [60, 125[ | 1 | [Reference] | |
| <60 | 0.64 | [0.42, 0.97] | |
| ***No recognition for BC*** | | | <0.0001 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 2.19 | [1.32, 3.63] | |
| <60 | 2.88 | [1.79, 4.64] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model, type III; clustering of patients into campuses (i.e. centre of main treatment) was taken into account; 3 021 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with low volume were excluded.*
*Source: BCR-IMA-HDD*

## Appendix 12.4. Adjusted association between recognition status and campus volume, and 1-, 3- and 5-year observed survival since diagnosis

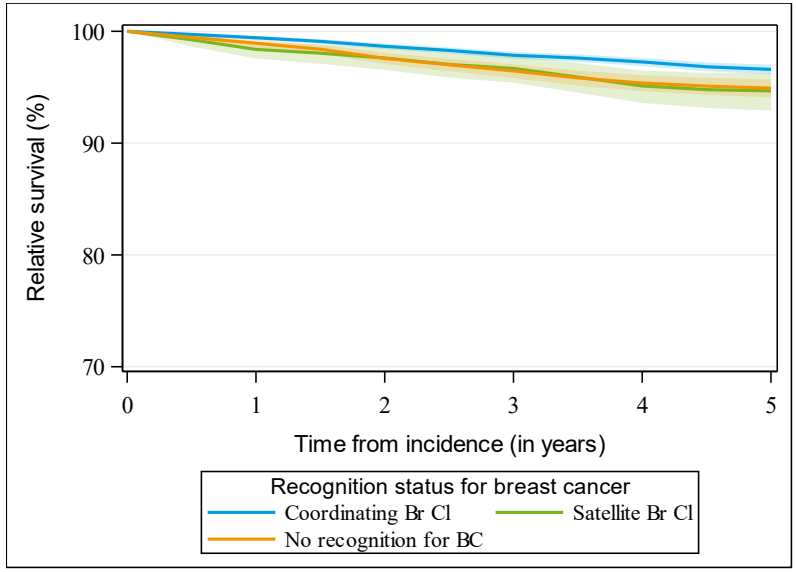
**Table 97 – Observed survival, adjusted HR for patients with IBC, by recognition status and campus volume**

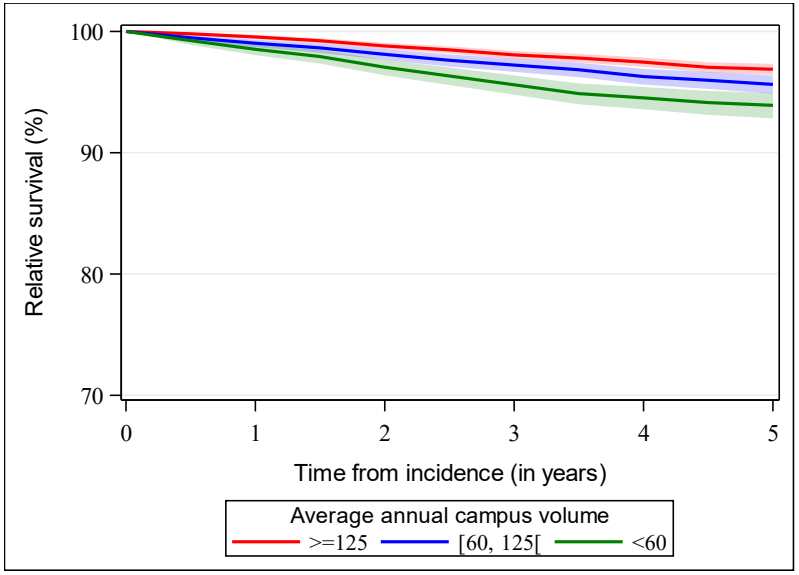
| | Adjusted HR** | 95% CI | p-value, type III$ |
|---|---|---|---|
| **Recognition status for BC** | | | 0.045 |
| Coordinating breast clinic | 1 | [Reference] | |
| Satellite breast clinic | 1.05 | [0.89, 1.24] | |
| No recognition for BC | 1.12 | [1.03, 1.23] | |
| **Average annual campus volume*** | | | 0.006 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.14 | [1.03, 1.26] | |
| <60 | 1.17 | [1.05, 1.30] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.116 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.11 | [0.97, 1.26] | |
| ***Satellite breast clinics*** | | | 0.028 |
| [60, 125[ | 1 | [Reference] | |
| <60 | 0.60 | [0.38, 0.94] | |
| ***No recognition for BC*** | | | 0.294 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.28 | [0.88, 1.85] | |
| <60 | 1.32 | [0.93, 1.87] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model, type III; **: adjusted for: age at diagnosis, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiac and respiratory diseases, and diabetes), combined tumour stage and tumour differentiation grade; clustering of patients into campuses (i.e. centre of main treatment) was taken into account; 3 021 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with low volume were excluded.*
*Source: BCR-IMA-HDD*

## Appendix 12.5. Unadjusted association between the recognition status and volume of a campus, and relative survival since diagnosis

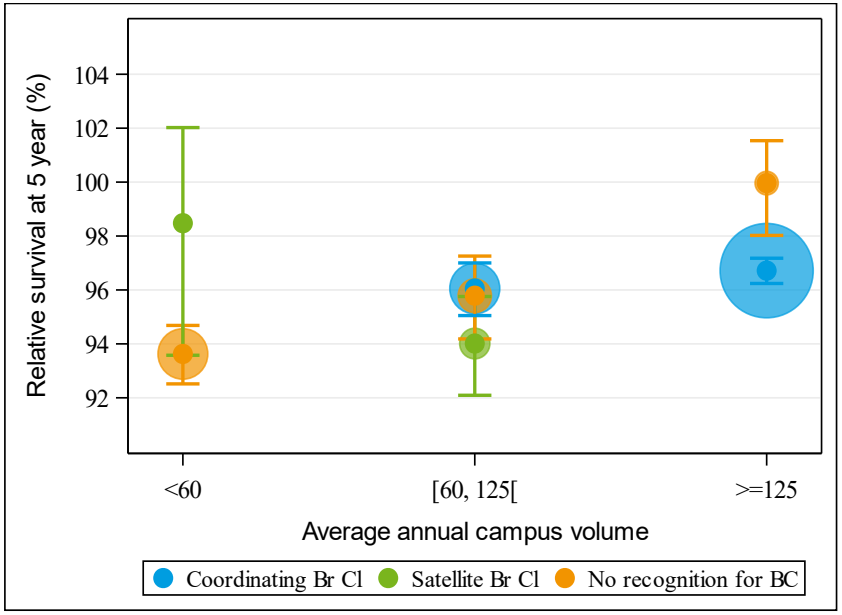
**Figure 29 – Relative survival, by campus recognition status (left) and average annual campus volume (right)**




*Source: BCR-IMA-HDD*

**Figure 30 – Relative survival at 5 year after diagnosis by campus recognition status and average annual campus volume, bubble plot**




*Source: BCR-IMA-HDD*



**Table 98 – 1-, 3-, and 5-year unadjusted relative survival for patients with IBC, by recognition status and campus volume**

| | | Unadjusted relative survival after incidence (%, 95% CI) | | | | | |
|---|---|---|---|---|---|---|---|
| | N patients | 1-year | | 3-year | | 5-year | |
| **Overall** | 42 872 | 99.2 | [99.1, 99.4] | 97.4 | [97.2, 97.7] | 96.1 | [95.7, 96.4] |
| **Recognition status for BC** | | | | | | | |
| Coordinating breast clinic | 30 190 | 99.4 | [99.2, 99.6] | 97.8 | [97.5, 98.1] | 96.6 | [96.1, 97.0] |
| Satellite breast clinic | 2 453 | 98.4 | [97.6, 99.0] | 96.7 | [95.4, 97.8] | 94.7 | [92.9, 96.3] |
| No recognition for BC | 10 229 | 98.9 | [98.6, 99.2] | 96.4 | [95.8, 97.0] | 94.9 | [94.1, 95.7] |
| **Average annual campus volume*** | | | | | | | |
| ≥125 | 24 744 | 99.5 | [99.4, 99.7] | 98.1 | [97.7, 98.4] | 96.9 | [96.4, 97.3] |
| [60, 125[ | 11 306 | 99.0 | [98.7, 99.3] | 97.2 | [96.6, 97.7] | 95.6 | [94.8, 96.3] |
| <60 | 6 822 | 98.5 | [98.0, 98.9] | 95.6 | [94.8, 96.4] | 93.9 | [92.8, 94.9] |
| **Volume groups per recognition status** | | | | | | | |
| ***Coordinating breast clinics*** | | | | | | | |
| ≥125 | 23 665 | 99.5 | [99.3, 99.7] | 97.9 | [97.6, 98.3] | 96.7 | [96.2, 97.2] |
| [60, 125[ | 6 525 | 99.2 | [98.7, 99.5] | 97.5 | [96.8, 98.2] | 96.1 | [95.0, 97.0] |
| ***Satellite breast clinics*** | | | | | | | |
| [60, 125[ | 2 109 | 98.1 | [97.1, 98.8] | 96.0 | [94.6, 97.3] | 94.0 | [92.1, 95.8] |
| <60 | 344 | 100.4 | [98.5, 101.1] | 100.6 | [97.6, 102.5] | 98.5 | [93.6, 102.0] |
| ***No recognition for BC*** | | | | | | | |
| ≥125 | 1 079 | 100.7 | [100.0, 101.0] | 100.6 | [99.3, 101.6] | 100.0 | [98.0, 101.5] |
| [60, 125[ | 2 672 | 99.4 | [98.7, 100.0] | 97.4 | [96.2, 98.5] | 95.8 | [94.2, 97.3] |
| <60 | 6 478 | 98.4 | [97.9, 98.9] | 95.3 | [94.5, 96.1] | 93.6 | [92.5, 94.7] |

**Table 99 – Relative survival, unadjusted relative excess risk to die for patients with IBC, by recognition status and campus volume**

| | Unadjusted EHR | 95% CI | p-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | <0.001 |
| Coordinating breast clinic | 1 | [Reference] | |
| Satellite breast clinic | **1.66** | [1.19, 2.30] | |
| No recognition for BC | **1.60** | [1.31, 1.95] | |
| **Average annual campus volume*** | | | <0.001 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | **1.43** | [1.14, 1.78] | |
| <60 | **2.10** | [1.69, 2.63] | |
| **Volume groups per recognition status** | | | |
| **Coordinating breast clinic** | | | 0.258 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 1.18 | [0.89, 1.57] | |
| **Satellite breast clinic** | | | 0.258 |
| ≥125 | 1 | [Reference] | |
| <60 | 0.17 | [0.01, 2.05] | |
| **No recognition for BC** | | | 0.009 |
| ≥125 | 1 | [Reference] | |
| [60, 125[ | 7.88 | [0.60, 103.0] | |
| <60 | 12.03 | [0.93, 155.1] | |

*IBC: invasive breast cancer; EHR: excess hazard ratio; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model; clustering of patients into campuses (i.e. centre of main treatment) was not taken into account; 3 021 out of 45 893 patients could not be assigned to a campus, and were thus excluded from the analyses; 142 patients assigned to a coordinating breast clinic with a low volume were excluded.*

*Source: BCR-IMA-HDD*



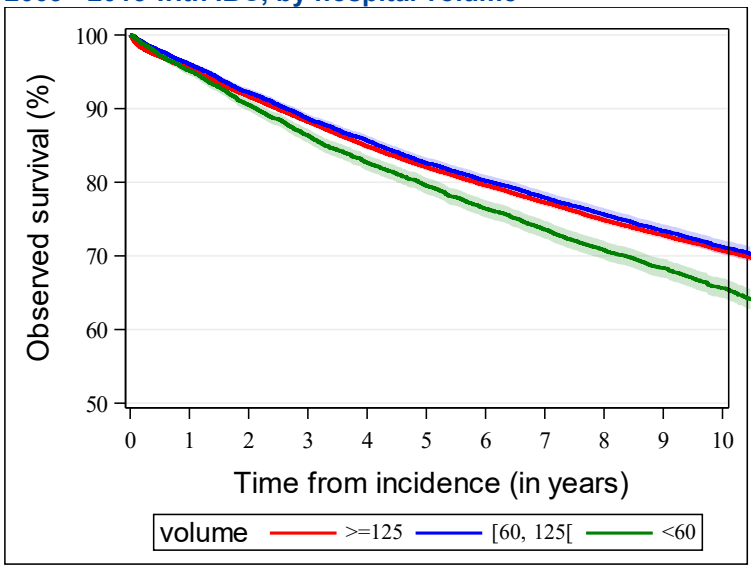
## Appendix 12.6. Association between hospital volume and observed survival since diagnosis in the comparison cohort (2009 - 2013)

**Table 100 – 1-, 3-, 5-, and 10-year unadjusted observed survival for patients diagnosed in 2009 - 2013 with IBC, by hospital volume**

| | | Unadjusted observed survival (%, 95% CI) | | | | | | | | p-value$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | N patients | 1-year | | 3-year | | 5-year | | 10-year | | |
| **Overall** | 43 506 | 95.5 | [95.3, 95.7] | 88.1 | [87.8, 88.4] | 81.9 | [81.5, 82.2] | 70.2 | [69.8, 70.7] | |
| **Average annual hospital volume*** | | | | | | | | | | <0.0001 |
| ≥125 | 29 026 | 95.3 | [95.1, 95.6] | 88.2 | [87.8, 88.6] | 82.1 | [81.6, 82.5] | 70.7 | [70.2, 71.3] | |
| [60, 125[ | 9 413 | 96.0 | [95.6, 96.4] | 88.7 | [88.0, 89.3] | 82.6 | [81.8, 83.4] | 71.2 | [70.3, 72.2] | |
| <60 | 5 067 | 95.1 | [94.5, 95.7] | 86.4 | [85.4, 87.3] | 79.5 | [78.4, 80.6] | 65.6 | [64.3, 67.0] | |

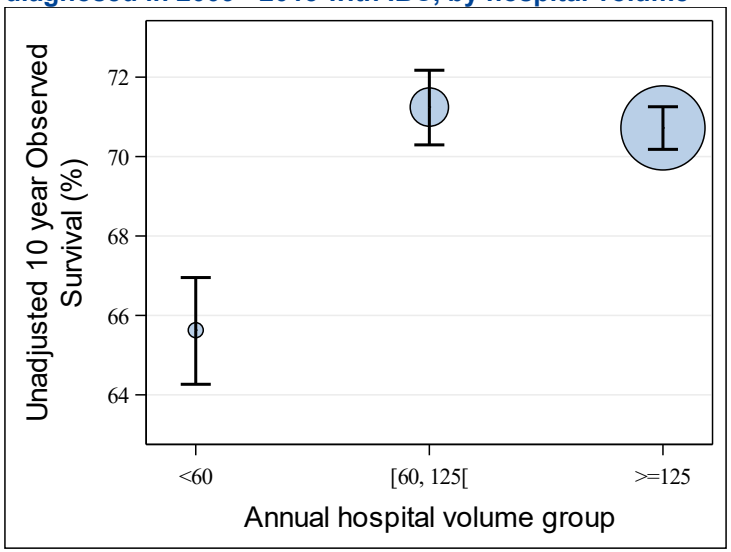
*IBC: invasive breast cancer; *: the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model.*
*Source: BCR-IMA*

**Figure 31 – Observed survival probability for patients diagnosed in 2009 - 2013 with IBC, by hospital volume**




*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Figure 32 – 10-year observed survival probability for patients diagnosed in 2009 - 2013 with IBC, by hospital volume**




*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Table 101 – Observed survival, unadjusted HR for patients diagnosed in 2009 - 2013 with IBC, by hospital volume**

| | Unadjusted HR | 95% CI | p-value£ | p-value, type III$ |
|---|---|---|---|---|
| **Average annual hospital volume*** | | | | <0.001 |
| ≥125 | 1 | [Reference] | | |
| [60, 125[ | 1.02 | [0.88, 1.20] | 0.770 | |
| <60 | 1.34 | [1.15, 1.56] | <0.001 | |

*IBC: invasive breast cancer; *: the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model; £: p-value from Wald test; clustering of patients into hospitals (i.e. centre of main treatment) was taken into account.*
*Source: BCR-IMA*

**Table 102 – Observed survival, adjusted HR for patients diagnosed in 2009 - 2013 with IBC, by hospital volume**

| | Adjusted HR[#] | 95% CI | p-value[£] | p-value, type III[$] |
|---|---|---|---|---|
| **Average annual hospital volume*** | | | | 0.364 |
| ≥125 | 1 | [Reference] | | |
| [60, 125[ | 1.02 | [0.93, 1.11] | 0.750 | |
| <60 | 1.07 | [0.97, 1.17] | 0.164 | |

*IBC: invasive breast cancer; *: the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Cox proportional hazards regression model; £: p-value from Wald test; #: adjusted for age at diagnosis, WHO performance status at diagnosis, the number of inpatient bed days the year preceding the incidence year, comorbidities (cardiac and respiratory diseases, and diabetes), combined tumour stage and tumour differentiation grade; clustering of patients into hospitals (i.e. centre of main treatment) was taken into account.*
*Source: BCR-IMA*

# APPENDIX 13. MAMMOGRAPHY AND SONOGRAPHY

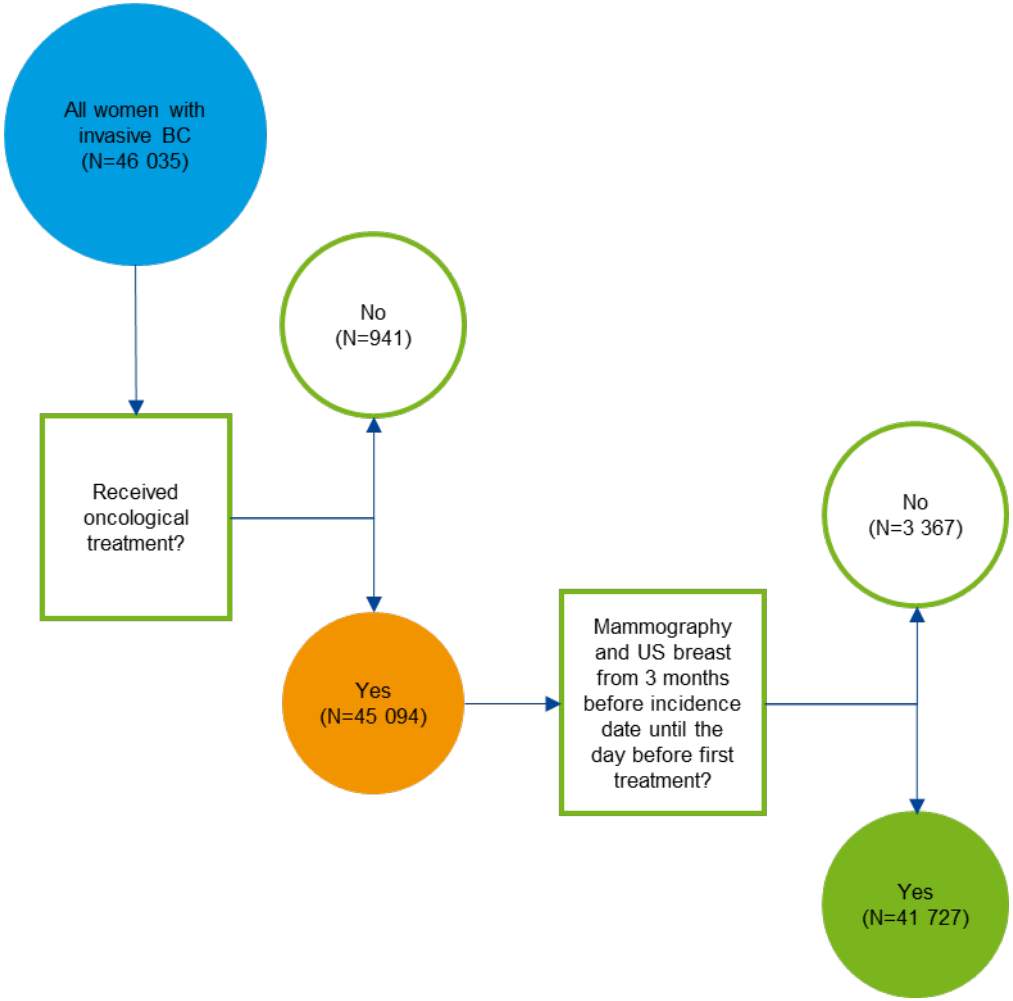
## Appendix 13.1. Documentation sheet

| Title | Proportion of women with IBC who received mammography and breast sonography before any oncological treatment |
|---|---|
| **Rationale** | The diagnosis of BC is based on a clinical examination in combination with imaging and should be confirmed by pathological assessment. To allow a proper diagnostic approach and to identify size, site and possible multifocal and/or contralateral disease, imaging includes bilateral mammography and sonography (ultrasound, US) of the breast and regional lymph nodes.<br><br>Magnetic resonance imaging (MRI) of the breast is more sensitive in determining the extent of the tumour but it may also overestimate the tumour size.[82] An MRI of the breast is not routinely recommended, but should be considered in cases of specific situations (e.g. familial BC associated with BRCA mutations, dense breasts, suspicion of multifocality/multicentricity (particularly in lobular BC)).[83] |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women with mammography and breast sonography (US) from 3 months before incidence date until the day before first treatment<br><br>Denominator: All women diagnosed with IBC who received oncological treatment |
| **Target** | 95% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26– Appendix 5)<br><br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br><br>Oncological treatment includes:<br>- Surgery, for nomenclature codes, see Table 44, Table 45, Table 46, Table 47<br>- Radiotherapy, for nomenclature codes, see Table 49<br>- Chemotherapy, for ATC codes, see Table 50<br>- Endocrine therapy, for ATC codes, see Table 52<br>- Targeted therapy, for ATC codes, see Table 51<br><br>Mammography: for nomenclature codes, see Table 36 |

| Title | Proportion of women with IBC who received mammography and breast sonography before any oncological treatment |
|---|---|
| | US breast: for nomenclature codes, see Table 37<br>Given the prevailing cumulation rules for the use of nomenclature codes, the QI was calculated as follows:<br>• Mammography within 3 months before incidence and 1 day before oncological treatment AND a breast ultrasound (excluding echo-guided biopsy) in the same time frame<br>OR<br>• Mammography within 3 months before incidence and 1 day before oncological treatment AND one of the non-specific nomenclature codes for US (limited list see Table 53) on the same day as the mammography<br>OR<br>• [Breast puncture OR breast biopsy] AND additional fee when punctures are performed under US or radiological guidance (nomenclature code 355913-355924) are invoiced together with a mammography on the same day; it is considered that these patients had mammography & US (i.e. the US was not billed since the puncture was taken under US guidance)<br>OR<br>• [Breast puncture OR breast biopsy] AND additional fee when punctures are performed under US or radiological guidance (nomenclature code 355913-355924) are invoiced together with a breast or non-specific US on the same day; it is considered that these patients had mammography & US (i.e. the mammography was not billed since the puncture was taken under mammography guidance) |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | While the guidelines stipulate to have a bilateral mammography and ultrasound of both breast and axillae, based on the nomenclature codes it is not possible to distinguish between procedures performed in the breast and procedures performed in the lymph nodes. In addition, for US it cannot be verified whether both breasts were examined as the nomenclature code is too vague ('460132 – 460143: US of one or both breast(s) with axillae'). |
| **Subgroup analyses** | • Clinical stage<br>• Age at diagnosis<br>• WHO performance status at time of diagnosis<br>• Number of inpatient bed days the year preceding the incidence date<br>• Number and type of comorbidities<br>• Year of incidence<br>• Treatment modality |
| **Sensitivity analyses** | • Incidence year 2009 - 2013 vs 2014 - 2018 |

| Title | Proportion of women with IBC who received mammography and breast sonography before any oncological treatment |
|---|---|
| | • Excluding patients younger than 30 year<br>• Excluding cT4b/c cases<br>• Types of imaging performed per clinical stage |
| **Benchmarking** | Centre of first treatment |
| **Level of benchmarking** | Campus level |
| **Comments** | |

## Appendix 13.2. Flowchart



## Appendix 13.3. Results

**Table 103 – Proportion of women with IBC with mammography and breast sonography before any treatment, by patient and tumour characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 45 094 | 41 727 | 92.5 |
| **Age at diagnosis** | | | |
| <40 years | 2 239 | 1 950 | 87.1 |
| 40-49 years | 6 741 | 6 293 | 93.4 |
| 50-59 years | 10 497 | 9 806 | 93.4 |
| 60-69 years | 11 473 | 10 734 | 93.6 |
| 70-79 years | 8 127 | 7 587 | 93.4 |
| 80+ years | 6 017 | 5 357 | 89.0 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 24 810 | 23 325 | 94.0 |
| 1 – Symptomatic but completely ambulatory | 15 713 | 14 409 | 91.7 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 722 | 561 | 77.7 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 249 | 179 | 71.9 |
| 4 – Completely disabled; totally confined to bed or chair | 77 | 45 | 58.4 |
| Missing | 3 523 | 3 208 | 91.1 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 33 727 | 31 486 | 93.4 |
| 1-5 days | 7 760 | 7 061 | 91.0 |
| 6-15 days | 2 228 | 1 980 | 88.9 |
| >15 days | 1 379 | 1 200 | 87.0 |
| **Number of comorbidities** | | | |
| 0 | 23 989 | 22 136 | 92.3 |
| 1 | 15 946 | 14 837 | 93.0 |
| 2 | 4 771 | 4 397 | 92.2 |
| 3 | 388 | 357 | 92.0 |
| **Cardiovascular disease** | | | |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| Absent | 26 014 | 24 003 | 92.3 |
| Present | 19 080 | 17 724 | 92.9 |
| **Respiratory disease** | | | |
| Absent | 42 011 | 38 885 | 92.6 |
| Present | 3 083 | 2 842 | 92.2 |
| **Diabetes** | | | |
| Absent | 40 605 | 37 591 | 92.6 |
| Present | 4 489 | 4 136 | 92.1 |
| **Incidence year** | | | |
| 2014 | 8 794 | 8 152 | 92.7 |
| 2015 | 8 808 | 8 155 | 92.6 |
| 2016 | 9 167 | 8 519 | 92.9 |
| 2017 | 8 983 | 8 273 | 92.1 |
| 2018 | 9 342 | 8 628 | 92.4 |
| **Clinical stage** | | | |
| 0 | 568 | 526 | 92.6 |
| I | 18 548 | 17 474 | 94.2 |
| II | 15 507 | 14 591 | 94.1 |
| III | 2 951 | 2 624 | 88.9 |
| IV | 2 677 | 2 147 | 80.2 |
| Unknown | 4 843 | 4 365 | 90.1 |
| **Treatment modality** | | | |
| Surgery < adjuvant RT | 899 | 828 | 92.1 |
| Surgery < adjuvant systemic Tx | 5 176 | 4 798 | 92.7 |
| Surgery < adjuvant RT + systemic Tx | 27 374 | 25 913 | 94.7 |
| Neoadjuvant Tx < surgery (<adjuvant Tx) | 5 976 | 5 541 | 92.7 |
| Surgery only | 808 | 687 | 85.0 |
| Primary systemic and/or radiotherapy | 4 861 | 3 960 | 81.5 |

*IBC: invasive breast cancer; WHO: World Health Organization.*
*Source: BCR-IMA*

### Table 104 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 45 094 | 41 727 | 92.5 |
| **Comparison period (2009 - 2013)** | 42 589 | 39 318 | 92.3 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

### Table 105 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, excluding patients <30 year

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 45 094 | 41 727 | 92.5 |
| **Excluding patients <30 years old** | 44 856 | 41 546 | 92.6 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

### Table 106 – Sensitivity analysis: Proportion of women with IBC with mammography and breast sonography before any treatment, excluding cT4b/c/d cases

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 45 094 | 41 727 | 92.5 |
| **Excluding cT4b/c/d cases** | 43 848 | 40 695 | 92.8 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

### Table 107 – Sensitivity analysis: Type of breast imaging in women with IBC before any treatment, by clinical stage

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Only mammography** | **45 094** | **376** | **0.8** |
| **Per clinical stage** | | | |
| 0 | 568 | 15 | 2.6 |
| I | 18 548 | 143 | 0.8 |
| II | 15 507 | 104 | 0.7 |
| III | 2 951 | 18 | 0.6 |
| IV | 2 677 | 47 | 1.8 |
| Unknown | 4 843 | 49 | 1.8 |
| **Only breast sonography** | **45 094** | **973** | **2.2** |
| **Per clinical stage** | | | |
| 0 | 568 | 4 | 0.7 |
| I | 18 548 | 258 | 1.4 |
| II | 15 507 | 250 | 1.6 |
| III | 2 951 | 112 | 3.8 |
| IV | 2 677 | 212 | 7.9 |
| Unknown | 4 843 | 137 | 2.8 |
| **Only breast MRI** | **45 094** | **149** | **0.3** |
| **Per clinical stage** | | | |
| 0 | 568 | 4 | 0.7 |
| I | 18 548 | 56 | 0.3 |
| II | 15 507 | 44 | 0.3 |
| III | 2 951 | 12 | 0.4 |
| IV | 2 677 | 10 | 0.4 |
| Unknown | 4 843 | 23 | 0.5 |
| **Mammography and breast MRI but no breast sonography** | **45 094** | **356** | **0.8** |
| **Per clinical stage** | | | |
| 0 | 568 | 13 | 2.3 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| I | 18 548 | 124 | 0.7 |
| II | 15 507 | 137 | 0.9 |
| III | 2 951 | 17 | 0.6 |
| IV | 2 677 | 8 | 0.3 |
| Unknown | 4 843 | 57 | 1.2 |
| **Breast sonography and breast MRI but no mammography** | **45 094** | **906** | **2.0** |
| **Per clinical stage** | | | |
| 0 | 568 | 6 | 1.1 |
| I | 18 548 | 405 | 2.2 |
| II | 15 507 | 278 | 1.8 |
| III | 2 951 | 70 | 2.4 |
| IV | 2 677 | 48 | 1.8 |
| Unknown | 4 843 | 99 | 2.0 |
| **No mammography nor breast sonography nor breast MRI in the defined time frame** | **45 094** | **607** | **1.3** |
| **Per clinical stage** | | | |
| 0 | 568 | 0 | 0.0 |
| I | 18 548 | 88 | 0.5 |
| II | 15 507 | 103 | 0.7 |
| III | 2 951 | 98 | 3.3 |
| IV | 2 677 | 205 | 7.7 |
| Unknown | 4 843 | 113 | 2.3 |
| **Mammography and breast sonography and breast MRI** | **45 094** | **21 543** | **47.7** |
| **Per clinical stage** | | | |
| 0 | 568 | 295 | 51.9 |
| I | 18 548 | 8 949 | 48.2 |
| II | 15 507 | 8 015 | 51.7 |
| III | 2 951 | 1 406 | 47.6 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| IV | 2 677 | 672 | 25.1 |
| Unknown | 4 843 | 2 206 | 45.6 |
| **Mammography and breast sonography but no breast MRI** | **45 094** | **20 184** | **44.8** |
| **Per clinical stage** | | | |
| 0 | 568 | 231 | 40.7 |
| I | 18 548 | 8 525 | 46.0 |
| II | 15 507 | 6 576 | 42.4 |
| III | 2 951 | 1 218 | 41.3 |
| IV | 2 677 | 1 475 | 55.1 |
| Unknown | 4 843 | 2 159 | 44.6 |

*IBC: invasive breast cancer; note: based on the nomenclature codes it is not possible to distinguish between procedures performed in the breast and procedures performed in the lymph nodes; categories mammography only, US only, MRI only, mammography & MRI, US & MRI and no mammography, no US and no MRI are calculated on patients included in the denominator but NOT in the numerator while categories mammography & US & MRI and mammography & US are calculated only on patients included in numerator.*
*Source: BCR-IMA*

### Table 108 – Proportion of women with IBC with mammography and breast sonography before any treatment, by recognition status for BC and campus volume

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 41 593 | 38 954 | 93.7 | [93.4, 93.9] | |
| **Recognition status for BC** | | | | | 0.2252 |
| Coordinating breast clinic | 29 039 | 27 216 | 93.7 | [93.4, 94.0] | |
| Satellite breast clinic | 2 402 | 2 262 | 94.2 | [93.2, 95.1] | |
| No recognition for BC | 10 152 | 9 476 | 93.3 | [92.8, 93.8] | |
| **Average annual campus volume*** | | | | | <0.0001 |
| ≥125 | 23 783 | 22 398 | 94.2 | [93.9, 94.5] | |
| [60, 125[ | 10 902 | 10 167 | 93.3 | [92.8, 93.7] | |
| <60 | 6 908 | 6 389 | 92.5 | [91.8, 93.1] | |
| **Volume groups per recognition status** | | | | | |

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| ***Coordinating breast clinics*** | | | | | <0.0001 |
| ≥125 | 22 794 | 21 444 | 94.1 | [93.8, 94.4] | |
| [60, 125[ | 6 245 | 5 772 | 92.4 | [91.7, 93.1] | |
| ***Satellite breast clinics*** | | | | | 0.0901 |
| [60, 125[ | 2 056 | 1 943 | 94.5 | [93.4, 95.4] | |
| <60 | 346 | 319 | 92.2 | [88.8, 94.8] | |
| ***No recognition for BC*** | | | | | <0.0001 |
| ≥125 | 989 | 954 | 96.5 | [95.1, 97.5] | |
| [60, 125[ | 2 601 | 2 452 | 94.3 | [93.3, 95.1] | |
| <60 | 6 562 | 6 070 | 92.5 | [91.8, 93.1] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 3 304 patients could not be assigned to a campus, and were thus excluded from the analyses; 196 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on the algorithm for centre of first treatment) to a campus with no main treatment volume, were excluded.*

*Source: BCR-IMA-HDD*

**Table 109 – Association between recognition status for BC and campus volume, and the odds of having mammography and breast sonography before any treatment in women with IBC, including volume analyses by recognition status**

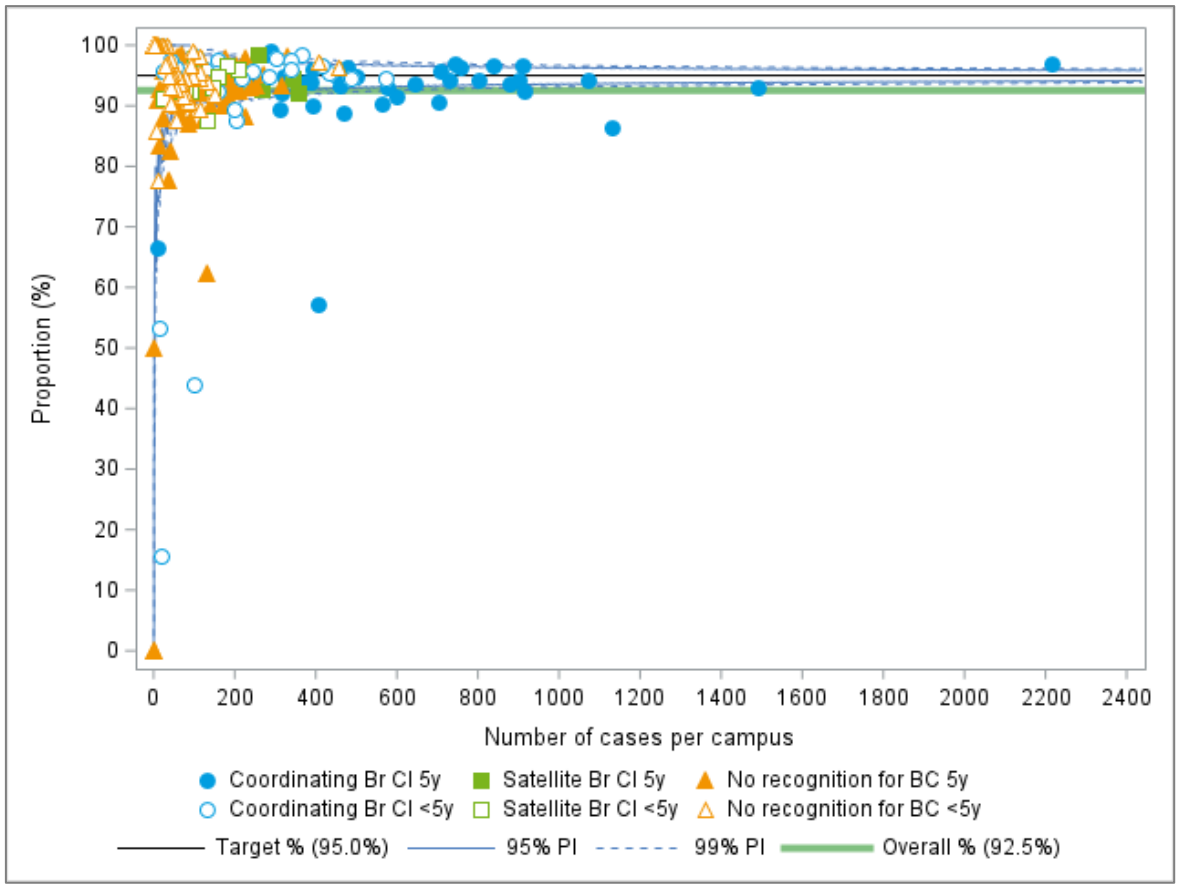
| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.206 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.96 | [0.65, 1.41] | |
| No recognition for BC | 0.82 | [0.66, 1.02] | |
| **Average annual campus volume*** | | | 0.015 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.02 | [0.78, 1.32] | |
| <60 | 0.74 | [0.58, 0.95] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.796 |

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.05 | [0.73, 1.51] | |
| ***Satellite breast clinics*** | | | 0.327 |
| [60, 125[ | 1 | [reference] | |
| <60 | 0.71 | [0.36, 1.40] | |
| ***No recognition for BC*** | | | 0.041 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.71 | [0.34, 1.48] | |
| <60 | 0.51 | [0.26, 1.01] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first treatment) was taken into account; 3 304 patients could not be assigned to a campus, and were thus excluded from the analyses; 196 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on the algorithm for centre of first treatment) to a campus with no main treatment volume.*

*Source: BCR-IMA-HDD*

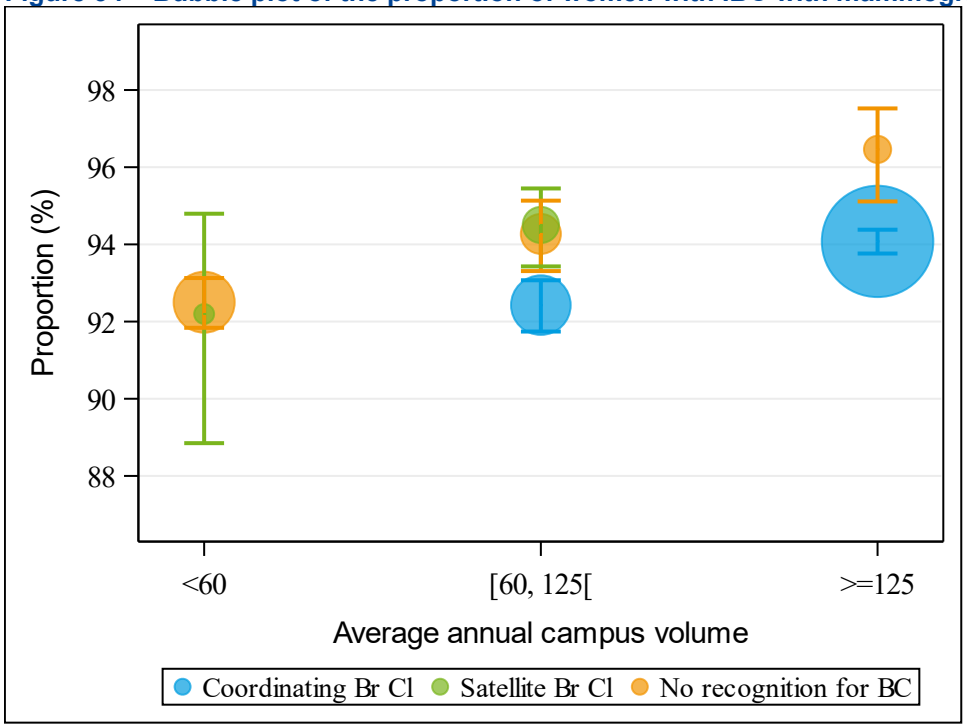
**Figure 33 – Funnel plot of the proportion of women with IBC with mammography and breast sonography before any treatment, by campus of first treatment**




*IBC: invasive breast cancer; Note: there were 184 units of analysis presented in the funnel plot, of which 20 had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 3 304 patients for whom the campus could not be identified, are not represented in the funnel plot.*

*Source: BCR-IMA-HDD*

**Figure 34 – Bubble plot of the proportion of women with IBC with mammography and breast sonography before any treatment, by campus volume***




*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 3 304 patients could not be assigned to a campus, and were thus excluded from the analyses; 196 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on the algorithm for centre of first treatment) to a campus with no main treatment volume.*

*Source: BCR-IMA-HDD*

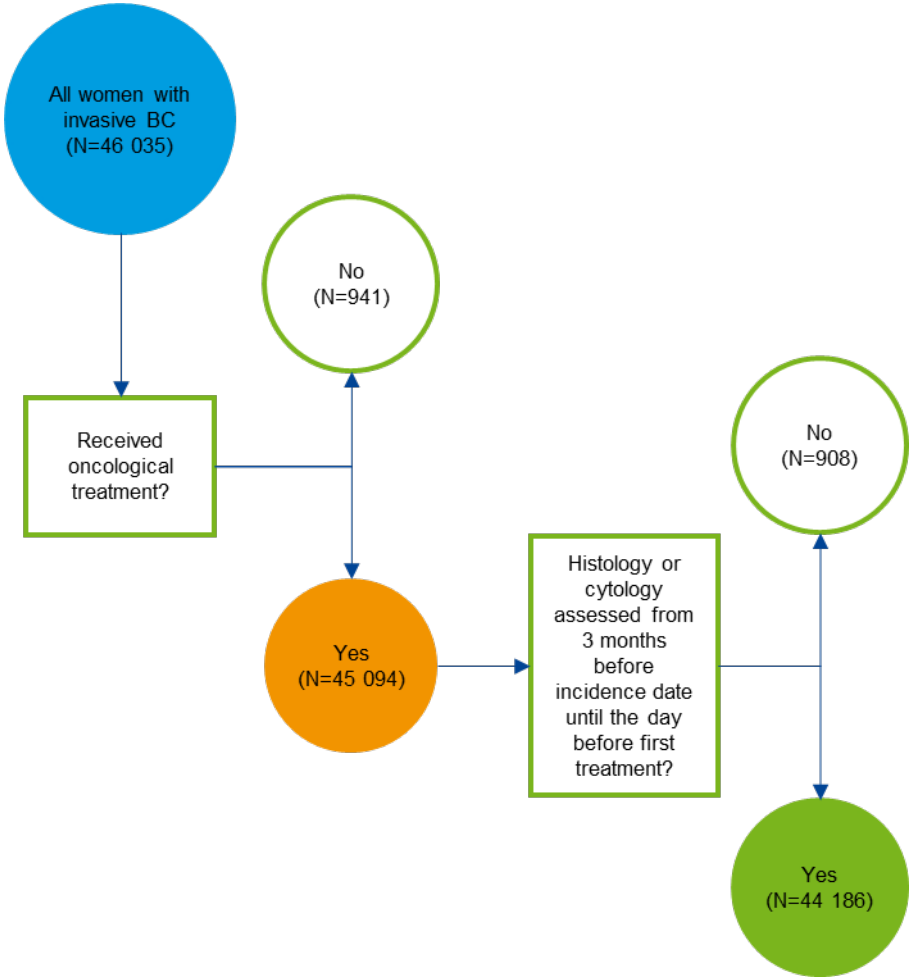
# APPENDIX 14. ASSESSMENT OF HISTOLOGY AND/OR CYTOLOGY BEFORE TREATMENT

## Appendix 14.1. Documentation sheet

| Title | Proportion of women with IBC with histological or cytological assessment before any oncological treatment |
|---|---|
| **Rationale** | The KCE guideline on the diagnosis, treatment and follow-up of BC in women stated that a lesion in the breast 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.[86]<br><br>Although the cytological assessment of breast tumours before treatment is nowadays obsolete, cytological assessment was still included in the calculation of this quality indicator as exploration of the administrative database revealed that the nomenclature codes intended for cytology were often used for a histological assessment and vice versa. In addition, the present study includes incidence years 2014 - 2018, when cytology was still being performed.<br><br>The clinical experts involved in this report further proposed not to restrict this quality indicator to women who had surgery, but to enlarge the target group to all women with IBC who had any type of treatment. |
| **Selection** | This QI was selected by all (n=17) experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women with histological or cytological assessment from 3 months before incidence date until the day before first treatment<br><br>Denominator: All women diagnosed with IBC who received oncological treatment |
| **Target** | >90% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br><br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br><br>Oncological treatment includes:<br><br>- Surgery, for nomenclature codes, see Table 44, Table 45, Table 46, Table 47 |

| Title | Proportion of women with IBC with histological or cytological assessment before any oncological treatment |
|---|---|
| | - Radiotherapy, for nomenclature codes, see Table 49<br>- Chemotherapy, for ATC codes, see Table 50<br>- Endocrine therapy, for ATC codes, see Table 52<br>- Targeted therapy, for ATC codes, see Table 51<br><br>Cytological and/or histological assessment: for nomenclature codes, see Table 30, Table 31, Table 32 |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | The administrative data only reveal when the examination was performed but not if this examination led to the confirmation of the diagnosis. |
| **Subgroup analyses** | - Clinical stage, combined stage<br>- Age at diagnosis<br>- Year of incidence<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Treatment modality |
| **Sensitivity analyses** | Incidence year 2009 - 2013 vs 2014 - 2018<br><br>Types of histological/cytological assessment performed |
| **Benchmarking** | Diagnostic centre & centre of main treatment |
| **Level of benchmarking** | Hospital level (diagnostic centre) & campus level (main treatment centre) |
| **Comments** | |

## Appendix 14.2. Flowchart



## Appendix 14.3. Results

**Table 110 – Proportion of women with IBC with histological or cytological assessment before any treatment, by patient and tumour characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 45 094 | 44 186 | 98.0 |
| **Age at diagnosis** | | | |
| <40 years | 2 239 | 2 177 | 97.2 |
| 40-49 years | 6 741 | 6 633 | 98.4 |
| 50-59 years | 10 497 | 10 320 | 98.3 |
| 60-69 years | 11 473 | 11 265 | 98.2 |
| 70-79 years | 8 127 | 7 976 | 98.1 |
| 80+ years | 6 017 | 5 815 | 96.6 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 24 810 | 24 403 | 98.4 |
| 1 – Symptomatic but completely ambulatory | 15 713 | 15 345 | 97.7 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 722 | 684 | 94.7 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 249 | 234 | 94.0 |
| 4 – Completely disabled; totally confined to bed or chair | 77 | 73 | 94.8 |
| Missing | 3 523 | 3 447 | 97.8 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 33 727 | 33 124 | 98.2 |
| 1-5 days | 7 760 | 7 548 | 97.3 |
| 6-15 days | 2 228 | 2 177 | 97.7 |
| >15 days | 1 379 | 1 337 | 97.0 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Number of comorbidities** | | | |
| 0 | 23 989 | 23 497 | 97.9 |
| 1 | 15 946 | 15 643 | 98.1 |
| 2 | 4 771 | 4 667 | 97.8 |
| 3 | 388 | 379 | 97.7 |
| **Cardiovascular disease** | | | |
| Absent | 26 014 | 25 482 | 98.0 |
| Present | 19 080 | 18 704 | 98.0 |
| **Respiratory disease** | | | |
| Absent | 42 011 | 41 178 | 98.0 |
| Present | 3 083 | 3 008 | 97.6 |
| **Diabetes** | | | |
| Absent | 40 605 | 39 784 | 98.0 |
| Present | 4 489 | 4 402 | 98.1 |
| **Incidence year** | | | |
| 2014 | 8 794 | 8 538 | 97.1 |
| 2015 | 8 808 | 8 613 | 97.8 |
| 2016 | 9 167 | 9 004 | 98.2 |
| 2017 | 8 983 | 8 822 | 98.2 |
| 2018 | 9 342 | 9 209 | 98.6 |
| **Clinical stage** | | | |
| 0 | 568 | 560 | 98.6 |
| I | 18 548 | 18 271 | 98.5 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| II | 15 507 | 15 278 | 98.5 |
| III | 2 951 | 2 872 | 97.3 |
| IV | 2 677 | 2 588 | 96.7 |
| Unknown | 4 843 | 4 617 | 95.3 |
| **Combined stage** | | | |
| (y)0 | 1 065 | 1 052 | 98.8 |
| yis | 337 | 336 | 99.7 |
| (y)I | 20 009 | 19 629 | 98.1 |
| (y)II | 15 307 | 15 044 | 98.3 |
| (y)III | 4 857 | 4 731 | 97.4 |
| (y)IV | 2 758 | 2 666 | 96.7 |
| Unknown | 761 | 728 | 95.7 |
| **Treatment modality** | | | |
| Surgery < adjuvant RT | 899 | 863 | 96.0 |
| Surgery < adjuvant systemic Tx | 5 176 | 5 046 | 97.5 |
| Surgery < adjuvant RT + systemic Tx | 27 374 | 26 931 | 98.4 |
| Neoadjuvant Tx < surgery (<adjuvant Tx) | 5 976 | 5 883 | 98.4 |
| Surgery only | 808 | 753 | 93.2 |
| Primary systemic and/or radiotherapy | 4 861 | 4 710 | 96.9 |

*IBC: invasive breast cancer; WHO: World Health Organization; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis; Tx: treatment; <: followed by.*
*Source: BCR-IMA*

**Table 111 – Sensitivity analysis: Proportion of women with IBC with histological or cytological assessment before any treatment, by time period**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 45 094 | 44 186 | 98.0 |
| **Comparison period (2009 - 2013)** | 42 589 | 40 813 | 95.8 |

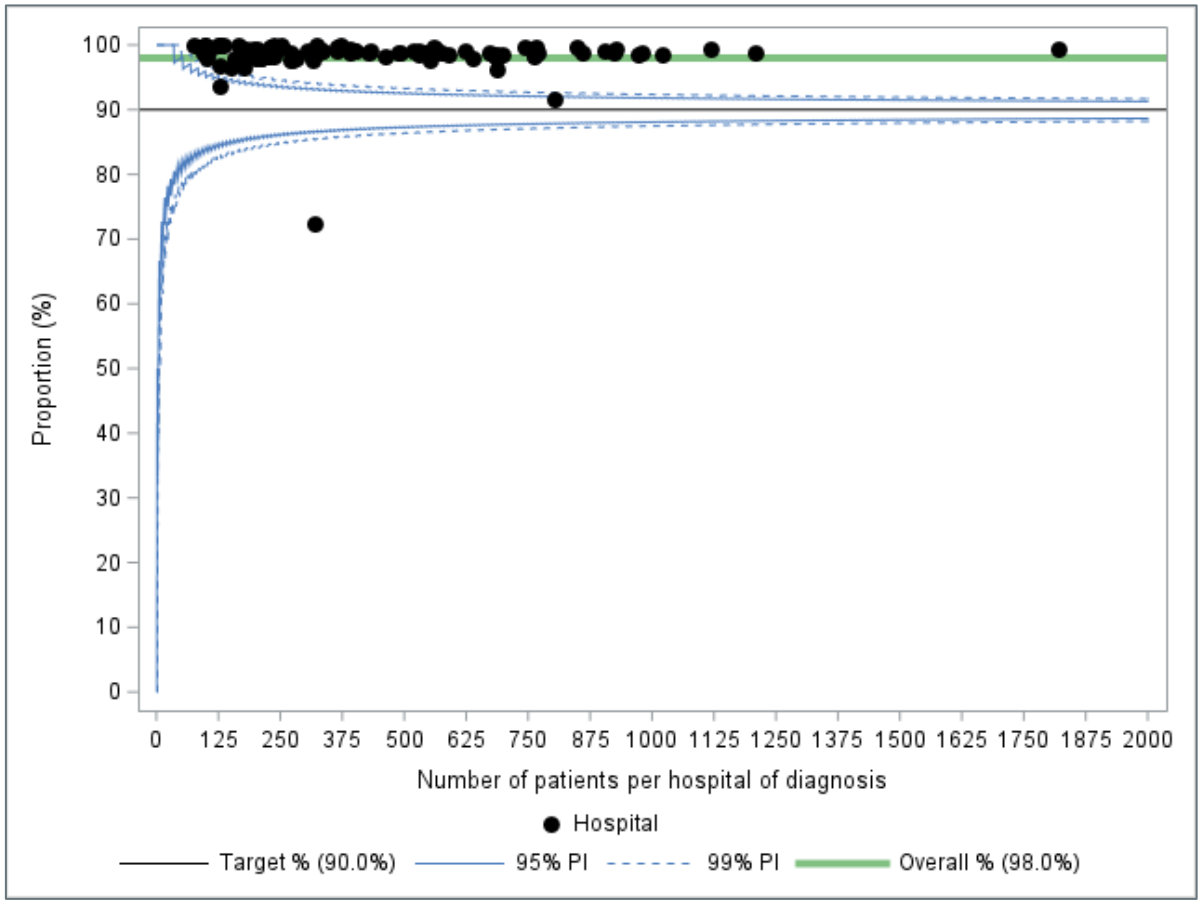
*IBC: invasive breast cancer*
*Source: BCR-IMA*

**Table 112 – Sensitivity analysis: Proportion of women with IBC with histological or cytological assessment before any treatment, by type of histological or cytological assessment**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Only cytological examination** | 45 094 | 625 | 1.4 |
| **Only histological examination** | 45 094 | 389 | 0.9 |
| **Only IHC** | 45 094 | 61 | 0.1 |
| **Cytological & histological examination** | 45 094 | 156 | 0.4 |
| **Cytological examination + IHC** | 45 094 | 100 | 0.2 |
| **Histological examination + IHC** | 45 094 | 29 898 | 66.3 |
| **Cytological & histological examination + IHC** | 45 094 | 12 957 | 28.7 |

*IBC: invasive breast cancer; IHC: immunohistochemical testing.*
*Note: based on the nomenclature codes it is not possible to distinguish between procedures performed in the breast and procedures performed in the lymph nodes.*
*Source: BCR-IMA*

**Figure 35 – Proportion of women with IBC with histological or cytological assessment before any treatment, by hospital of diagnosis**




*Note: There were 100 hospitals reported in the funnel plot; one out of hundred hospitals were situated below the 99% prediction interval, while 97 were situated above the 99% prediction interval; 1 719 patients, who could not be assigned to a centre of diagnosis, are not represented in the funnel plot.*
*Source: BCR-IMA*

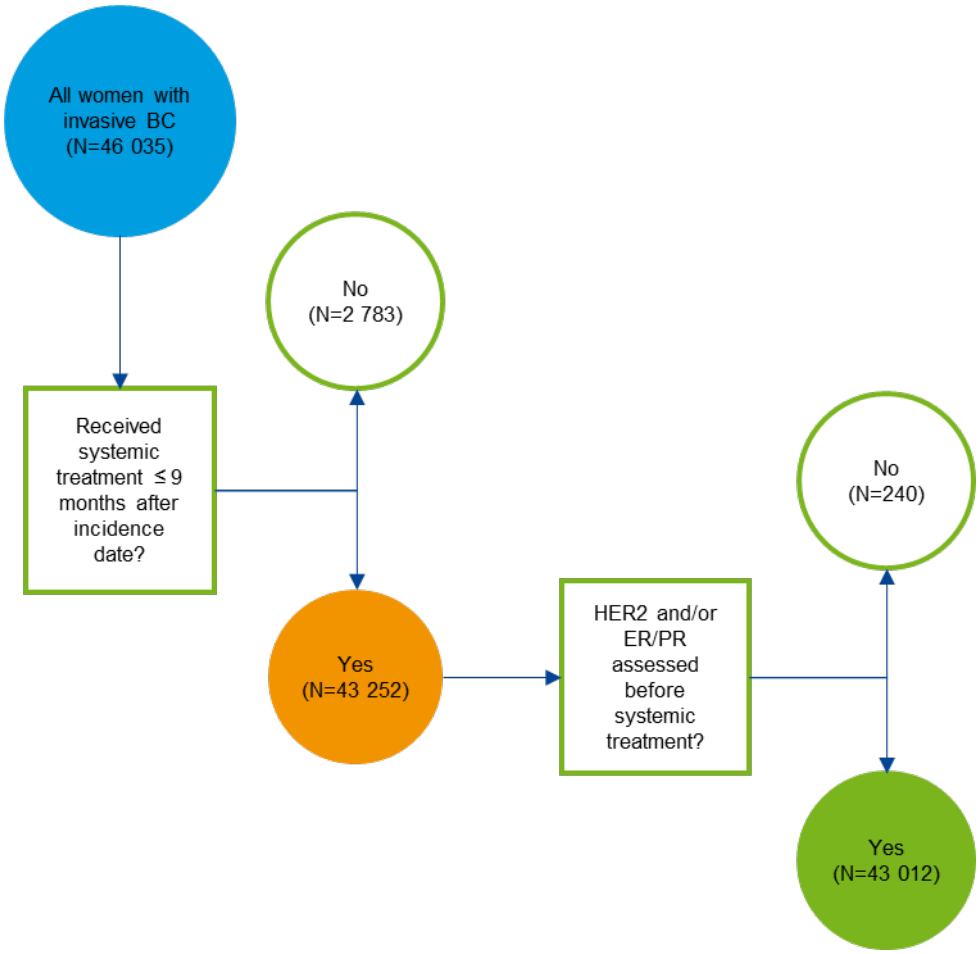
# APPENDIX 15. ASSESSMENT OF RECEPTOR STATUS BEFORE ANY SYSTEMIC TREATMENT

## Appendix 15.1. Documentation sheet

| Title | Proportion of women with IBC in whom human epidermal growth factor receptor 2 (HER2) status and/or oestrogen receptor (ER) and/or progesterone receptor (PR) status were assessed before any systemic treatment |
|---|---|
| **Rationale** | Information on oestrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor 2 (HER2) receptor status is essential in determining the need and type of (neo)adjuvant therapy in BC. Hence, it is recommended to have these biomarkers routinely tested for all IBC.[90]<br><br>This QI was already included in a previous BCR study on the quality of care in BC in Belgium (2012-2014). The QI is slightly different from the EUSOMA QI ('Proportion of invasive cancer cases for which the following prognostic/predictive parameters have been recorded: histological type, grading, ER, HER 2/neu and optional are the PR and Proliferation index (Ki67) which do not need to be included in the calculation for compliance with the QI'),[46] because the EUSOMA QI combines more predictive parameters in the same QI, while our selected QI focuses on the HER2, ER and PR status. |
| **Selection** | This QI was selected by all (n=17) experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women in whom HER2 status and/or ER and/or PR status was assessed before the start of systemic treatment<br><br>Denominator: All women diagnosed with IBC who have systemic treatment within 9 months after incidence date |
| **Target** | 98%: although this QI is slightly different from the EUSOMA QI on this aspect of care, 88% of experts agreed to use this target. |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26<br><br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br><br>Systemic treatment: chemotherapy, endocrine therapy, targeted therapy within 1m before until 9m after incidence date, for ATC codes, see Table 50, Table 51, Table 52<br><br>ER-PR-HER2 tests: from 3 months before incidence date until start of systemic therapy (date of start therapy not included), for nomenclature codes, see Table 32, Table 33, Table 34 |

| Title | Proportion of women with IBC in whom human epidermal growth factor receptor 2 (HER2) status and/or oestrogen receptor (ER) and/or progesterone receptor (PR) status were assessed before any systemic treatment |
|---|---|
| **Risk adjustment** | None (process indicator) |
| **Limitations** | - During the study period (2014 - 2018) there was neither a dedicated nomenclature code for HER2 IHC test, nor a billing code for ER and PR testing separately. In addition, exploration of the data revealed that the ER/PR specific nomenclature codes (546416 - 546420 and 435831-435842) were not billed. Instead, more general immunohistochemical test codes were used (588070 - 588081 and 588976 - 588980, describing the testing for tumour antigen) to bill ER-PR-HER2 IHC testing collectively. It was thus impossible to disentangle whether in all these cases ER as well as PR as well as HER2 IHC testing was performed. (For HER2-ISH the following codes were included: 588556-588560; 594436-594440; 594451-594462) |
| **Subgroup analyses** | - Clinical and combined stage<br>- Age at diagnosis<br>- Year of incidence<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Type of systemic therapy (chemotherapy – endocrine therapy – targeted therapy) |
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs 2014 - 2018<br>- Proportion of women with IBC in whom HER2 status and/or ER/PR status were assessed within a time frame of 3 months around incidence date<br>- Proportion of women with IBC in whom HER2 status and/or ER/PR status were assessed within a time frame of 3 months around incidence date, irrespective of treatment |
| **Benchmarking** | Diagnostic centre & centre of main treatment |
| **Level of benchmarking** | Hospital level (diagnostic centre) & campus level (main treatment centre) |
| **Comments** | |

## Appendix 15.2. Flowchart



## Appendix 15.3. Results

**Table 113 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed before any systemic treatment**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 43 252 | 43 012 | 99.4 |
| **Age at diagnosis** | | | |
| <40 years | 2 198 | 2 181 | 99.2 |
| 40-49 years | 6 570 | 6 555 | 99.8 |
| 50-59 years | 10 243 | 10 204 | 99.6 |
| 60-69 years | 11 138 | 11 089 | 99.6 |
| 70-79 years | 7 731 | 7 689 | 99.5 |
| 80+ years | 5 372 | 5 294 | 98.5 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 23 919 | 23 829 | 99.6 |
| 1 – Symptomatic but completely ambulatory | 15 068 | 14 991 | 99.5 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 660 | 640 | 97.0 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 228 | 220 | 96.5 |
| 4 – Completely disabled; totally confined to bed or chair | 70 | 66 | 94.3 |
| Missing | 3 307 | 3 266 | 98.8 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 32 467 | 32 313 | 99.5 |
| 1-5 days | 7 428 | 7 384 | 99.4 |
| 6-15 days | 2 109 | 2 083 | 98.8 |
| >15 days | 1 248 | 1 232 | 98.7 |
| **Number of comorbidities** | | | |
| 0 | 23 208 | 23 101 | 99.5 |
| 1 | 15 159 | 15 059 | 99.3 |
| 2 | 4 521 | 4 489 | 99.3 |
| 3 | 364 | 363 | 99.7 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Cardiovascular disease** | | | |
| Absent | 25 174 | 25 051 | 99.5 |
| Present | 18 078 | 17 961 | 99.4 |
| **Respiratory disease** | | | |
| Absent | 40 324 | 40 114 | 99.5 |
| Present | 2 928 | 2 898 | 99.0 |
| **Diabetes** | | | |
| Absent | 38 965 | 38 745 | 99.4 |
| Present | 4 287 | 4 267 | 99.5 |
| **Incidence year** | | | |
| 2014 | 8 419 | 8 373 | 99.5 |
| 2015 | 8 442 | 8 385 | 99.3 |
| 2016 | 8 818 | 8 776 | 99.5 |
| 2017 | 8 610 | 8 561 | 99.4 |
| 2018 | 8 963 | 8 917 | 99.5 |
| **Clinical stage** | | | |
| 0 | 463 | 462 | 99.8 |
| I | 17 909 | 17 858 | 99.7 |
| II | 14 879 | 14 802 | 99.5 |
| III | 2 819 | 2 793 | 99.1 |
| IV | 2 614 | 2 576 | 98.5 |
| Unknown | 4 568 | 4 521 | 99.0 |
| **Combined stage** | | | |
| (y)0 | 1 059 | 1 048 | 99.0 |
| yis | 337 | 333 | 98.8 |
| (y)I | 19 124 | 19 073 | 99.7 |
| (y)II | 14 686 | 14 613 | 99.5 |
| (y)III | 4 649 | 4 615 | 99.3 |
| (y)IV | 2 693 | 2 652 | 98.5 |
| Unknown | 704 | 678 | 96.3 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Chemotherapy within 9 months of incidence** | | | |
| No | 25 059 | 24 920 | 99.4 |
| Yes | 18 193 | 18 092 | 99.4 |
| **Endocrine therapy within 9 months of incidence** | | | |
| No | 8 252 | 8 209 | 99.5 |
| Yes | 35 000 | 34 803 | 99.4 |
| **Targeted therapy within 9 months of incidence** | | | |
| No | 37 154 | 36 944 | 99.4 |
| Yes | 6 098 | 6 068 | 99.5 |

*IBC: invasive breast cancer; WHO: World Health Organization; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis.*
*Source: BCR-IMA*

### Table 114 – Sensitivity analysis: Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed before any systemic treatment, by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 43 252 | 43 012 | 99.4 |
| **Comparison period (2009 - 2013)** | 40 481 | 40 025 | 98.9 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 115 – Sensitivity analysis: Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status were assessed within 3 months around incidence date

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 43 252 | 43 012 | 99.4 |
| **Systemic therapy and receptor status assessed within 3 months around incidence date** | 43 252 | 43 062 | 99.6 |

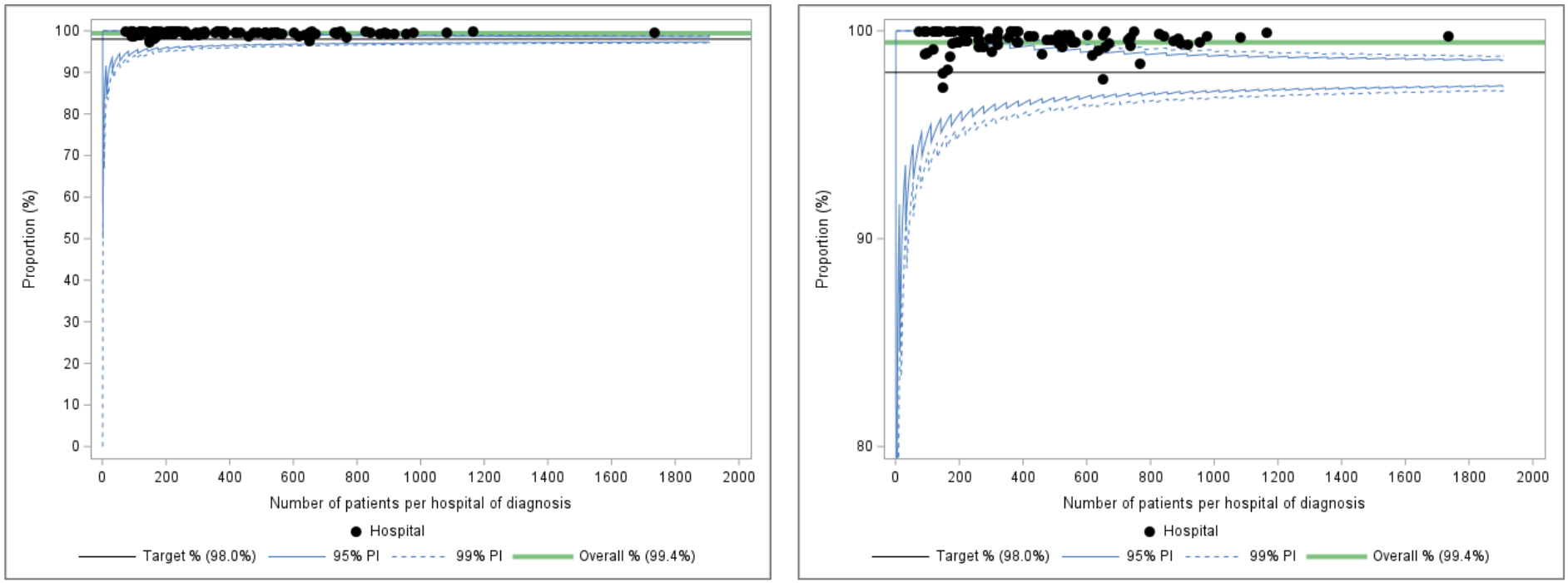
*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Table 116 – Sensitivity analysis: Proportion of women with IBC in whom HER2 status and/or ER and/or PR status were assessed within 3 months around incidence date (irrespective of treatment)**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 43 252 | 43 012 | 99.4 |
| **Receptor status assessed within 3 months around incidence date** | 46 035 | 45 648 | 99.2 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Figure 36 – Proportion of women with IBC treated with systemic therapy in whom HER2 status and/or ER and/or PR status was assessed before any systemic treatment (left) and zoom on the highest proportions (right), by hospital of diagnosis**




*Note: There were 100 hospitals reported in the funnel plot, none of them having less than ten patients in denominator; no hospital was situated below the 99% prediction interval, while 38 were situated above the 99% prediction interval; 1 599 patients, who could not be assigned to a centre of diagnosis, were not represented in the funnel plot.*
*Source: BCR-IMA*

# APPENDIX 16. MULTIDISCIPLINARY TEAM (MDT) MEETING

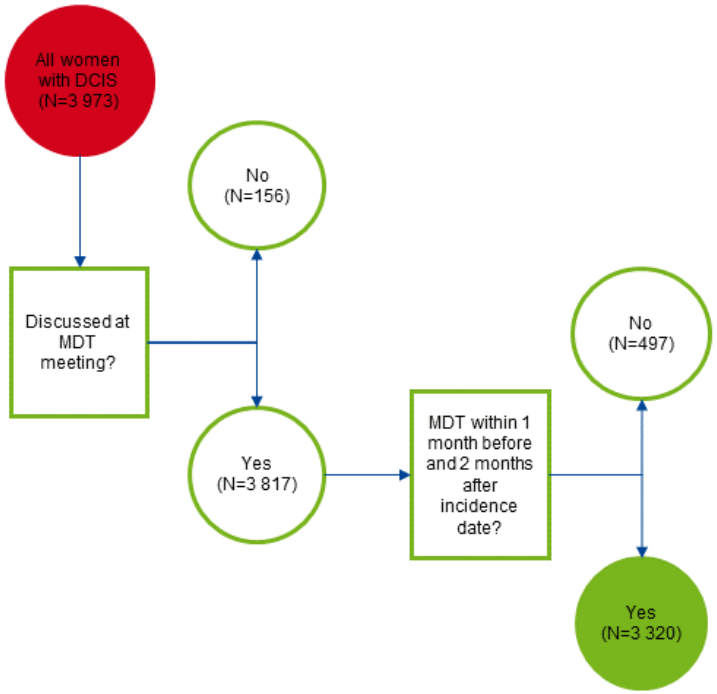
## Appendix 16.1. Documentation sheet

| Title | Proportion of women with BC discussed during a multidisciplinary team meeting |
|---|---|
| **Rationale** | So far, there is little evidence indicating that multidisciplinary team (MDT) meetings, where professionals from different specialties (among others, medical oncologists, radiologists, surgeons, radiotherapists, pathologists and nurse specialists) discuss cancer patients, resulted in improvements in clinical outcomes.[151] Yet, it has been suggested that MDT meetings have a positive impact upon patient assessment and management practices: between 4% and 45% of patients discussed at MDT meetings experienced changes in diagnostic reports following the meeting. In addition, patients discussed at MDT meetings were more likely to receive more accurate and complete pre-operative staging, and neoadjuvant/adjuvant treatment.[151] |
| **Selection** | This QI was selected by all (n=17) experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | • DCIS<br>Numerator: Number of women who were discussed during a billed multidisciplinary team meeting within the time frame of 1 month before and 2 months after incidence date<br>Denominator: All women diagnosed with DCIS<br>• IBC<br>Numerator: Number of women who were discussed during a billed multidisciplinary team meeting within the time frame of 1 month before and 2 months after incidence date<br>Denominator: All women diagnosed with IBC |
| **Target** | Given the limitations of the dedicated nomenclature codes (see section 4.10.2), it was decided to elaborate this indicator as a descriptive indicator (without target) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with<br>• DCIS (ICD-10: D05; for ICD-O-3 morphology codes see Table 26)<br>• IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>'First' MDT (MOC-COM), for nomenclature codes, see Table 55 |
| **Risk adjustment** | None (process indicator) |

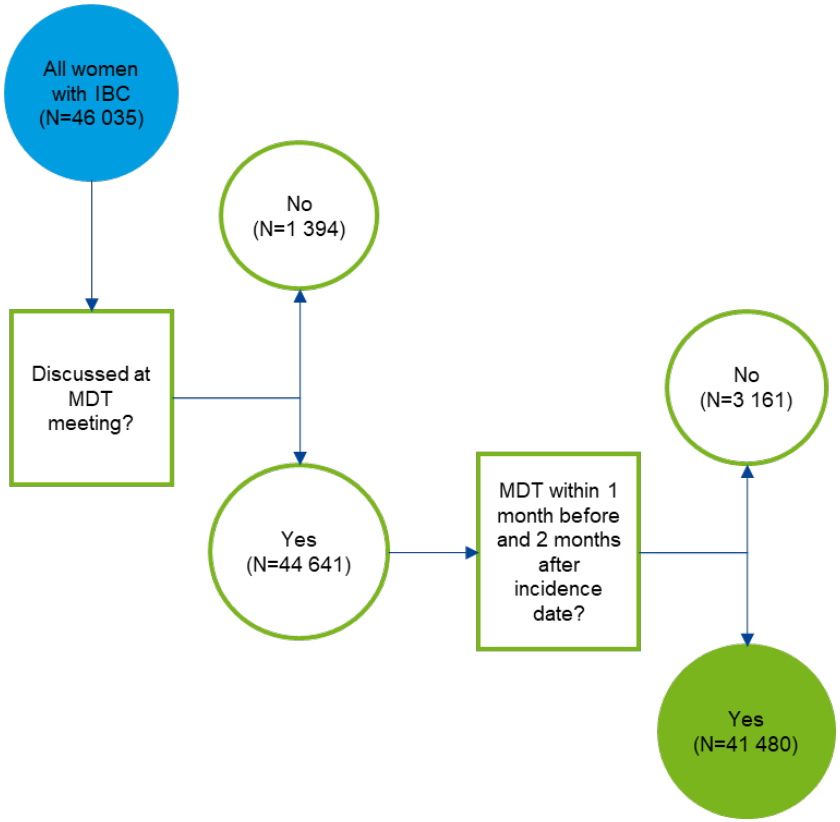
| Title | Proportion of women with BC discussed during a multidisciplinary team meeting |
|---|---|
| **Limitations** | Based on the administrative data, only the MDT meetings that have been charged can be identified. Due to the invoicing rules, which imply that only one MDT meeting can be billed per patient and per calendar year, these data may underestimate the real frequency of MDTs.[79] From the administrative data it cannot be deduced how many times a patient was discussed during a MDT meeting and when these were scheduled. Due to the limitations of the IMA – AIM data, a time frame of 1 month before and 2 months after incidence date has been chosen.<br>Another limitation is that we do not have any information on the quality of the multidisciplinary meeting itself, nor on the multidisciplinary approach during the entire care pathway.<br>Finally, during the validation study, a few hospitals pointed out that for some cases the 'centre of diagnosis' only performed diagnostic procedures on the demand of an external physician. They do not identify themselves as the 'centre of diagnosis' for these patients, as 'they do not really know these patients'. |
| **Subgroup analyses** | • Clinical and combined stage<br>• Treatment modality<br>• Age at diagnosis<br>• Year of incidence<br>• WHO performance status at time of diagnosis<br>• Number of inpatient bed days the year preceding the incidence date<br>• Number and type of comorbidities |
| **Sensitivity analyses** | • Incidence year 2009 - 2013 vs. 2014 - 2018<br>• MDT within 1 month before to 3, 6, 9, 12 months after incidence<br>• Excluding those patients who died within 2 months after incidence date |
| **Benchmarking** | Diagnostic centre |
| **Level of benchmarking** | Hospital level |
| **Comments** | |

# Appendix 16.2. Flowcharts

## *Appendix 16.2.1. Women with DCIS*



## *Appendix 16.2.2. Women with IBC*



## Appendix 16.3. Results

**Table 117 – Proportion of women with BC for whom a multidisciplinary team (MDT) meeting was billed within 1 month before until 2 months after incidence date, by patient, tumour and treatment characteristics**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Overall** | 3 973 | 3 320 | 83.6 | 46 035 | 41 480 | 90.1 |
| **Age at diagnosis** | | | | | | |
| <40 years | 164 | 129 | 78.7 | 2 261 | 2 087 | 92.3 |
| 40-49 years | 716 | 579 | 80.9 | 6 798 | 6 229 | 91.6 |
| 50-59 years | 1 238 | 1 069 | 86.3 | 10 580 | 9 682 | 91.5 |
| 60-69 years | 1 194 | 997 | 83.5 | 11 611 | 10 573 | 91.1 |
| 70-79 years | 481 | 396 | 82.3 | 8 294 | 7 419 | 89.5 |
| 80+ years | 180 | 150 | 83.3 | 6 491 | 5 490 | 84.6 |
| **WHO performance status at time of diagnosis** | | | | | | |
| 0 – Asymptomatic | 2 809 | 2 407 | 85.7 | 24 975 | 22 874 | 91.6 |
| 1 – Symptomatic but completely ambulatory | 711 | 633 | 89.0 | 16 016 | 14 913 | 93.1 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 19 | 17 | 89.5 | 794 | 701 | 88.3 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 8 | 7 | 87.5 | 299 | 260 | 87.0 |
| 4 – Completely disabled; totally confined to bed or chair | 9 | 9 | 100.0 | 103 | 90 | 87.4 |
| Missing | 417 | 247 | 59.2 | 3 848 | 2 642 | 68.7 |
| **Number of inpatient bed days in year prior to incidence** | | | | | | |
| 0 days | 3 005 | 2 507 | 83.4 | 34 199 | 30 902 | 90.4 |
| 1-5 days | 773 | 649 | 84.0 | 7 927 | 7 208 | 90.9 |
| 6-15 days | 143 | 118 | 82.5 | 2 379 | 2 090 | 87.9 |
| >15 days | 52 | 46 | 88.5 | 1 530 | 1 280 | 83.7 |
| **Number of comorbidities** | | | | | | |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| 0 | 2 442 | 2 057 | 84.2 | 24 330 | 22 188 | 91.2 |
| 1 | 1 207 | 1 007 | 83.4 | 16 362 | 14 592 | 89.2 |
| 2 | 301 | 240 | 79.7 | 4 938 | 4 345 | 88.0 |
| 3 | 23 | 16 | 69.6 | 405 | 355 | 87.7 |
| **Cardiovascular disease** | | | | | | |
| Absent | 2 638 | 2 233 | 84.6 | 26 390 | 24 048 | 91.1 |
| Present | 1 335 | 1 087 | 81.4 | 19 645 | 17 432 | 88.7 |
| **Respiratory disease** | | | | | | |
| Absent | 3 710 | 3 097 | 83.5 | 42 861 | 38 673 | 90.2 |
| Present | 263 | 223 | 84.8 | 3 174 | 2 807 | 88.4 |
| **Diabetes** | | | | | | |
| Absent | 3 693 | 3 095 | 83.8 | 41 401 | 37 372 | 90.3 |
| Present | 280 | 225 | 80.4 | 4 634 | 4 108 | 88.6 |
| **Incidence year** | | | | | | |
| 2014 | 807 | 669 | 82.9 | 8 980 | 8 073 | 89.9 |
| 2015 | 777 | 654 | 84.2 | 8 973 | 8 096 | 90.2 |
| 2016 | 808 | 668 | 82.7 | 9 363 | 8 488 | 90.7 |
| 2017 | 771 | 644 | 83.5 | 9 193 | 8 254 | 89.8 |
| 2018 | 810 | 685 | 84.6 | 9 526 | 8 569 | 90.0 |
| **Clinical stage** | | | | | | |
| 0 | 2 646 | 2 292 | 86.6 | 569 | 479 | 84.2 |
| I | - | - | | 18 658 | 17 253 | 92.5 |
| II | - | - | | 15 697 | 14 445 | 92.0 |
| III | - | - | | 3 023 | 2 732 | 90.4 |
| IV | - | - | | 2 921 | 2 683 | 91.9 |
| Unknown | 1 327 | 1 028 | 77.5 | 5 167 | 3 888 | 75.2 |
| **Combined stage** | | | | | | |
| (y)0 | 3 774 | 3 221 | 85.3 | 1 065 | 935 | 87.8 |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| yis | - | - | | 337 | 299 | 88.7 |
| (y)I | - | - | | 20 126 | 18 372 | 91.3 |
| (y)II | - | - | | 15 507 | 14 152 | 91.3 |
| (y)III | - | - | | 4 930 | 4 532 | 91.9 |
| (y)IV | - | - | | 3 009 | 2 755 | 91.6 |
| Unknown | 199 | 99 | 49.7 | 1 061 | 435 | 41.0 |
| **Treatment modality** | | | | | | |
| Surgery < adjuvant RT | 1 216 | 1 067 | 87.7 | 899 | 789 | 87.8 |
| Surgery < adjuvant systemic Tx | 411 | 336 | 81.8 | 5 176 | 4 598 | 88.8 |
| Surgery < adjuvant RT + systemic Tx | 1 015 | 901 | 88.8 | 27 374 | 25 510 | 93.2 |
| Neoadjuvant Tx < Surgery (< adjuvant Tx) | 20 | 14 | 70.0 | 5 976 | 5 277 | 88.3 |
| Surgery only | 1 147 | 902 | 78.6 | 808 | 649 | 80.3 |
| Primary systemic and/or RT (no surgery) | 55 | 50 | 90.9 | 4 861 | 4 169 | 85.8 |
| No oncological treatment | 109 | 50 | 45.9 | 941 | 488 | 51.9 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; WHO: World Health Organization; RT: radiotherapy; Tx: treatment; <: followed by.*
*Source: BCR-IMA*

### Table 118 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, by time period

| Category | DCIS | | IBC | |
|---|---|---|---|---|
| | N | % | N | % |
| **Multidisciplinary team (MDT) meeting** | | | | |
| ***Study period 2014 - 2018*** | | | | |
| **All patients with BC** | 3 973 | | 46 035 | |
| MDT meeting within -1 to +2 months of incidence | 3 320 | 83.6 | 41 480 | 90.1 |
| MDT meeting within -1 to +3 months of incidence | 3 660 | 92.1 | 43 303 | 94.1 |
| MDT meeting within -1 to +6 months of incidence | 3 784 | 95.2 | 43 957 | 95.5 |
| MDT meeting within -1 to +9 months of incidence | 3 796 | 95.5 | 44 370 | 96.4 |
| MDT meeting within -1 to +12 months of incidence | 3 800 | 95.7 | 44 430 | 96.5 |
| **Comparison period 2009 - 2013** | | | | |
| **All patients with BC** | 3 830 | | 43 507 | |
| MDT meeting within -1 to +2 months of incidence | 3 088 | 80.6 | 38 071 | 87.5 |
| MDT meeting within -1 to +3 months of incidence | 3 404 | 88.9 | 39 732 | 91.3 |
| MDT meeting within -1 to +6 months of incidence | 3 548 | 92.6 | 40 533 | 93.2 |
| MDT meeting within -1 to +9 months of incidence | 3 562 | 93.0 | 40 903 | 94.0 |
| MDT meeting within -1 to +12 months of incidence | 3 566 | 93.1 | 40 991 | 94.2 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; MDT: multidisciplinary team meeting.*
*Source: BCR-IMA*

**Table 119 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, by time period and treatment modalities**

| Category | DCIS (N=3 973) | | IBC (N=46 035) | |
|---|---|---|---|---|
| | N | % | N | % |
| **Multidisciplinary team (MDT) meeting** | | | | |
| **Operated patients without neoadjuvant therapy*** | 3 789 | | 34 257 | |
| MDT meeting within -1 to +2 months of incidence | 3 206 | 84.6 | 31 546 | 92.1 |
| MDT meeting within -1 to +3 months of incidence | 3 537 | 93.3 | 33 178 | 96.9 |
| MDT meeting within -1 to +6 months of incidence | 3 656 | 96.5 | 33 530 | 97.9 |
| MDT meeting within -1 to +9 months of incidence | 3 667 | 96.8 | 33 580 | 98.0 |
| MDT meeting within -1 to +12 months of incidence | 3 669 | 96.8 | 33 586 | 98.0 |
| **Operated patients treated with neoadjuvant therapy*** | 20 | | 5 976 | |
| MDT meeting within -1 to +2 months of incidence | 14 | 70.0 | 5 277 | 88.3 |
| MDT meeting within -1 to +3 months of incidence | 17 | 85.0 | 5 353 | 89.6 |
| MDT meeting within -1 to +6 months of incidence | 20 | 100.0 | 5 571 | 93.2 |
| MDT meeting within -1 to +9 months of incidence | 20 | 100.0 | 5 882 | 98.4 |
| MDT meeting within -1 to +12 months of incidence | 20 | 100.0 | 5 890 | 98.6 |
| **Non operated patients** | 164 | | 5 802 | |
| MDT meeting within -1 to +2 months of incidence | 100 | 61.0 | 4 657 | 80.3 |
| MDT meeting within -1 to +3 months of incidence | 106 | 64.6 | 4 772 | 82.2 |
| MDT meeting within -1 to +6 months of incidence | 108 | 65.9 | 4 856 | 83.7 |
| MDT meeting within -1 to +9 months of incidence | 109 | 66.5 | 4 908 | 84.6 |
| MDT meeting within -1 to +12 months of incidence | 111 | 67.7 | 4 954 | 85.4 |

** Neoadjuvant therapy is defined as chemotherapy, targeted therapy, endocrine therapy or radiotherapy; DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; MDT: multidisciplinary team meeting.*
*Source: BCR-IMA*

**Table 120 – Sensitivity analyses: Multidisciplinary team (MDT) meeting, excluding patients who died within two months after incidence**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 3 973 | 3 320 | 83.6 | 46 035 | 41 480 | 90.1 |
| **Excluding patients who died within two months after incidence** | 3 969 | 3 317 | 83.6 | 45 499 | 41 094 | 90.3 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; MDT: multidisciplinary team meeting.*
*Source: BCR-IMA*

# APPENDIX 17. TNM STAGE REPORTING TO THE BCR

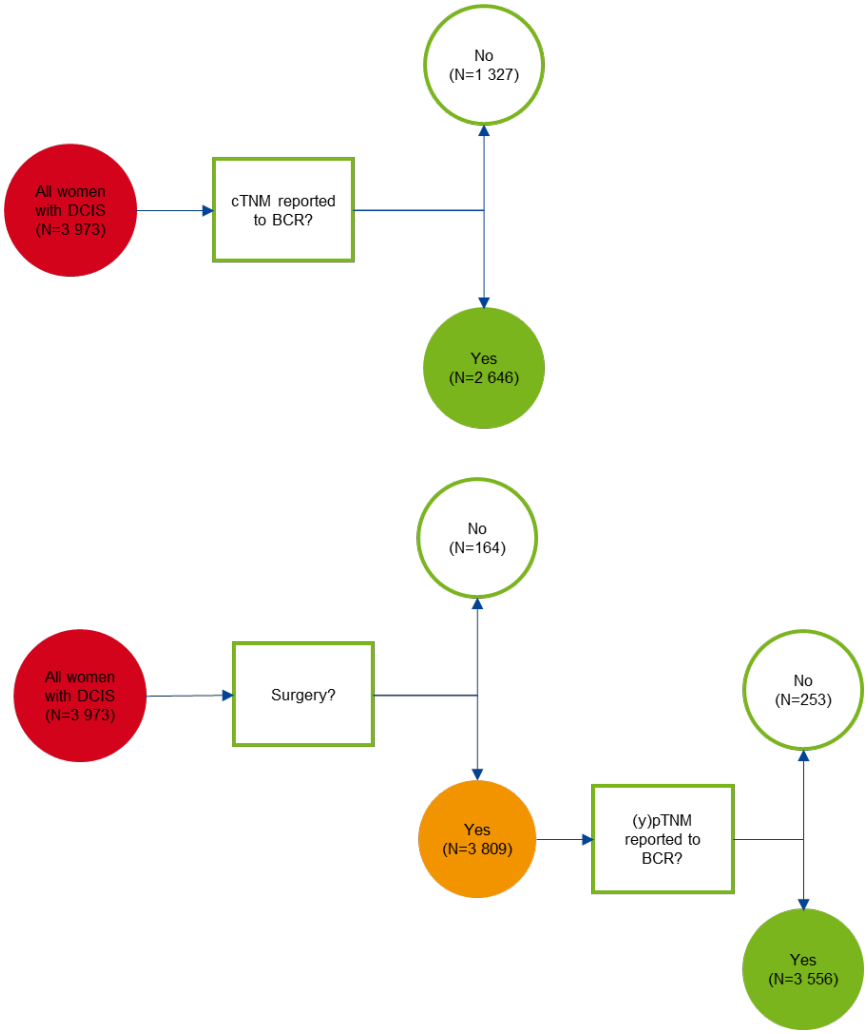
## Appendix 17.1. Documentation sheet

| | |
|---|---|
| **Title** | • **Proportion of women with BC for whom a valid cTNM stage is reported to the Belgian Cancer Registry (BCR)**<br>• **Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR** |
| **Rationale** | Staging is an essential step in the clinical cancer pathway, as it helps in planning the treatment (or the renouncement of treatment) and in predicting the patient's prognosis. It also contributes to a high quality cancer care.<br>In Belgium, cancer stage (clinical and pathological TNM) reporting is one of the legal obligations of the responsible physician of the MDT meeting in order to keep the recognition as oncological care program. Despite this legal requirement, the reporting of the clinical stage to the BCR is not yet optimal. There is also a substantial variability between centres.[79]<br>The second source of information for the staging process are the laboratories for anatomical pathology. They encode the received specimens following classification rules approved by the Consilium Pathological Belgicum/Committee for Pathological Anatomy. In Flanders most laboratories followed the CODAP-2007 classification till incidence year 2016. From incidence year 2017 onwards CODAP-2017 version is used. Various coding systems are used in the Walloon and Brussels Capital Regions. The French speaking laboratories predominantly use the SNOMED classification. Also here, the SNOMED 2017 is in use starting from incidence year 2017. Every (pre) malignant diagnosis is encoded and transferred to the BCR, accompanied by the protocols as stated in the law.[79]<br>At the BCR, these (clinical and pathological) data are linked by tumour, and quality control and consistency checks are performed. When indicated, the data source is consulted to provide additional information.[79]<br>As in reality it is impossible to check the medical files of all BC patients in Belgium, a proxy approach is used by evaluating the quality of the data transferred to the BCR. |
| **Selection** | This QI was selected by 94% (cTNM) and 100% (pTNM) of experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | DCIS<br>○ Numerator: Number of women for whom a valid cTNM stage is reported to the BCR<br>Denominator: All women diagnosed with DCIS<br>○ Numerator: Number of women for whom a valid (y)pTNM stage is reported to the BCR<br>Denominator: All women diagnosed with DCIS treated with surgery<br>IBC<br>○ Numerator: Number of women for whom a valid cTNM stage is reported to the BCR<br>Denominator: All women diagnosed with IBC<br>○ Numerator: Number of women for whom a valid (y)pTNM stage is reported to the BCR<br>Denominator: All women diagnosed with IBC treated with surgery |
| **Target** | 98% (EUSOMA[46]) |
| **Data sources** | Belgian Cancer Registry (BCR): incidence years 2014 – 2018 |

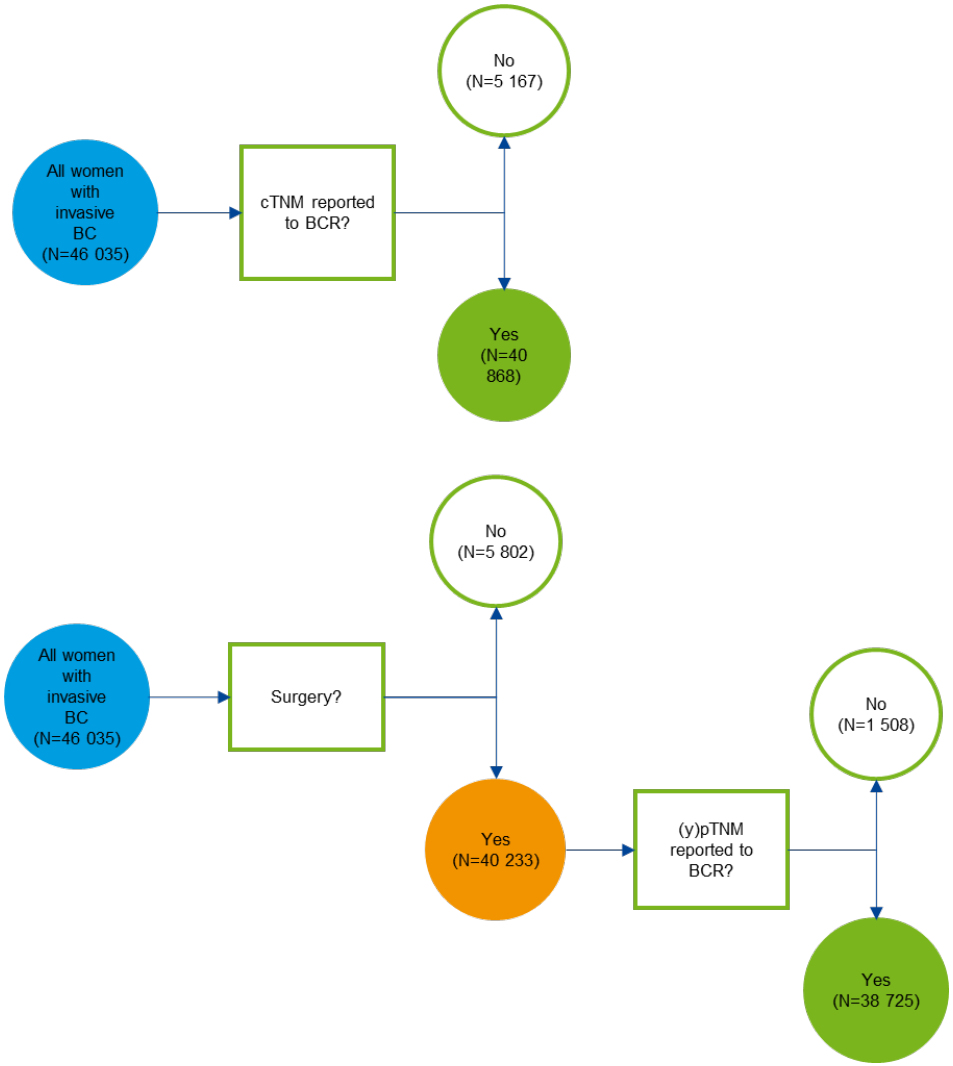
| Title | • Proportion of women with BC for whom a valid cTNM stage is reported to the Belgian Cancer Registry (BCR)<br>• Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR |
|---|---|
| | IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with:<br>DCIS (ICD-10: D05; for ICD-O-3 morphology codes see Table 26<br>IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Invalid cTNM: combinations of T0/x N0/x M0/x (at least one of the parameters T, N or M should be different from x and 0); in all other situations the cTNM is considered 'valid'.<br>Invalid (y)pTNM: combinations of Tx N0/x M0/x. In contrast to the cTNM, the combination (y)pT0 No/x M0/x leads to stage (y)0; in all other situations the (y)pTNM is considered 'valid'.<br>For DCIS, c/(y)pTNM values not compatible with in situ behaviour are categorised as 'not reported'.<br>Surgery: for nomenclature codes, see Table 44, Table 45, Table 46, Table 47<br>Neoadjuvant treatment (to calculate ypTNM), for nomenclature and ATC codes, see Table 49, Table 50, Table 51, Table 52 |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | A proxy approach is used by evaluating the quality of the data transferred to the BCR (cf. rationale). |
| **Subgroup analyses** | - Treatment modality<br>- Age at diagnosis<br>- Year of incidence<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Discussed at a billed MDT |
| **Sensitivity analyses** | Incidence year 2009 - 2013 vs 2014 - 2018 |
| **Benchmarking** | - cTNM stage reporting: diagnostic centre<br>- (y)pTNM stage reporting: main treatment centre |
| **Level of benchmarking** | - cTNM stage reporting: hospital level (as patients are in general not admitted in hospital for diagnostic procedures, no campus identification can be performed)<br>- (y)pTNM stage reporting: campus level |

# Appendix 17.2. Flowcharts

## *Appendix 17.2.1. Women with DCIS*



## *Appendix 17.2.2. Women with IBC*



# Appendix 17.3. Results

## *Appendix 17.3.1. cTNM reporting*

**Table 121 – Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by patient, tumour and treatment characteristics**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Overall** | 3 973 | 2 646 | 66.6 | 46 035 | 40 868 | 88.8 |
| **Age at diagnosis** | | | | | | |
| <40 years | 164 | 110 | 67.1 | 2 261 | 2 092 | 92.5 |
| 40-49 years | 716 | 481 | 67.2 | 6 798 | 6 098 | 89.7 |
| 50-59 years | 1 238 | 858 | 69.3 | 10 580 | 9 478 | 89.6 |
| 60-69 years | 1 194 | 790 | 66.2 | 11 611 | 10 264 | 88.4 |
| 70-79 years | 481 | 307 | 63.8 | 8 294 | 7 314 | 88.2 |
| 80+ years | 180 | 100 | 55.6 | 6 491 | 5 622 | 86.6 |
| **WHO performance status at time of diagnosis** | | | | | | |
| 0 – Asymptomatic | 2 809 | 1 974 | 70.3 | 24 975 | 22 725 | 91.0 |
| 1 – Symptomatic but completely ambulatory | 711 | 462 | 65.0 | 16 016 | 14 664 | 91.6 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 19 | 14 | 73.7 | 794 | 740 | 93.2 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 8 | 6 | 75.0 | 299 | 274 | 91.6 |
| 4 – Completely disabled; totally confined to bed or chair | 9 | 6 | 66.7 | 103 | 98 | 95.1 |
| Missing | 417 | 184 | 44.1 | 3 848 | 2 367 | 61.5 |
| **Number of inpatient bed days in year prior to incidence** | | | | | | |
| 0 days | 3 005 | 2 044 | 68.0 | 34 199 | 30 514 | 89.2 |
| 1-5 days | 773 | 479 | 62.0 | 7 927 | 6 986 | 88.1 |
| 6-15 days | 143 | 88 | 61.5 | 2 379 | 2 065 | 86.8 |
| >15 days | 52 | 35 | 67.3 | 1 530 | 1 303 | 85.2 |
| **Number of comorbidities** | | | | | | |
| 0 | 2 442 | 1 665 | 68.2 | 24 330 | 21 763 | 89.4 |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| 1 | 1 207 | 785 | 65.0 | 16 362 | 14 439 | 88.2 |
| 2 | 301 | 181 | 60.1 | 4 938 | 4 320 | 87.5 |
| 3 | 23 | 15 | 65.2 | 405 | 346 | 85.4 |
| **Cardiovascular disease** | | | | | | |
| Absent | 2 638 | 1 809 | 68.6 | 26 390 | 23 599 | 89.4 |
| Present | 1 335 | 837 | 62.7 | 19 645 | 17 269 | 87.9 |
| **Respiratory disease** | | | | | | |
| Absent | 3 710 | 2 462 | 66.4 | 42 861 | 38 091 | 88.9 |
| Present | 263 | 184 | 70.0 | 3 174 | 2 777 | 87.5 |
| **Diabetes** | | | | | | |
| Absent | 3 693 | 2 475 | 67.0 | 41 401 | 36 797 | 88.9 |
| Present | 280 | 171 | 61.1 | 4 634 | 4 071 | 87.9 |
| **Incidence year** | | | | | | |
| 2014 | 807 | 459 | 56.9 | 8 980 | 7 338 | 81.7 |
| 2015 | 777 | 476 | 61.3 | 8 973 | 7 723 | 86.1 |
| 2016 | 808 | 510 | 63.1 | 9 363 | 8 136 | 86.9 |
| 2017 | 771 | 591 | 76.7 | 9 193 | 8 672 | 94.3 |
| 2018 | 810 | 610 | 75.3 | 9 526 | 8 999 | 94.5 |
| **Treatment modality** | | | | | | |
| Surgery < adjuvant RT | 1 216 | 831 | 68.3 | 899 | 783 | 87.1 |
| Surgery < adjuvant systemic Tx | 411 | 259 | 63.0 | 5 176 | 4 449 | 86.0 |
| Surgery < adjuvant RT + systemic Tx | 1 015 | 717 | 70.6 | 27 374 | 24 379 | 89.1 |
| Neoadjuvant Tx < surgery (< adjuvant Tx) | 20 | 13 | 65.0 | 5 976 | 5 660 | 94.7 |
| Surgery only | 1 147 | 740 | 64.5 | 808 | 661 | 81.8 |
| Primary systemic and/or radiotherapy (no surgery) | 55 | 37 | 67.3 | 4 861 | 4 319 | 88.9 |
| No oncological treatment | 109 | 49 | 45.0 | 941 | 617 | 65.6 |
| **Discussed at multidisciplinary team (MDT) meeting (within -1 to +2 months of incidence)** | | | | | | |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| Yes | 3 320 | 2 292 | 69.0 | 41 480 | 37 592 | 90.6 |
| No | 653 | 354 | 54.2 | 4 555 | 3 276 | 71.9 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; WHO: World Health Organization; RT: radiotherapy; Tx: treatment; <: followed by*
*Source: BCR-IMA*

### Table 122 – Sensitivity analyses: Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by time period

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 3 973 | 2 646 | 66.6 | 46 035 | 40 868 | 88.8 |
| **Comparison period (2009 - 2013)** | 3 830 | 1 711 | 44.7 | 43 507 | 33 964 | 78.1 |

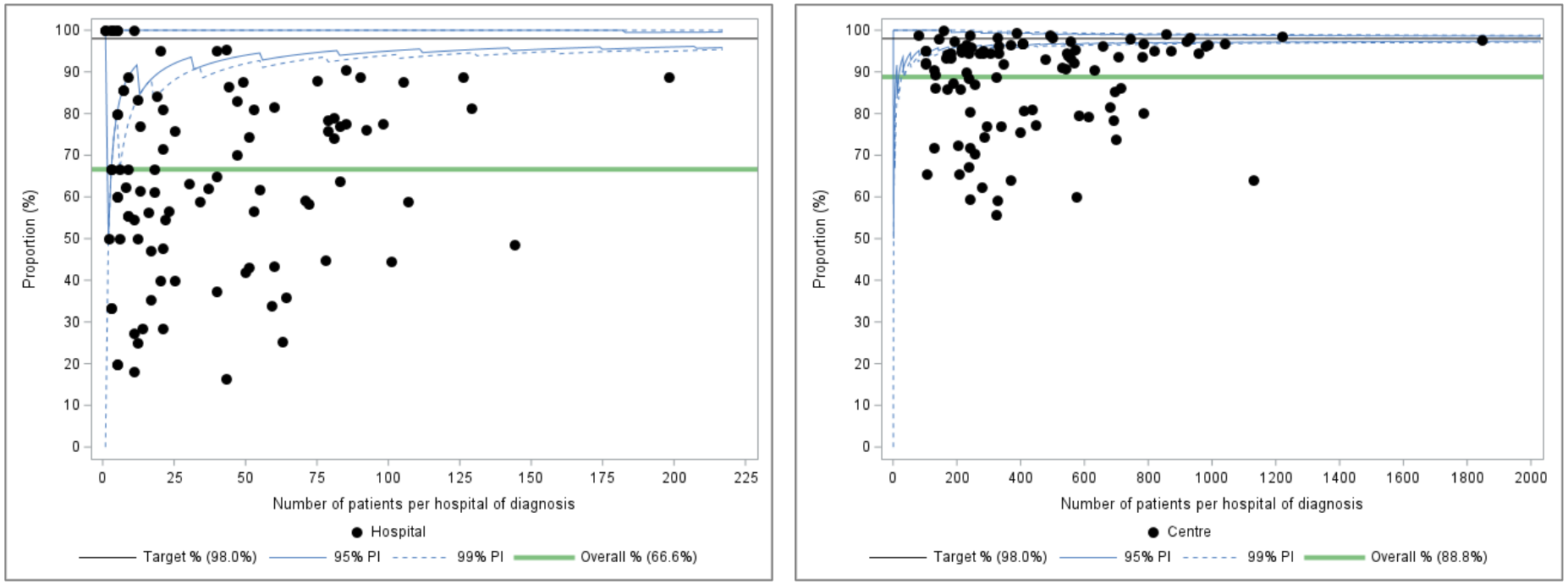
*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer*
*Source: BCR-IMA*

### Table 123 – Proportion of women with BC for whom a valid cTNM stage is reported to the BCR, by hospital volume

| | DCIS | | | | | IBC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | n | n/N (%) | 95% CI | P-value$ | N | n | n/N (%) | 95% CI | P-value$ |
| **Overall** | 3 835 | 2 591 | 67.6 | [66.1, 69.0] | | 44 176 | 39 379 | 89.1 | [88.8, 89.4] | |
| **Average annual hospital volume*** | | | | | <0.0001 | | | | | <0.0001 |
| ≥125 | 2 937 | 2 045 | 69.6 | [67.9, 71.3] | | 29 038 | 26 479 | 91.2 | [90.9, 91.5] | |
| [60, 125[ | 561 | 337 | 60.1 | [55.9, 64.2] | | 7 792 | 6 621 | 85.0 | [84.2, 85.8] | |
| <60 | 337 | 209 | 62.0 | [56.6, 67.2] | | 7 346 | 6 279 | 85.5 | [84.6, 86.3] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 138 patients with DCIS and 1 859 patients with IBC could not be assigned to a hospital, and were thus excluded from these analyses.*
*Source: BCR-IMA-HDD*

**Figure 37 – Proportion of women with DCIS (left) and IBC (right) for whom a valid cTNM stage is reported to the BCR, by hospital of diagnosis**



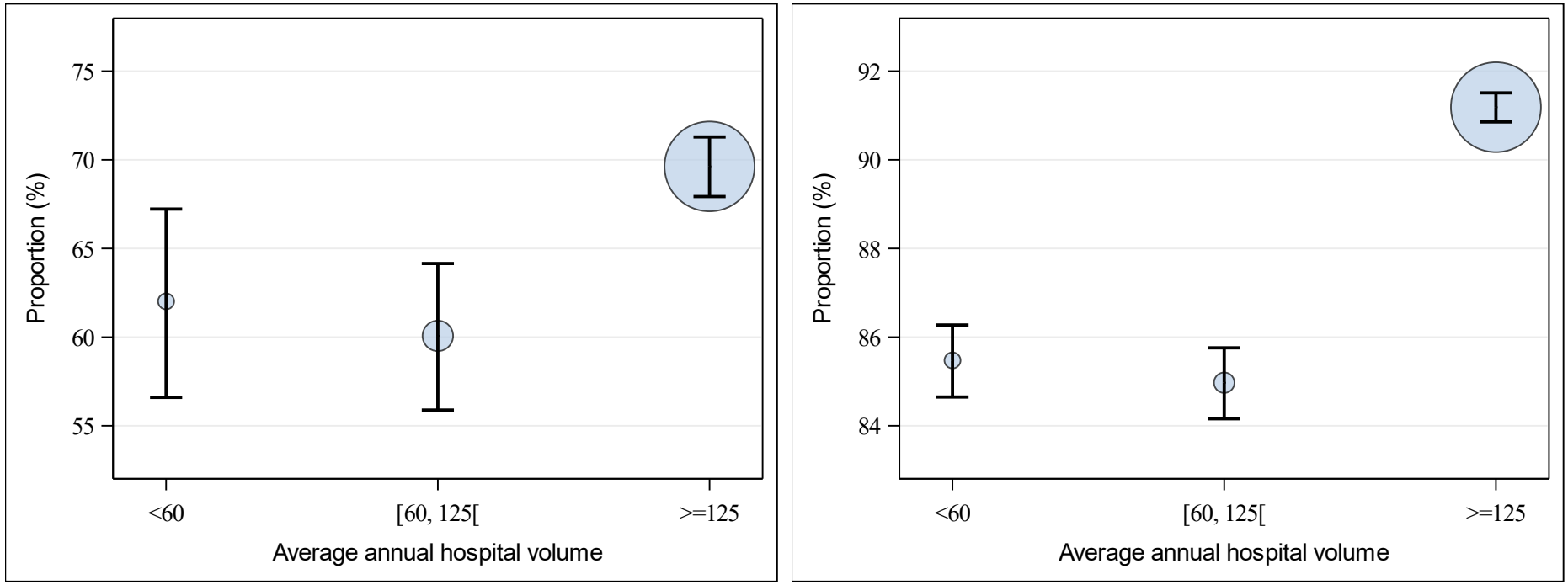

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer.*

*Note for DCIS: There were 98 hospitals reported in the funnel plot, with 76/98 below the 99% PI; 27 hospitals had less than ten patients in the denominator; N=138 patients could not be allocated to a hospital and are thus not represented in the funnel plot.*

*Note for IBC: There were 100 hospitals reported in the funnel plot, with 72/100 below 99%PI; there were no hospitals with less than ten patients in the denominator; N=1 859 patients could not be allocated to a hospital and are thus not represented in the funnel plot.*

*Source: BCR-IMA*

**Figure 38 – Bubble plots of the proportion of women with DCIS (left) and IBC (right) for whom the cTNM stage is reported to the BCR, by hospital volume**




*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 138 patients with DCIS and 1 859 patients with IBC could not be assigned to a hospital, and were thus excluded from these analyses.*
*Source: BCR-IMA*

## *Appendix 17.3.2. (y)pTNM reporting*

**Table 124 – Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by patient, tumour and treatment characteristics**

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Overall** | 3 809 | 3 556 | 93.4 | 40 233 | 38 725 | 96.3 |
| **Age at diagnosis** | | | | | | |
| <40 years | 158 | 148 | 93.7 | 2 124 | 1 940 | 91.3 |
| 40-49 years | 682 | 621 | 91.1 | 6 467 | 6 166 | 95.3 |
| 50-59 years | 1 199 | 1 120 | 93.4 | 9 937 | 9 577 | 96.4 |
| 60-69 years | 1 164 | 1 103 | 94.8 | 10 694 | 10 335 | 96.6 |
| 70-79 years | 460 | 426 | 92.6 | 7 178 | 6 975 | 97.2 |
| 80+ years | 146 | 138 | 94.5 | 3 833 | 3 732 | 97.4 |
| **WHO performance status at time of diagnosis** | | | | | | |
| 0 – Asymptomatic | 2 728 | 2 589 | 94.9 | 23 552 | 22 868 | 97.1 |
| 1 – Symptomatic but completely ambulatory | 686 | 652 | 95.0 | 13 380 | 12 805 | 95.7 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 16 | 16 | 100.0 | 316 | 302 | 95.6 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 2 | 2 | 100.0 | 82 | 78 | 95.1 |
| 4 – Completely disabled; totally confined to bed or chair | 9 | 8 | 88.9 | 25 | 25 | 100.0 |
| Missing | 368 | 289 | 78.5 | 2 878 | 2 647 | 92.0 |
| **Number of inpatient bed days in year prior to incidence** | | | | | | |
| 0 days | 2 891 | 2 693 | 93.2 | 30 833 | 29 646 | 96.2 |
| 1-5 days | 749 | 712 | 95.1 | 6 837 | 6 603 | 96.6 |
| 6-15 days | 127 | 115 | 90.6 | 1 656 | 1 598 | 96.5 |
| >15 days | 42 | 36 | 85.7 | 907 | 878 | 96.8 |
| **Number of comorbidities** | | | | | | |
| 0 | 2 360 | 2 202 | 93.3 | 22 364 | 21 457 | 95.9 |
| 1 | 1 151 | 1 070 | 93.0 | 13 676 | 13 221 | 96.7 |
| 2 | 276 | 262 | 94.9 | 3 885 | 3 751 | 96.6 |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| 3 | 22 | 22 | 100.0 | 308 | 296 | 96.1 |
| **Cardiovascular disease** | | | | | | |
| Absent | 2 548 | 2 377 | 93.3 | 24 200 | 23 225 | 96.0 |
| Present | 1 261 | 1 179 | 93.5 | 16 033 | 15 500 | 96.7 |
| **Respiratory disease** | | | | | | |
| Absent | 3 567 | 3 322 | 93.1 | 37 616 | 36 203 | 96.2 |
| Present | 242 | 234 | 96.7 | 2 617 | 2 522 | 96.4 |
| **Diabetes** | | | | | | |
| Absent | 3 543 | 3 309 | 93.4 | 36 513 | 35 136 | 96.2 |
| Present | 266 | 247 | 92.9 | 3 720 | 3 589 | 96.5 |
| **Incidence year** | | | | | | |
| 2014 | 790 | 718 | 90.9 | 7 914 | 7 557 | 95.5 |
| 2015 | 745 | 695 | 93.3 | 7 963 | 7 677 | 96.4 |
| 2016 | 780 | 730 | 93.6 | 8 196 | 7 792 | 95.1 |
| 2017 | 734 | 695 | 94.7 | 7 991 | 7 826 | 97.9 |
| 2018 | 760 | 718 | 94.5 | 8 169 | 7 873 | 96.4 |
| **Treatment modality** | | | | | | |
| Surgery < adjuvant RT | 1 216 | 1 153 | 94.8 | 899 | 864 | 96.1 |
| Surgery < adjuvant systemic Tx | 411 | 378 | 92.0 | 5 176 | 5 076 | 98.1 |
| Surgery < adjuvant RT + systemic Tx | 1 015 | 965 | 95.1 | 27 374 | 27 041 | 98.8 |
| Neoadjuvant Tx < surgery (<adjuvant Tx) | 20 | 20 | 100.0 | 5 976 | 5 003 | 83.7 |
| Surgery only | 1 147 | 1 040 | 90.7 | 808 | 741 | 91.7 |
| **Discussed at multidisciplinary team meeting (MDT) (within -1 to +2 months of incidence)** | | | | | | |
| Yes | 3 220 | 3 035 | 94.3 | 36 823 | 35 499 | 96.4 |
| No | 589 | 521 | 88.5 | 3 410 | 3 226 | 94.6 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; WHO: World Health Organization; RT: radiotherapy; Tx: treatment; <: followed by.*
*Source: BCR-IMA*

### Table 125 – Sensitivity analyses: Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by time period

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Denominator | Numerator | Proportion (%) | Denominator | Numerator | Proportion (%) |
| **Study period (2014 - 2018)** | 3 809 | 3 556 | 93.4 | 40 233 | 38 725 | 96.3 |
| **Comparison period (2009 - 2013)** | 3 708 | 3 142 | 84.7 | 38 440 | 36 424 | 94.8 |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer*
*Source: BCR-IMA*

### Table 126 – Proportion of women with BC who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by recognition status for BC and campus volume, including volume analyses by recognition status

| | DCIS | | | | | IBC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | n | n/N (%) | 95% CI | P-value[$] | N | n | n/N (%) | 95% CI | P-value[$] |
| **Overall** | 3 794 | 3 542 | 93.4 | [92.5, 94.1] | | 40 060 | 38 567 | 96.3 | [96.1, 96.5] | |
| **Recognition status for BC** | | | | | 0.011 | | | | | 0.346 |
| Coordinating breast clinic | 2 824 | 2 656 | 94.1 | [93.1, 94.9] | | 28 270 | 27 194 | 96.2 | [96.0, 96.4] | |
| Satellite breast clinic | 188 | 174 | 92.6 | [87.8, 95.9] | | 2 279 | 2 193 | 96.2 | [95.4, 97.0] | |
| No recognition for BC | 782 | 712 | 91.0 | [88.8, 93.0] | | 9 511 | 9 180 | 96.5 | [96.1, 96.9] | |
| **Average annual campus volume*** | | | | | <0.0001 | | | | | <0.0001 |
| ≥125 | 2 361 | 2 242 | 95.0 | [94.0, 95.8] | | 23 179 | 22 418 | 96.7 | [96.5, 96.9] | |
| [60, 125[ | 968 | 880 | 90.9 | [88.9, 92.6] | | 10 617 | 10 170 | 95.8 | [95.4, 96.2] | |
| <60 | 465 | 420 | 90.3 | [87.3, 92.9] | | 6 264 | 5 979 | 95.5 | [94.9, 96.0] | |
| **Volume groups per recognition status** | | | | | | | | | | |
| ***Coordinating breast clinic*** | | | | | <0.0001 | | | | | <0.0001 |
| ≥125 | 2 248 | 2 134 | 94.9 | [93.9, 95.8] | | 22 100 | 21 348 | 96.6 | [96.3, 96.8] | |
| [60, 125[ | 576 | 522 | 90.6 | [87.9, 92.9] | | 6 170 | 5 846 | 94.7 | [94.2, 95.3] | |
| ***Satellite breast clinic*** | | | | | 0.959 | | | | | <0.001 |
| [60, 125[ | 162 | 150 | 92.6 | [87.4, 96.1] | | 1 956 | 1 894 | 96.8 | [96.0, 97.6] | |
| <60 | 26 | 24 | 92.3 | [74.9, 99.1] | | 323 | 299 | 92.6 | [89.1, 95.2] | |

| | DCIS | | | | | IBC | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | N | n | n/N (%) | 95% CI | P-value[$] | N | n | n/N (%) | 95% CI | P-value[$] |
| ***No recognition for BC*** | | | | | 0.189 | | | | | <0.0001 |
| ≥125 | 113 | 108 | 95.6 | [90.0, 98.5] | | 1 079 | 1 070 | 99.2 | [98.4, 99.6] | |
| [60, 125[ | 230 | 208 | 90.4 | [85.9, 93.9] | | 2 491 | 2 430 | 97.6 | [96.9, 98.1] | |
| <60 | 439 | 396 | 90.2 | [87.0, 92.8] | | 5 941 | 5 680 | 95.6 | [95.1, 96.1] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 7 patients with DCIS and 60 patients with IBC could not be assigned to a campus, and were thus excluded from the analyses; 8 patients with DCIS and 113 patients with IBC assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

**Table 127 – Association between recognition status for BC and campus volume, and (y)pTNM stage reporting to the BCR, including volume analyses by recognition status**

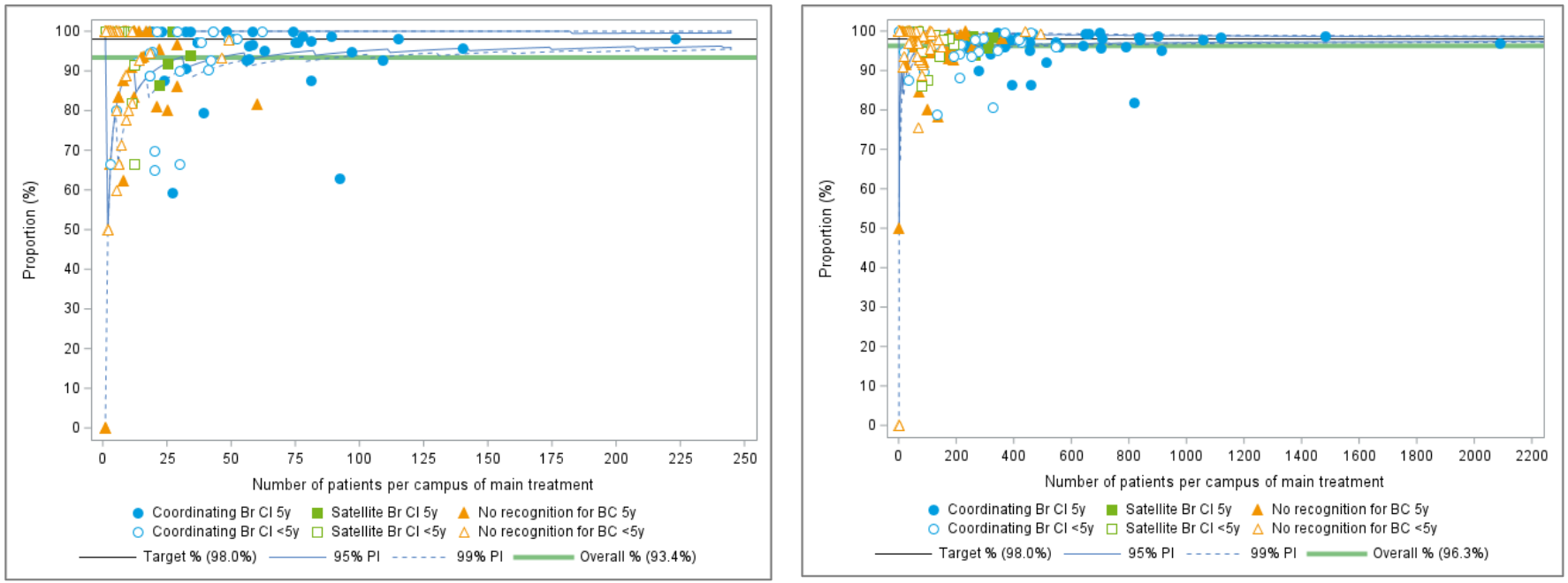
| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Unadjusted OR | 95% CI | P-value, type III[$] | Unadjusted OR | 95% CI | P-value, type III[$] |
| **Recognition status for BC** | | | 0.078 | | | 0.948 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 0.73 | [0.30, 1.77] | | 0.93 | [0.50, 1.72] | |
| No recognition for BC | 0.56 | [0.34, 0.93] | | 1.03 | [0.72, 1.47] | |
| **Average annual campus volume** | | | 0.003 | | | 0.191 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.53 | [0.31, 0.92] | | 0.78 | [0.51, 1.18] | |
| <60 | 0.39 | [0.22, 0.68] | | 0.69 | [0.46, 1.03] | |
| **Volume groups per recognition status** | | | | | | |
| ***Coordinating breast clinics*** | | | 0.069 | | | 0.121 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.50 | [0.24, 1.06] | | 0.65 | [0.38, 1.12] | |
| ***Satellite breast clinics*** | | | 0.992 | | | 0.161 |
| [60, 125[ | 1 | [reference] | | 1 | [reference] | |
| <60 | 1.01 | [0.13, 7.61] | | 0.46 | [0.16, 1.36] | |

| | DCIS | | | IBC | | |
|---|---|---|---|---|---|---|
| | Unadjusted OR | 95% CI | P-value, type III[$] | Unadjusted OR | 95% CI | P-value, type III[$] |
| ***No recognition for BC*** | | | 0.311 | | | 0.043 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.57 | [0.16, 2.05] | | 0.35 | [0.09, 1.32] | |
| <60 | 0.43 | [0.13, 1.40] | | 0.24 | [0.07, 0.82] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of main treatment) was taken into account; 7 patients with DCIS and 60 patients with IBC could not be assigned to a campus, and were thus excluded from the analyses; 8 patients with DCIS and 113 patients with IBC assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*

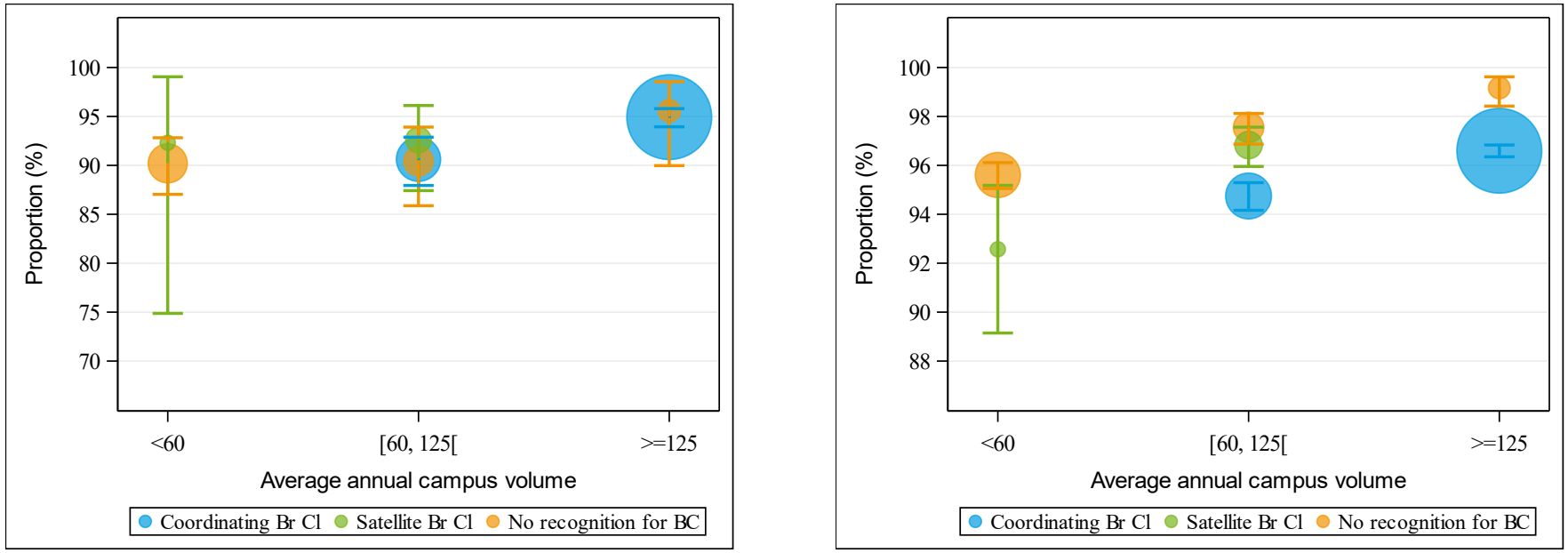
*Source: BCR-IMA-HDD*

**Figure 39 – Proportion of women with DCIS (left) and IBC (right) who had surgery, for whom a valid (y)pTNM stage is reported to the BCR, by campus of main treatment**




*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer.*
*Note for DCIS: There were 155 units of analysis reported in the funnel plot, including 65 having less than ten patients in the denominator; fifteen out of 155 units were situated below the 99% prediction interval; 7 patients, who could not be assigned to a campus of main treatment, are not represented in the funnel plot.*
*Note* for IBC*: There were 175 units of analysis reported in the funnel plot, including 21 units with less than ten patients in denominator; 38 out of 175 units were situated below the 99% prediction interval; 60 patients, who could not be assigned to a campus of main treatment, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

**Figure 40 – Bubble plots of the proportion of women with DCIS (left) and IBC (right) who were operated for whom the (y)pTNM stage is reported to the BCR, by campus volume**




*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; the average annual hospital volume refers to the main treatment volume of a hospital, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 7 patients with DCIS and 60 patients with IBC could not be assigned to a campus, and were thus excluded from the analyses; 8 patients with DCIS and 113 patients with IBC assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

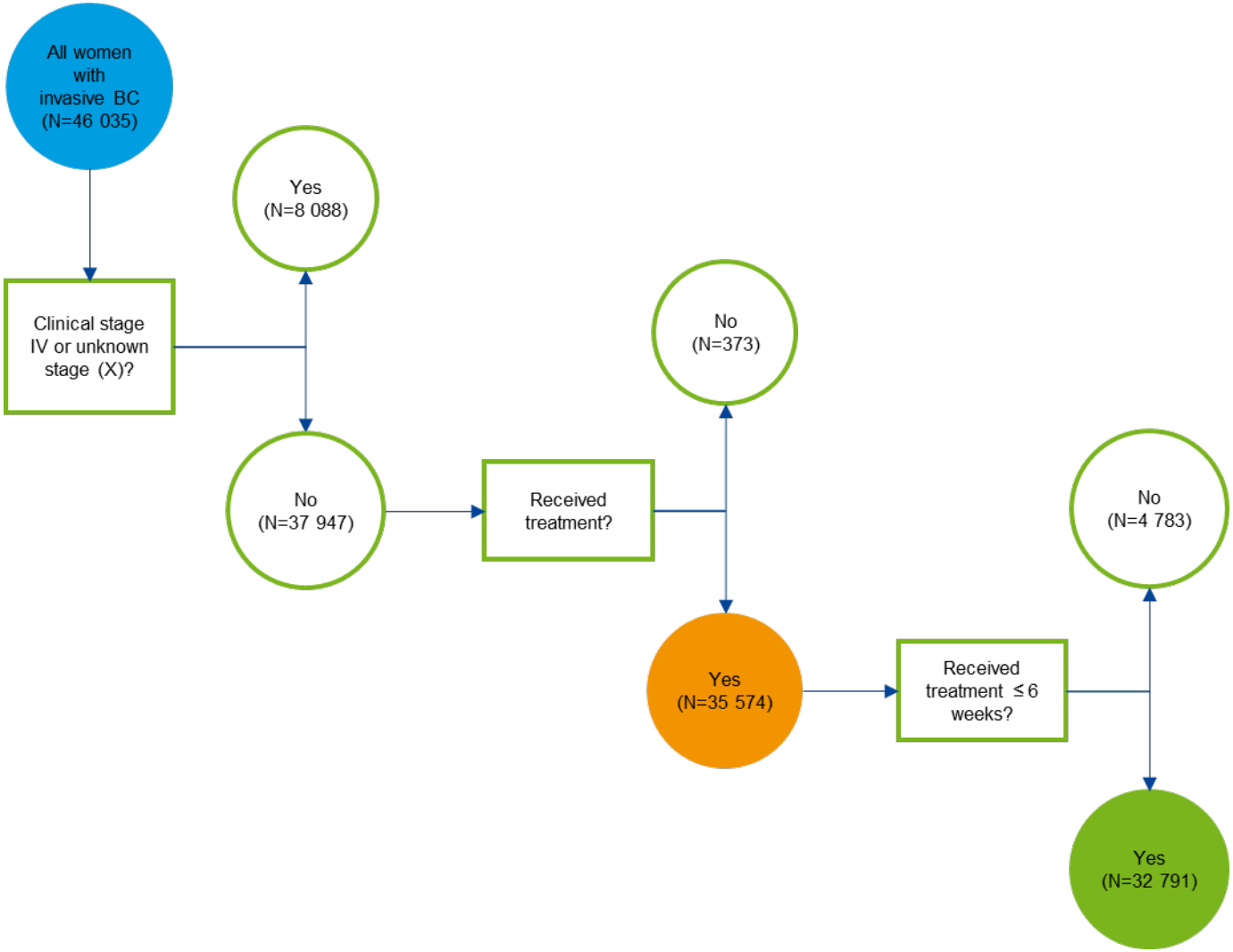
# APPENDIX 18. TIME TO TREATMENT

## Appendix 18.1. Documentation sheet

| Title | Proportion of women with IBC for whom the time interval between the incidence date and the date of first treatment was ≤ 6 weeks |
|---|---|
| **Rationale** | Timely treatment of cancer is essential, not only to increase the chances for cure, but also to alleviate the symptoms as soon as possible. |
| **Selection** | This QI was selected by all (n=17) experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women whose treatment starts within 6 weeks after incidence<br>Denominator: All women diagnosed with IBC who had any type of oncological treatment<br>'Any type of oncological treatment' includes:<br>• surgery<br>• radiotherapy<br>• chemotherapy<br>• endocrine therapy<br>• targeted therapy<br>Exclusion: patients with stage cIV or unknown clinical stage |
| **Target** | 90% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first histopathological confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Oncological treatment includes:<br>Surgery, for nomenclature codes, see Table 44, Table 45, Table 46,Table 47<br>- Radiotherapy, for nomenclature codes, see Table 49<br>- Chemotherapy, for ATC codes, see Table 50<br>- Endocrine therapy, for ATC codes, see Table 52<br>- Targeted therapy, for ATC codes, see Table 51 |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | - Due to some small administrative errors based on the definition of incidence date, e.g. date of pathology report used instead of date of medical procedure, 70 patients had a negative time-to first treatment (-30 days till -1 day). For these 70 patients the time to first treatment was set at 0 days. The negative time to first treatment were more frequently observed in patients who had neoadjuvant treatment. |

| Title | Proportion of women with IBC for whom the time interval between the incidence date and the date of first treatment was ≤ 6 weeks |
|---|---|
| | - Start date of radiotherapy was not always available in IMA-data; for these cases the BCR estimated the start date of radiotherapy based on the simulation date. If the simulation date was not available either, the start date was estimated based on the end date and duration of the series of similar patients for whom the start date was available in IMA-data.<br>- When the first treatment was part of a clinical trial (not visible in health insurance data) this could not be taken into account and the start date of treatment was based on the first billed treatment modality.<br>- It is impossible to deduce reasons for delayed treatment initiation from the data. Therefore, benchmarking is performed based on centre of diagnosis and centre of first treatment. Reasons for delayed treatment initiation can also be non-related to the centre, e.g. patient related. |
| **Subgroup analyses** | - Clinical stage<br>- Treatment modality<br>- Age at diagnosis<br>- Year of incidence<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Referral status during the diagnostic process (i.e. patients whose diagnostic procedures were performed in more than one hospital); when the hospital was unknown for some procedures (i.e. most probably because the procedure was performed in private practice) the patient was included in the subgroup 'no referral'<br>- Referral for treatment (i.e. patients whose diagnostic procedures were performed in another hospital than the hospital of first treatment) |
| **Sensitivity analyses** | - Median time (days) between incidence and first treatment for patients with IBC, excluding patients with time to treatment <0 days<br>- Incidence year 2009 - 2013 vs 2014 - 2018<br>- Patients with stage cIV or unknown clinical stage<br>- Excluding patients for whom the time to first treatment was ≤0 days (n=471 with TTT = 0 and n=70 with TTT <0)<br>- Number of women whose treatment starts within 4 weeks after incidence |
| **Benchmarking** | Diagnostic centre & centre of first treatment |
| **Level of benchmarking** | Diagnostic centre: hospital level<br>Centre of first treatment: campus level |
| **Comments** | / |

## Appendix 18.2. Flowchart



## Appendix 18.3. Results

**Table 128 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by patient, tumour and treatment characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 37 574 | 32 791 | 87.3 |
| **Age at diagnosis** | | | |
| <40 years | 1 963 | 1 796 | 91.5 |
| 40-49 years | 5 810 | 5 217 | 89.8 |
| 50-59 years | 8 973 | 8 027 | 89.5 |
| 60-69 years | 9 556 | 8 363 | 87.5 |
| 70-79 years | 6 537 | 5 582 | 85.4 |
| 80+ years | 4 735 | 3 806 | 80.4 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 21 888 | 18 927 | 86.5 |
| 1 – Symptomatic but completely ambulatory | 12 919 | 11 621 | 90.0 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 455 | 372 | 81.8 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 145 | 109 | 75.2 |
| 4 – Completely disabled; totally confined to bed or chair | 48 | 39 | 81.3 |
| Missing | 2 119 | 1 723 | 81.3 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 28 576 | 24 956 | 87.3 |
| 1-5 days | 6 229 | 5 534 | 88.8 |
| 6-15 days | 1 693 | 1 435 | 84.8 |
| >15 days | 1 076 | 866 | 80.5 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Number of comorbidities** | | | |
| 0 | 20 370 | 18 168 | 89.2 |
| 1 | 13 064 | 11 160 | 85.4 |
| 2 | 3 833 | 3 217 | 83.9 |
| 3 | 307 | 246 | 80.1 |
| **Cardiovascular disease** | | | |
| Absent | 22 061 | 19 616 | 88.9 |
| Present | 15 513 | 13 175 | 84.9 |
| **Respiratory disease** | | | |
| Absent | 35 044 | 30 673 | 87.5 |
| Present | 2 530 | 2 118 | 83.7 |
| **Diabetes** | | | |
| Absent | 33 966 | 29 752 | 87.6 |
| Present | 3 608 | 3 039 | 84.2 |
| **Incidence year** | | | |
| 2014 | 6 760 | 5 961 | 88.2 |
| 2015 | 7 122 | 6 315 | 88.7 |
| 2016 | 7 491 | 6 571 | 87.7 |
| 2017 | 7 989 | 6 954 | 87.0 |
| 2018 | 8 212 | 6 990 | 85.1 |
| **Clinical stage** | | | |
| 0* | 568 | 420 | 73.9 |
| I | 18 548 | 16 266 | 87.7 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| II | 15 507 | 13 527 | 87.2 |
| III | 2 951 | 2 578 | 87.4 |
| **Treatment modality** | | | |
| Surgery < adjuvant RT | 778 | 619 | 79.6 |
| Surgery < adjuvant systemic Tx | 4 370 | 3 638 | 83.2 |
| Surgery < adjuvant RT + systemic Tx | 24 272 | 21 803 | 89.8 |
| Neoadjuvant Tx < surgery (<adjuvant Tx) | 5 381 | 4 824 | 89.6 |
| Surgery only | 647 | 468 | 72.3 |
| Primary systemic and/or radiotherapy (no surgery) | 2 126 | 1 439 | 67.7 |
| **Referral between hospitals during diagnostic process°** | | | |
| No referral | 29 860 | 26 452 | 88.6 |
| Referral | 6 360 | 5 140 | 80.8 |
| Unknown centre of diagnosis | 1 354 | 1 199 | 88.6 |
| **Referral between diagnosis and treatment** | | | |
| No referral | 30 212 | 26 863 | 88.9 |
| Referral | 5 930 | 4 675 | 78.8 |
| Unknown centre of diagnosis or treatment | 1 432 | 1 253 | 87.5 |

*IBC: invasive breast cancer; WHO: World Health Organization; RT: radiotherapy; Tx: treatment; <: followed by; *: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; patients whose diagnostic procedures were performed in more than one hospital. When the hospital was unknown for some procedures (i.e. most probably because the procedure was performed in private practice) the patient was included in the subgroup 'no referral'.*
*Source: BCR-IMA*

### Table 129 – Median time (days) between incidence and first treatment for patients with IBC

| | N | Min | Q1 | Median | Q3 | Max |
|---|---|---|---|---|---|---|
| **Overall** | 37 574 | 0 | 15 | 22 | 33 | 266 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 130 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 37 574 | 32 791 | 87.3 |
| **Comparison period (2009 - 2013)** | 31 207 | 28 072 | 90.0 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 131 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by clinical stage

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Clinical stage 0-III (Main quality indicator)** | 37 574 | 32 791 | 87.3 |
| **Clinical stage IV** | 2 677 | 2 288 | 85.5 |
| **Unknown clinical stage** | 4 843 | 4 018 | 83.0 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 132 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, excluding patients with time to treatment ≤0 days

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator)** | 37 574 | 32 791 | 87.3 |
| **Excluding TTT ≤0 days** | 37 033 | 32 250 | 87.1 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 133 – Sensitivity analyses: Proportion of women with IBC for whom first treatment was initiated within 6 (42 days) versus 4 (28 days) weeks of incidence

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Within 6 weeks (Main quality indicator)** | 37 574 | 32 791 | 87.3 |
| **Within 4 weeks** | 37 574 | 24 862 | 66.2 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 134 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by recognition status and campus volume

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 35 715 | 31 356 | 87.8 | [87.5, 88.1] | |
| **Recognition status for BC** | | | | | <0.0001 |
| Coordinating breast clinic | 25 551 | 22 255 | 87.1 | [86.7, 87.5] | |
| Satellite breast clinic | 1 994 | 1 807 | 90.6 | [89.3, 91.9] | |
| No recognition for BC | 8 170 | 7 294 | 89.3 | [88.6, 89.9] | |
| **Average annual campus volume*** | | | | | 0.147 |
| ≥125 | 21 423 | 18 850 | 88.0 | [87.5, 88.4] | |
| [60, 125[ | 8 807 | 7 733 | 87.8 | [87.1, 88.5] | |
| <60 | 5 485 | 4 773 | 87.0 | [86.1, 87.9] | |

| Characteristic | N | n | n/N (%) | 95% CI | P-value$ |
|---|---|---|---|---|---|
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | <0.0001 |
| ≥125 | 20 502 | 17 959 | 87.6 | [87.1, 88.0] | |
| [60, 125[ | 5 049 | 4 296 | 85.1 | [84.1, 86.1] | |
| ***Satellite breast clinics*** | | | | | <0.0001 |
| [60, 125[ | 1 731 | 1 587 | 91.7 | [90.3, 92.9] | |
| <60 | 263 | 220 | 83.7 | [78.6, 87.9] | |
| ***No recognition for BC*** | | | | | <0.0001 |
| ≥125 | 921 | 891 | 96.7 | [95.4, 97.8] | |
| [60, 125[ | 2 027 | 1 850 | 91.3 | [90.0, 92.5] | |
| <60 | 5 222 | 4 553 | 87.2 | [86.3, 88.1] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 1 717 patients could not be assigned to a campus, and were thus excluded from the analyses; 141 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on algorithm for centre of first treatment) to a campus with no main treatment volume, were excluded.*
*Source: BCR-IMA-HDD*

**Table 135 – Association between recognition status for BC and campus volume of the campus of first treatment, and start of first treatment within 6 weeks (42 days) of incidence, including volume analyses by recognition status**

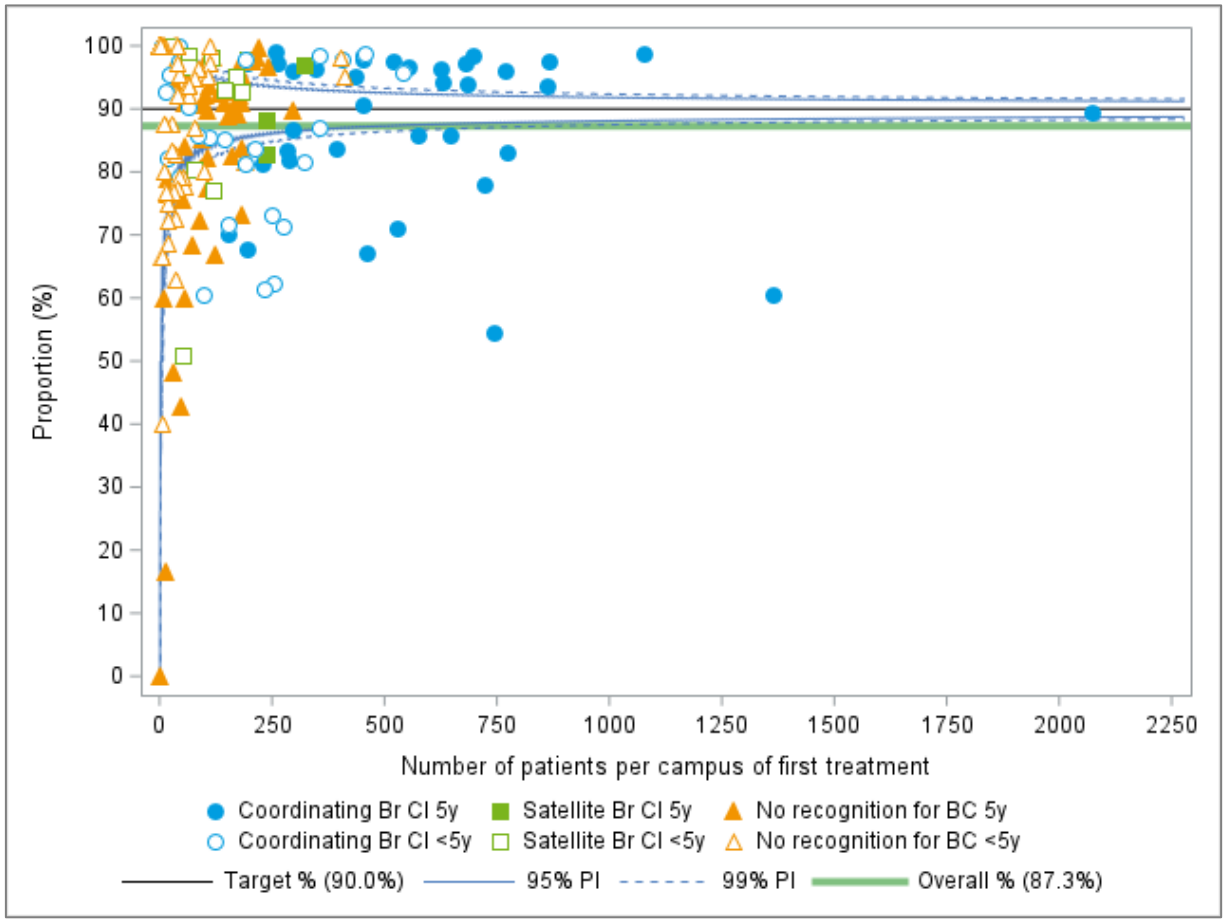
| | Unadjusted OR | 95% CI | P-value, type III$ | Adjusted** OR | 95% CI | P-value, type III$ |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.406 | | | 0.529 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 1.26 | [0.61, 2.58] | | 1.35 | [0.65, 2.78] | |
| No recognition for BC | 0.83 | [0.55, 1.24] | | 0.91 | [0.60, 1.36] | |
| **Average annual campus volume** | | | 0.047 | | | 0.140 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.83 | [0.50, 1.36] | | 0.87 | [0.53, 1.44] | |
| <60 | 0.58 | [0.36, 0.91] | | 0.64 | [0.40, 1.02] | |
| **Volume groups per recognition status** | | | | | | |
| ***Coordinating breast clinics*** | | | 0.266 | | | 0.297 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |

| | Unadjusted OR | 95% CI | P-value, type III[$] | Adjusted** OR | 95% CI | P-value, type III[$] |
|---|---|---|---|---|---|---|
| [60, 125[ | 0.68 | [0.34, 1.34] | | 0.69 | [0.35, 1.38] | |
| ***Satellite breast clinics*** | | | 0.417 | | | 0.368 |
| [60, 125[ | 1 | [reference] | | 1 | [reference] | |
| <60 | 0.54 | [0.12, 2.38] | | 0.49 | [0.10, 2.34] | |
| ***No recognition for BC*** | | | 0.021 | | | 0.051 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.35 | [0.09, 1.39] | | 0.39 | [0.10, 1.53] | |
| <60 | 0.21 | [0.06, 0.76] | | 0.25 | [0.07, 0.91] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that all levels of a categorical predictor have the same effect on the outcome as the reference category does; **Adjusted for the following case-mix variables: age at diagnosis, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiac and respiratory diseases, and diabetes); clustering of patients into campuses (i.e. centre of first treatment) was taken into account; 1 717 patients could not be assigned to a campus, and were thus excluded from the analyses; 141 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on algorithm for centre of first treatment) to a campus with no main treatment volume, were excluded.*

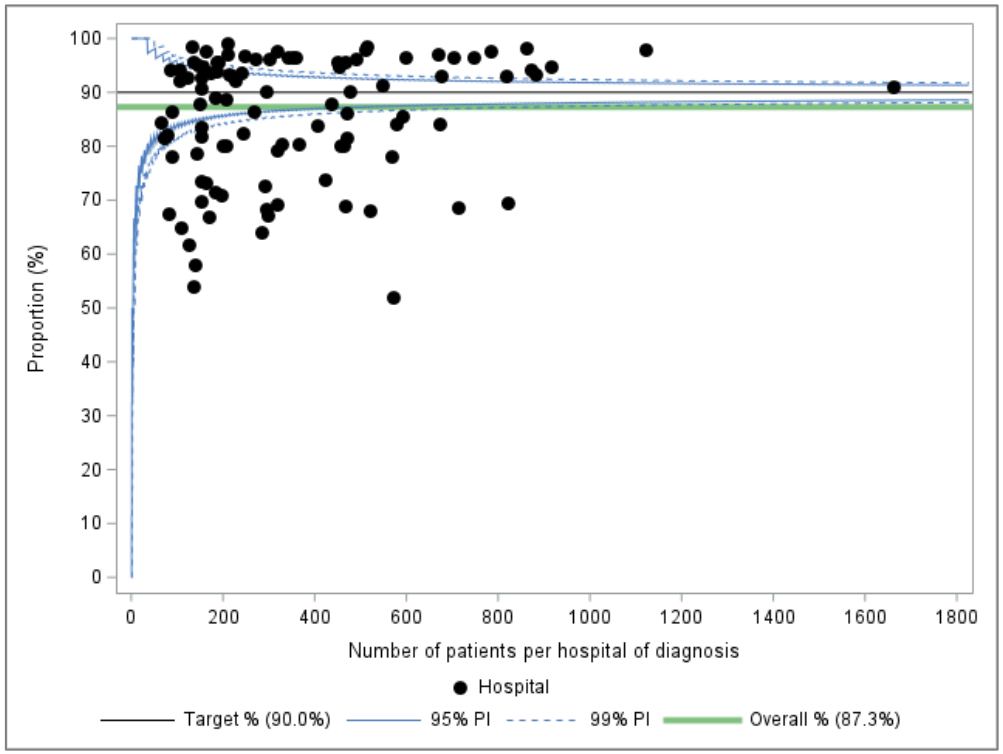
*Source: BCR-IMA-HDD*

**Figure 41 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by campus of first treatment**



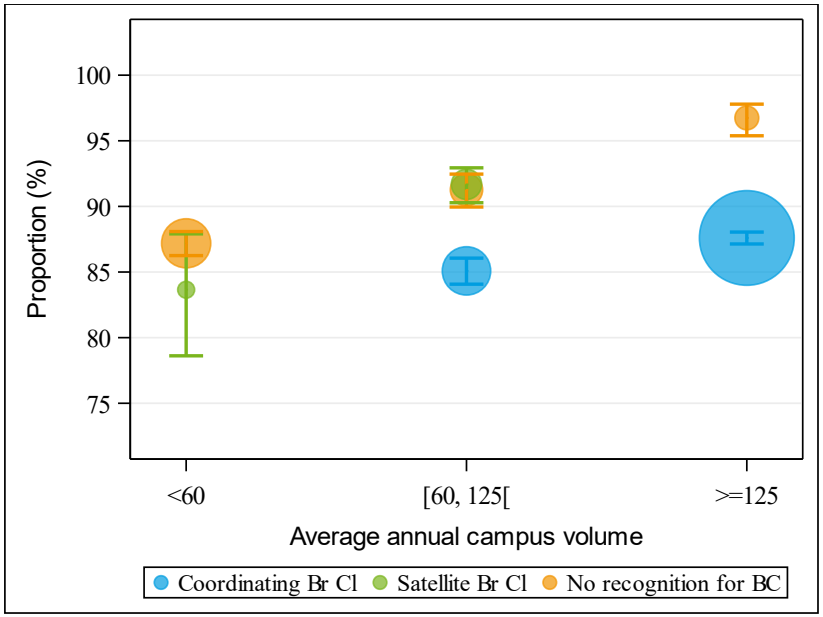

*IBC: invasive breast cancer.*
*Note: There were 178 units of analysis reported in the funnel plot, 19 of them having less than ten patients in the denominator; 43 out of 178 units were situated below the 99% prediction interval; 1 717 patients, who could not be assigned to a campus of first treatment, were not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

**Figure 42 – Proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by hospital of diagnosis**




*IBC: invasive breast cancer; There were 100 hospitals reported in the funnel plot, none of them having less than ten patients in the denominator; forty out of hundred hospitals were situated below the 99% prediction interval; 1 354 patients, who could not be assigned to a centre of diagnosis, were not represented in the funnel plot.*
*Source: BCR-IMA*

**Figure 43 – Bubble plot of the proportion of women with IBC for whom first treatment was initiated within 6 weeks (42 days) of incidence, by campus volume**




*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 1 717 patients could not be assigned to a campus, and were thus excluded from the analyses; 141 patients assigned to a coordinating breast clinic in volume group < 60 patients/year and 1 patient assigned (based on algorithm for centre of first treatment) to a campus with no main treatment volume, were excluded.*

*Source: BCR-IMA-HDD*

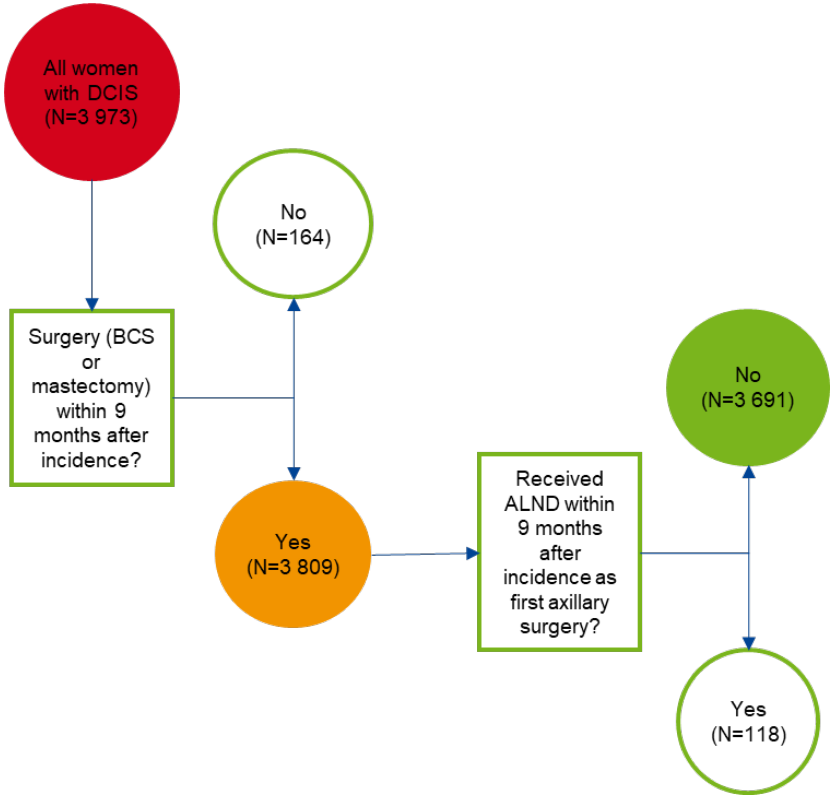
# APPENDIX 19. NO AXILLARY CLEARANCE IN PATIENTS WITH DCIS

## Appendix 19.1. Documentation sheet

| Title | Proportion of women with DCIS who do not undergo axillary lymph node dissection (ALND) as first axillary surgery |
|---|---|
| **Rationale** | While lymph node evaluation is standard for women with invasive cancer, there is no demonstrated benefit for lymph node assessment in women with DCIS. It has been estimated that axillary involvement is about 1-2% in DCIS (which by definition does not metastasise); it depends on grade and diameter (i.e. risk of occult invasive cancer).[46] Still, lymph node analysis is often unnecessarily performed in DCIS patients.[112] The additional morbidity caused by axillary evaluation is significant; axillary interventions, even limited intervention through use of sentinel node biopsy, carry the risk of long term sequelae such as chronic pain, decreased strength, oedema, and sensory disorder.[113] |
| **Selection** | This QI was selected by 94% of the experts who completed the online survey in spring 2020 |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women who did not undergo ALND as first axillary surgery<br>Denominator: All women diagnosed with DCIS who received surgery (BCS or mastectomy) within 9 months after incidence |
| **Target** | As the description of nomenclature codes is not specific enough (see section 4.10.3), it was decided to elaborate this indicator as a descriptive indicator (without target). |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with DCIS (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>ALND: for nomenclature codes, see Table 48<br>Breast surgery (BCS or mastectomy): for nomenclature codes, see Table 44, Table 45 |
| **Risk adjustment** | None (process indicator) |

| Title | Proportion of women with DCIS who do not undergo axillary lymph node dissection (ALND) as first axillary surgery |
|---|---|
| **Limitations** | As is described in section 4.10.3, the nomenclature codes related to sentinel lymph node resection and/or axillary lymph node resection are not specific: it is not clear whether patients for whom these codes were invoiced, underwent axillary lymph node resection or not. Moreover, during the discussion of this indicator, several experts expressed their doubts about the reliability of the calculation of this indicator based on nomenclature codes. They noted that these codes are not always/not in all Belgian hospitals used in a correct way (more precisely: nomenclature codes for ALND are used to attest SLNB as the fees for the former are higher). This may thus lead to an overestimation of ALND and underestimation of SLNB.<br>An alternative approach could be the identification of SLNB by pNsn, but this is not reported as meticulously to the Belgian Cancer Registry by every Belgian hospital/pathology lab. Hence, this approach may also lead to an underestimation and can thus not be considered reliable either. Therefore, it was decided not to provide benchmarking for this indicator. |
| **Subgroup analyses** | - Age at diagnosis<br>- Year of incidence<br>- Type of breast surgery (BCS vs. mastectomy) |
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs 2014 - 2018 |
| **Benchmarking** | Centre of first surgery |
| **Level of benchmarking** | Campus level |
| **Comments** | |

## Appendix 19.2. Flowchart



## Appendix 19.3. Results

**Table 136 – Proportion of women with DCIS who did not receive ALND as first axillary surgery, by patient characteristics and type of first surgery**

| | DCIS | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 3 809 | 3 691 | 96.9 |
| **Age at diagnosis** | | | |
| <40 years | 158 | 149 | 94.3 |
| 40-49 years | 682 | 660 | 96.8 |
| 50-59 years | 1 199 | 1 173 | 97.8 |
| 60-69 years | 1 164 | 1 139 | 97.9 |
| 70-79 years | 460 | 443 | 96.3 |
| 80+ years | 146 | 127 | 87.0 |
| **Incidence year** | | | |
| 2014 | 790 | 763 | 96.6 |
| 2015 | 745 | 724 | 97.2 |
| 2016 | 780 | 750 | 96.2 |
| 2017 | 734 | 711 | 96.9 |
| 2018 | 760 | 743 | 97.8 |
| **Type of first surgery** | | | |
| BCS | 2 993 | 2 944 | 98.4 |
| *BCS (stricto sensu[ss])* | 2 539 | 2 492 | 98.1 |
| *Surgery for benign breast lesions* | 409 | 407 | 99.5 |
| *Excision biopsy* | 15 | 15 | 100.0 |
| *Surgery leading to accidental findings** | 30 | 30 | 100.0 |
| Mastectomy | 816 | 747 | 91.5 |

*DCIS: ductal carcinoma in situ; BCS: breast conserving surgery; *: tumours which were found 'accidently' during breast reduction surgery.*
*Source: BCR-IMA*

### Table 137 – Sensitivity analysis: Proportion of women with DCIS who did not receive ALND as first axillary surgery, by time period

| | DCIS | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 3 809 | 3 691 | 96.9 |
| **Comparison period (2009 - 2013)** | 3 708 | 3 504 | 94.5 |

*DCIS: ductal carcinoma in situ*
*Source: BCR-IMA*

### Table 138 – Proportion of women with DCIS who did not receive ALND as first axillary surgery, by recognition status for BC and campus volume

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 3 796 | 3 679 | 96.9 | [96.3, 97.4] | |
| **Recognition status for BC** | | | | | 0.003 |
| Coordinating breast clinic | 2 824 | 2 750 | 97.4 | [96.7, 97.9] | |
| Satellite breast clinic | 188 | 184 | 97.9 | [94.6, 99.4] | |
| No recognition for BC | 784 | 745 | 95.0 | [93.3, 96.4] | |
| **Average annual campus volume*** | | | | | 0.214 |
| ≥125 | 2 363 | 2 299 | 97.3 | [96.6, 97.9] | |
| [60, 125[ | 968 | 931 | 96.2 | [94.8, 97.3] | |
| <60 | 465 | 449 | 96.6 | [94.5, 98.0] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.021 |
| ≥125 | 2 248 | 2 197 | 97.7 | [97.0, 98.3] | |
| [60, 125[ | 576 | 553 | 96.0 | [94.1, 97.5] | |
| ***Satellite breast clinics*** | | | | | 0.418 |
| [60, 125[ | 162 | 158 | 97.5 | [93.8, 99.3] | |
| <60 | 26 | 26 | 100.0 | [86.8, 100.0] | |
| ***No recognition for BC*** | | | | | 0.003 |
| ≥125 | 115 | 102 | 88.7 | [81.4, 93.8] | |
| [60, 125[ | 230 | 220 | 95.7 | [92.1, 97.9] | |
| <60 | 439 | 423 | 96.4 | [94.1, 97.9] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 5 patients could not be assigned to a campus, and were thus excluded from the analyses; 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

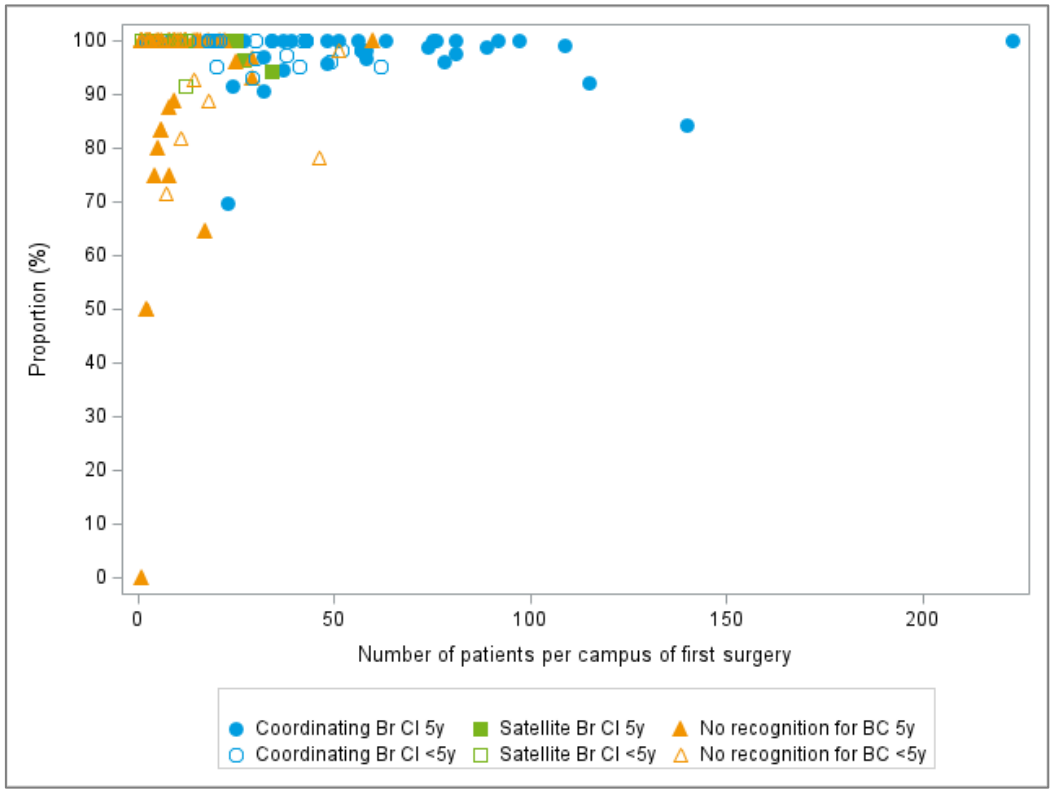
**Table 139 – Association between recognition status for BC and campus volume, and the odds of not receiving ALND as first axillary surgery in women with DCIS, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.035 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.99 | [0.26, 3.77] | |
| No recognition for BC | 0.44 | [0.23, 0.83] | |
| **Average annual campus volume*** | | | 0.088 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.51 | [0.25, 1.06] | |
| <60 | 0.45 | [0.20, 1.00] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.027 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.37 | [0.16, 0.89] | |
| ***Satellite breast clinics[#]*** | | | |
| ***No recognition for BC*** | | | 0.414 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 3.17 | [0.52, 19.22] | |
| <60 | 2.81 | [0.55, 14.29] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; #: the model for the satellite breast clinics did not converge, hence no results could be obtained; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 5 patients could not be assigned to a campus, and were thus excluded from the analyses; 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*

*Source: BCR-IMA-HDD*

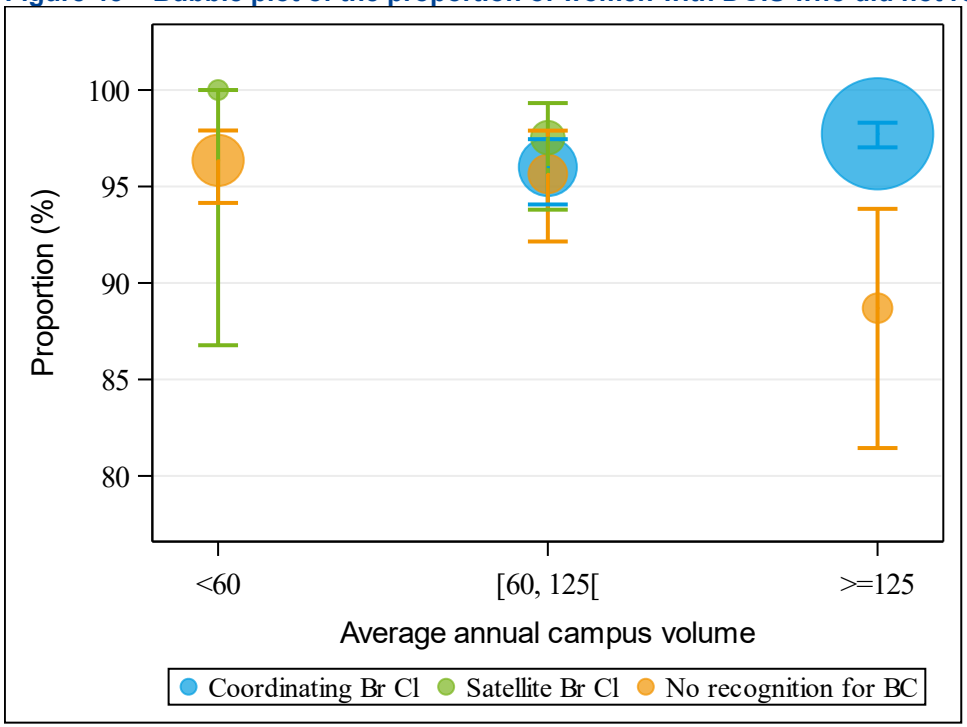
**Figure 44 – Scatter plot of the proportion of women with DCIS who did not receive ALND as first axillary surgery, by campus of first surgery**




*DCIS: ductal carcinoma in situ; ALND : axillary lymph node dissection.*

*Note: There were 155 units of analysis presented in the scatter plot, of which 65 campuses had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 5 patients for whom the campus could not be identified, are not represented in the scatter plot.*
*Source: BCR-IMA-HDD*

**Figure 45 – Bubble plot of the proportion of women with DCIS who did not receive ALND as first axillary surgery, by campus volume***




*DCIS: ductal carcinoma in situ; ALND : axillary lymph node dissection; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 5 patients could not be assigned to a campus, and were thus excluded from the analyses; 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*

*Source: BCR-IMA-HDD*

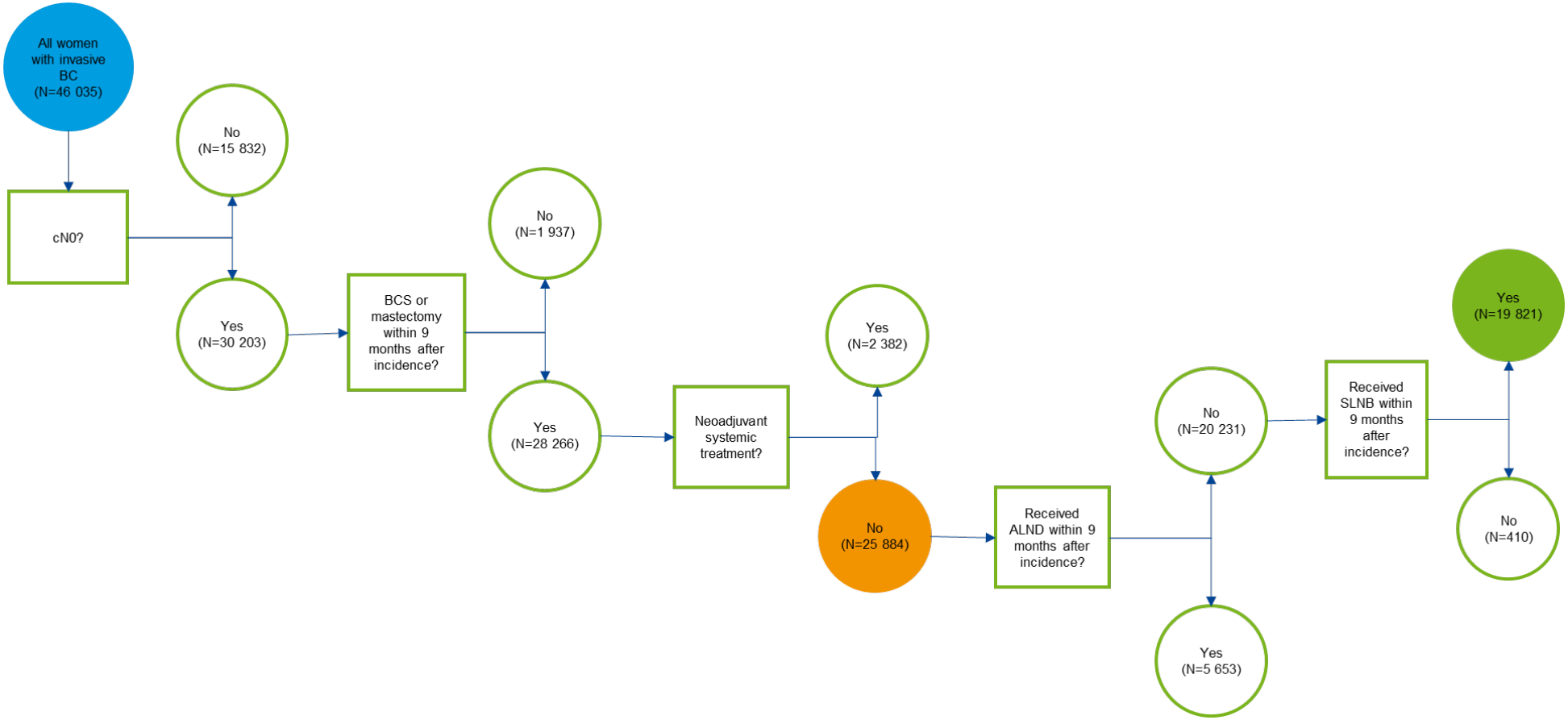
# APPENDIX 20. SENTINEL LYMPH-NODE BIOPSY (SLNB) ONLY IN PATIENTS WITH IBC

## Appendix 20.1. Documentation sheet

| Title | Proportion of patients with IBC and clinically negative axilla who undergo sentinel lymph-node biopsy (SLNB) only (excluding patients who received neoadjuvant systemic treatment) |
|---|---|
| **Rationale** | The axillary nodal status is the strongest prognostic factor in BC; it tailors many loco-regional and systemic treatment decisions.[46] Sentinel lymph node biopsy (SLNB) is an accepted and sufficient means of surgical and pathological staging of the axilla in patients who do not present with clinical evidence of lymph node involvement. Several randomised trials compared SLNB with full axillary lymph node dissection (ALND) in patients with clinically negative lymph nodes.[116-120] These trials did not reveal any difference with regard to overall survival or disease-free survival. Yet, morbidity and quality of life were significantly better in patients who underwent SLNB alone.[46, 121] SLNB is therefore regarded as the gold standard to assess the axillary lymph node status in patients with IBC and clinically negative axilla.[46] |
| **Selection** | This QI was selected by 94% of the experts who completed the online survey in spring 2020 |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women who undergo sentinel lymph-node biopsy (SLNB) only<br>Denominator: All women diagnosed with IBC and clinically negative axilla, who received surgery (BCS or mastectomy) within 9 months after incidence<br>Excluded: Women who received neoadjuvant systemic treatment |
| **Target** | As the description of nomenclature codes is not specific enough, it was decided to elaborate this indicator as a descriptive indicator (without target) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Clinically negative axilla: cN0 (unknown clinical status of lymph nodes i.e. cNx excluded)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>SLNB: for nomenclature codes, see Table 48<br>ALND: for nomenclature codes, see Table 48<br>Breast surgery (BCS or mastectomy): for nomenclature codes, see Table 44, Table 45<br>Systemic treatment includes chemotherapy, targeted therapy and endocrine therapy: for ATC codes, see Table 50, Table 51, Table 52 |
| **Risk adjustment** | None (process indicator) |

| Title | Proportion of patients with IBC and clinically negative axilla who undergo sentinel lymph-node biopsy (SLNB) only (excluding patients who received neoadjuvant systemic treatment) |
|---|---|
| **Limitations** | As is described in section 4.10.3, the nomenclature codes related to sentinel lymph node resection and/or axillary lymph node resection are not specific: it is not clear whether patients for whom these codes were invoiced, underwent axillary lymph node resection or not. Moreover, during the discussion of this indicator, several experts expressed their doubts about the reliability of the calculation of this indicator based on nomenclature codes. They noted that these codes are not always/not in all Belgian hospitals used in a correct way (more precisely: nomenclature codes for ALND are used to attest SLNB as the fees for the former are higher). This may thus lead to an overestimation of ALND and underestimation of SLNB.<br>An alternative approach could be the identification of SLNB by pNsn, but this is not reported as meticulously to the Belgian Cancer Registry by every Belgian hospital/pathology lab. Hence, this approach may also lead to an underestimation and can thus not be considered reliable either. Therefore, it was decided not to provide benchmarking for this indicator. |
| **Subgroup analyses** | - Age at diagnosis<br>- Year of incidence<br>- Clinical stage<br>- Type of breast surgery (BCS vs. mastectomy) |
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs 2014 - 2018<br>- Excluding vs. including cases with missing clinical node status (i.e. cNx)<br>- cN0 vs. cN0 and pN0 |
| **Benchmarking** | Centre of first surgery |
| **Level of benchmarking** | Campus level |
| **Comments** | |

## Appendix 20.2. Flowchart



## Appendix 20.3. Results

**Table 140 – Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by patient and tumour characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 25 884 | 19 821 | 76.6 |
| **Age at diagnosis** | | | |
| <40 years | 865 | 609 | 70.4 |
| 40-49 years | 3 901 | 2 961 | 75.9 |
| 50-59 years | 6 571 | 5 210 | 79.3 |
| 60-69 years | 7 345 | 5 841 | 79.5 |
| 70-79 years | 4 755 | 3 568 | 75.0 |
| 80+ years | 2 447 | 1 632 | 66.7 |
| **Incidence year** | | | |
| 2014 | 4 661 | 3 407 | 73.1 |
| 2015 | 5 011 | 3 660 | 73.0 |
| 2016 | 5 100 | 3 864 | 75.8 |
| 2017 | 5 525 | 4 372 | 79.1 |
| 2018 | 5 587 | 4 518 | 80.9 |
| **Clinical stage** | | | |
| 0 | 472 | 370 | 78.4 |
| I | 16 686 | 14 037 | 84.1 |
| II | 7 943 | 4 943 | 62.2 |
| III | 170 | 39 | 22.9 |
| IV[§] | 74 | 31 | 41.9 |
| Unknown | 539 | 401 | 74.4 |
| **Type of first surgery** | | | |
| BCS | 19 887 | 16 628 | 83.6 |
| *BCS (stricto sensu[ss])* | 19 578 | 16 406 | 83.8 |
| *Surgery for benign breast lesions* | 307 | 221 | 72.0 |
| *Excision biopsy* | 0 | 0 | - |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| *Surgery leading to accidental findings** | 2 | 1 | 50.0 |
| Mastectomy | 5 997 | 3 193 | 53.2 |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy; WHO: World Health Organization; §: there were 74 patients included who were clinically metastasized (cM1), but for whom no lymph node invasion was detected clinically (cN0); *: tumours which were found 'accidently' during breast reduction surgery.*
*Source: BCR-IMA*

### Table 141 – Sensitivity analysis: Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 25 884 | 19 821 | 76.6 |
| **Comparison period (2009 - 2013)** | 21 512 | 13 128 | 61.0 |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy.*
*Source: BCR-IMA*

### Table 142 – Sensitivity analysis: Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), including cases with missing cN category

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Excluding cNx (main quality indicator)** | 25 884 | 19 821 | 76.6 |
| **Including cNx** | 30 843 | 22 820 | 74.0 |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy.*
*Source: BCR-IMA*

### Table 143 – Sensitivity analysis: Proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment)

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Clinically negative axilla (cN0) only (main quality indicator)** | 25 884 | 19 821 | 76.6 |
| **Clinically and pathologically negative axilla (cN0 and pN0)** | 19 559 | 17 401 | 89.0 |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy.*
*Source: BCR-IMA*

**Table 144 – Proportion of women with IBC and clinically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 25 828 | 19 785 | 76.6 | [76.1, 77.1] | |
| **Recognition status for BC** | | | | | <0.0001 |
| Coordinating breast clinic | 18 556 | 14 422 | 77.7 | [77.1, 78.3] | |
| Satellite breast clinic | 1 411 | 1 112 | 78.8 | [76.6, 80.9] | |
| No recognition for BC | 5 861 | 4 251 | 72.5 | [71.4, 73.7] | |
| **Average annual campus volume*** | | | | | <0.0001 |
| ≥125 | 15 750 | 12 369 | 78.5 | [77.9, 79.2] | |
| [60, 125[ | 6 313 | 4 731 | 74.9 | [73.9, 76.0] | |
| <60 | 3 765 | 2 685 | 71.3 | [69.8, 72.8] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | <0.0001 |
| ≥125 | 14 944 | 11 752 | 78.6 | [78.0, 79.3] | |
| [60, 125[ | 3 612 | 2 670 | 73.9 | [72.5, 75.3] | |
| ***Satellite breast clinics*** | | | | | 0.377 |
| [60, 125[ | 1 254 | 984 | 78.5 | [76.1, 80.7] | |
| <60 | 157 | 128 | 81.5 | [74.6, 87.3] | |
| ***No recognition for BC*** | | | | | 0.001 |
| ≥125 | 806 | 617 | 76.6 | [73.5, 79.4] | |
| [60, 125[ | 1 447 | 1 077 | 74.4 | [72.1, 76.7] | |
| <60 | 3 608 | 2 557 | 70.9 | [69.4, 72.3] | |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 36 patients who could not be assigned to a campus, and 20 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

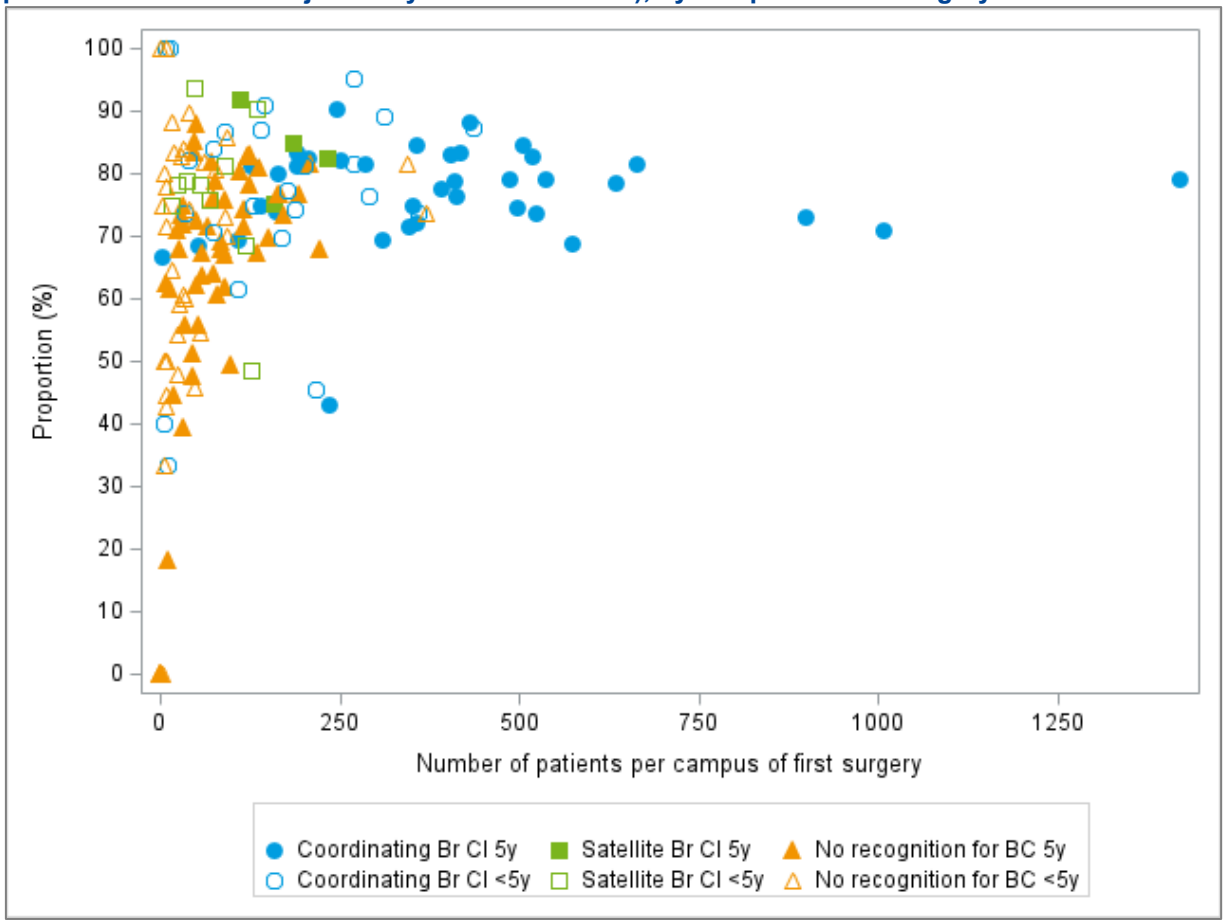
**Table 145 – Association between recognition status for BC and campus volume, and the odds of undergoing SLNB only (excluding pts who received neoadjuvant systemic treatment) in women with IBC and clinically negative axilla, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | <0.0001 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 1.08 | [0.77, 1.52] | |
| No recognition for BC | 0.64 | [0.52, 0.77] | |
| **Average annual campus volume*** | | | <0.0001 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.75 | [0.60, 0.95] | |
| <60 | 0.56 | [0.45, 0.71] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.019 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.72 | [0.54, 0.95] | |
| ***Satellite breast clinics*** | | | 0.730 |
| [60, 125[ | 1 | [reference] | |
| <60 | 1.17 | [0.47, 2.90] | |
| ***No recognition for BC*** | | | 0.270 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.89 | [0.47, 1.69] | |
| <60 | 0.72 | [0.40, 1.31] | |

*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 36 patients who could not be assigned to a campus, and 20 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*

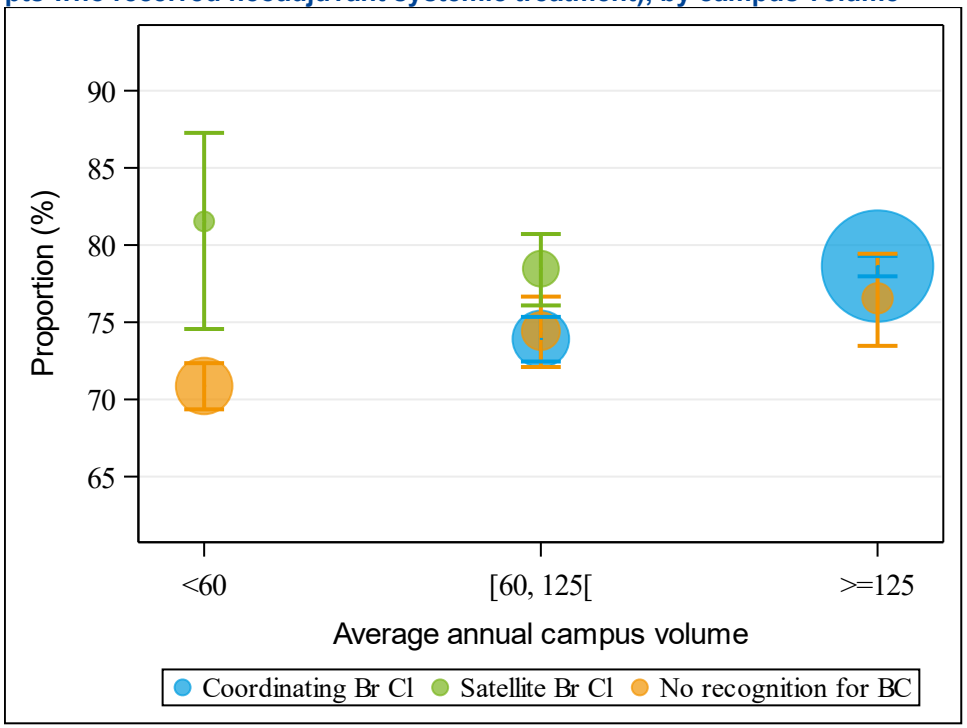
*Source: BCR-IMA-HDD*

**Figure 46 – Scatter plot of the proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by campus of first surgery**




*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy.*
*Note: There were 163 units of analysis presented in the scatter plot, of which 21 had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 36 patients for whom the campus could not be identified, are not represented in the scatter plot.*
*Source: BCR-IMA-HDD*

**Figure 47 – Bubble plot of the proportion of women with IBC and clinically AND pathologically negative axilla who underwent SLNB only (excluding pts who received neoadjuvant systemic treatment), by campus volume***




*IBC: invasive breast cancer; SLNB: sentinel lymph node biopsy; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 36 patients who could not be assigned to a campus, and 20 patients assigned to a coordinating breast clinic in volume group < 60 patients/year were excluded.*
*Source: BCR-IMA-HDD*

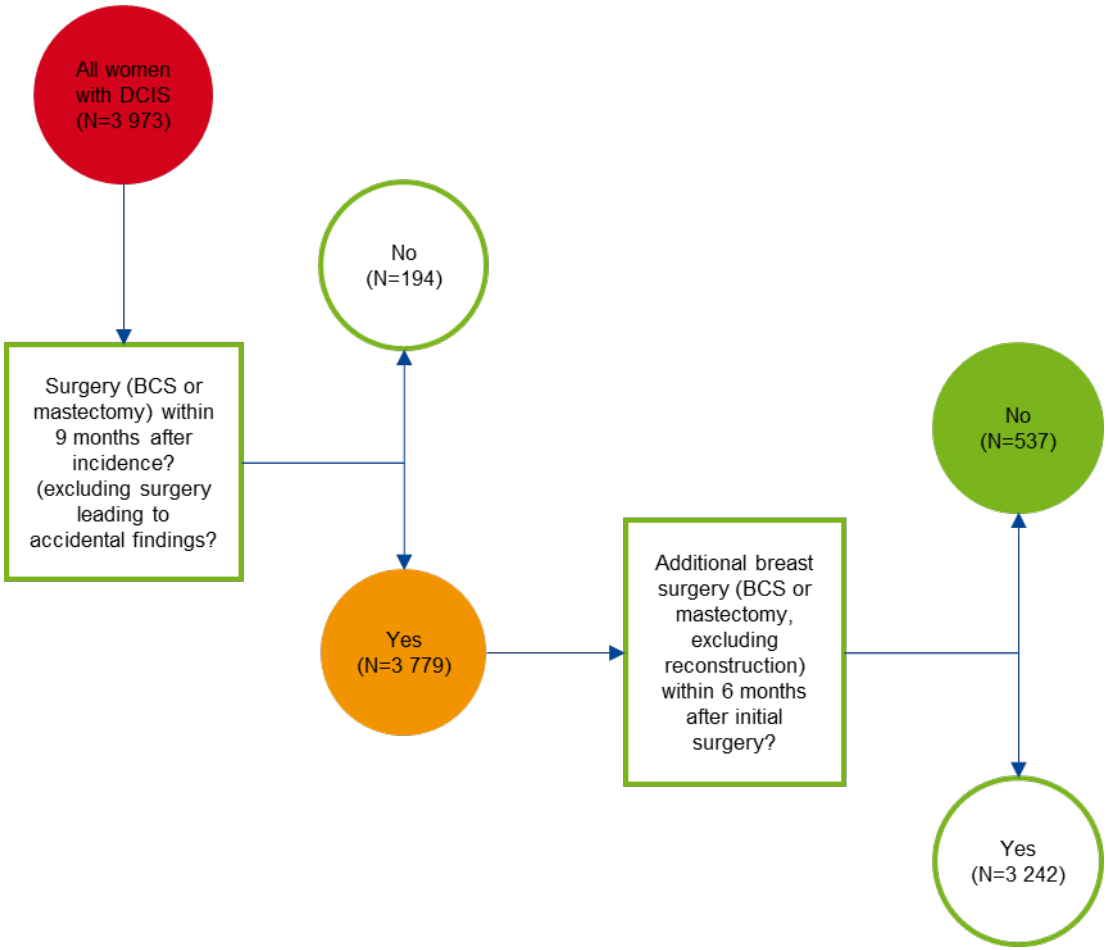
# APPENDIX 21. JUST ONE BREAST SURGERY IN DCIS

## Appendix 21.1. Documentation sheet

| Title | Proportion of women with DCIS who received just one breast operation (excluding reconstruction) |
|---|---|
| **Rationale** | It is estimated that approximately 30% of patients in whom wide excision for DCIS is attempted, require additional breast surgery to achieve negative surgical margins.[46] The financial, psychological, and cosmetic impact of these repeated surgeries is significant; they markedly increase the burden of BC therapy.[64] |
| **Selection** | This QI was selected by 82% of experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women who did not receive a second breast surgery (which is not reconstruction surgery) within 6 months after initial breast surgery<br>Denominator: All women diagnosed with DCIS who received surgery (BCS or mastectomy) within 9 months after incidence |
| **Target** | 90% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with DCIS (ICD-10: C50; for ICD-O-3 morphology codes, see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Breast surgery (BCS or mastectomy): for nomenclature codes, see Table 44, Table 45; nomenclature codes for surgery of benign breast lesions and excision biopsy (Table 46) were included in BCS. |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | The nomenclature codes do not provide any information on the laterality of procedures. Hence, in case of multiple surgical interventions identified for the same patient it cannot be revealed whether they were performed in the same breast or in the contralateral breast (e.g. preventive surgery). |
| **Subgroup analyses** | - Age at diagnosis<br>- Year of incidence<br>- Type of initial surgery (BCS vs. mastectomy) |
| **Sensitivity analyses** | Incidence year 2009 - 2013 vs. 2014 - 2018 |
| **Benchmarking** | Centre of first surgery |
| **Level of benchmarking** | Campus level |

| Title | Proportion of women with DCIS who received just one breast operation (excluding reconstruction) |
|---|---|
| **Comments** | In order to focus on surgery performed for BC, the nomenclature codes for surgery leading to accidental findings (i.e. breast reduction surgery) were not included in the analyses. |

## Appendix 21.2. Flowchart



## Appendix 21.3. Results

**Table 146 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by patient characteristics and type of first surgery**

| | DCIS | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 3 779 | 3 242 | 85.8 |
| **Age at diagnosis** | | | |
| <40 years | 153 | 115 | 75.2 |
| 40-49 years | 673 | 558 | 82.9 |
| 50-59 years | 1 189 | 1 001 | 84.2 |
| 60-69 years | 1 158 | 1 016 | 87.7 |
| 70-79 years | 460 | 420 | 91.3 |
| 80+ years | 146 | 132 | 90.4 |
| **Incidence year** | | | |
| 2014 | 782 | 666 | 85.2 |
| 2015 | 740 | 624 | 84.3 |
| 2016 | 773 | 666 | 86.2 |
| 2017 | 729 | 627 | 86.0 |
| 2018 | 755 | 659 | 87.3 |
| **Type of first surgery** | | | |
| BCS | 2 963 | 2 452 | 82.8 |
| *BCS (stricto sensu[ss])* | *2 539* | *2 123* | *83.6* |
| *Surgery for benign breast lesions* | *409* | *314* | *76.8* |
| *Excision biopsy* | *15* | *15* | *100.0* |
| Mastectomy | 816 | 790 | 96.8 |

*DCIS: ductal carcinoma in situ; BCS: breast conserving surgery.*
*Source: BCR-IMA*

**Table 147 – Proportion of women with DCIS who received breast surgery (excluding surgery leading to accidental findings), by type of first and second surgery (excluding breast reconstruction)**

| | DCIS | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **BCS as first surgery** | 2 963 | 2 452 | 82.8 |
| **More than one surgery[$]** | | 511 | |
| *BCS as second surgery** | | *278* | *54.4* |
| *Mastectomy as second surgery** | | *233* | *45.6* |
| **Mastectomy as first surgery** | 816 | 790 | 96.8 |
| **More than one surgery[$]** | | 26 | |
| *BCS as second surgery** | | *12* | *46.2* |
| *Mastectomy as second surgery** | | *14* | *53.8* |

*DCIS: ductal carcinoma in situ; BCS: Breast conserving surgery; $: as the nomenclature codes do not provide any information on the laterality of procedures, it cannot be revealed whether these patients underwent the second surgery in the same breast or in the contralateral breast (e.g. preventive surgery); *: the denominator for these percentages is the number of patients having more than one surgery.*
*Source: BCR-IMA*

**Table 148 – Sensitivity analysis: Proportion of women with DCIS who received just one operation (excluding reconstruction), by time period**

| | DCIS | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 3 779 | 3 242 | 85.8 |
| **Comparison period (2009 - 2013)** | 3 690 | 2 932 | 79.5 |

*DCIS: ductal carcinoma in situ*
*Source: BCR-IMA*

**Table 149 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 3 766 | 3 234 | 85.9 | [84.7, 87.0] | |
| **Recognition status for BC** | | | | | 0.182 |
| Coordinating breast clinic | 2 809 | 2 429 | 86.5 | [85.2, 87.7] | |

| Characteristic | N | n | n/N (%) | 95% CI | P-value$ |
|---|---|---|---|---|---|
| Satellite breast clinic | 185 | 154 | 83.2 | [77.1, 88.3] | |
| No recognition for BC | 772 | 651 | 84.3 | [81.6, 86.8] | |
| **Average annual campus volume** | | | | | 0.174 |
| ≥125 | 2 347 | 2 032 | 86.6 | [85.1, 87.9] | |
| [60, 125[ | 961 | 820 | 85.3 | [82.9, 87.5] | |
| <60 | 458 | 382 | 83.4 | [79.7, 86.7] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.883 |
| ≥125 | 2 233 | 1 932 | 86.5 | [85.0, 87.9] | |
| [60, 125[ | 576 | 497 | 86.3 | [83.2, 89.0] | |
| ***Satellite breast clinics*** | | | | | 0.057 |
| [60, 125[ | 159 | 129 | 81.1 | [74.2, 86.9] | |
| <60 | 26 | 25 | 96.2 | [80.4, 99.9] | |
| ***No recognition for BC*** | | | | | 0.314 |
| ≥125 | 114 | 100 | 87.7 | [80.3, 93.1] | |
| [60, 125[ | 226 | 194 | 85.8 | [80.6, 90.1] | |
| <60 | 432 | 357 | 82.6 | [78.7, 86.1] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Table 150 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with DCIS, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.518 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.82 | [0.48, 1.41] | |
| No recognition for BC | 0.85 | [0.62, 1.16] | |
| **Average annual campus volume** | | | 0.591 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.92 | [0.66, 1.28] | |
| <60 | 0.83 | [0.57, 1.19] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.889 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.03 | [0.67, 1.59] | |
| ***Satellite breast clinics*** | | | 0.098 |
| [60, 125[ | 1 | [reference] | |
| <60 | 5.87 | [0.72, 47.84] | |
| ***No recognition for BC*** | | | 0.492 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.83 | [0.36, 1.93] | |
| <60 | 0.67 | [0.31, 1.45] | |

*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

### Table 151 – Proportion of women with DCIS who received BCS, by recognition status for BC and campus volume

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 3 766 | 2 952 | 78.4 | [77.0, 79.7] | |
| **Recognition status for BC** | | | | | 0.049 |
| Coordinating breast clinic | 2 809 | 2 180 | 77.6 | [76.0, 79.1] | |
| Satellite breast clinic | 185 | 142 | 76.8 | [70.0, 82.6] | |
| No recognition for BC | 772 | 630 | 81.6 | [78.7, 84.3] | |
| **Average annual campus volume** | | | | | 0.010 |
| ≥125 | 2 347 | 1 803 | 76.8 | [75.1, 78.5] | |
| [60, 125[ | 961 | 775 | 80.6 | [78.0, 83.1] | |
| <60 | 458 | 374 | 81.7 | [77.8, 85.1] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.014 |
| ≥125 | 2 233 | 1 711 | 76.6 | [74.8, 78.4] | |
| [60, 125[ | 576 | 469 | 81.4 | [78.0, 84.5] | |
| ***Satellite breast clinics*** | | | | | 0.632 |
| [60, 125[ | 159 | 123 | 77.4 | [70.1, 83.6] | |
| <60 | 26 | 19 | 73.1 | [52.2, 88.4] | |
| ***No recognition for BC*** | | | | | 0.898 |
| ≥125 | 114 | 92 | 80.7 | [72.3, 87.5] | |
| [60, 125[ | 226 | 183 | 81.0 | [75.2, 85.9] | |
| <60 | 432 | 355 | 82.2 | [78.2, 85.7] | |

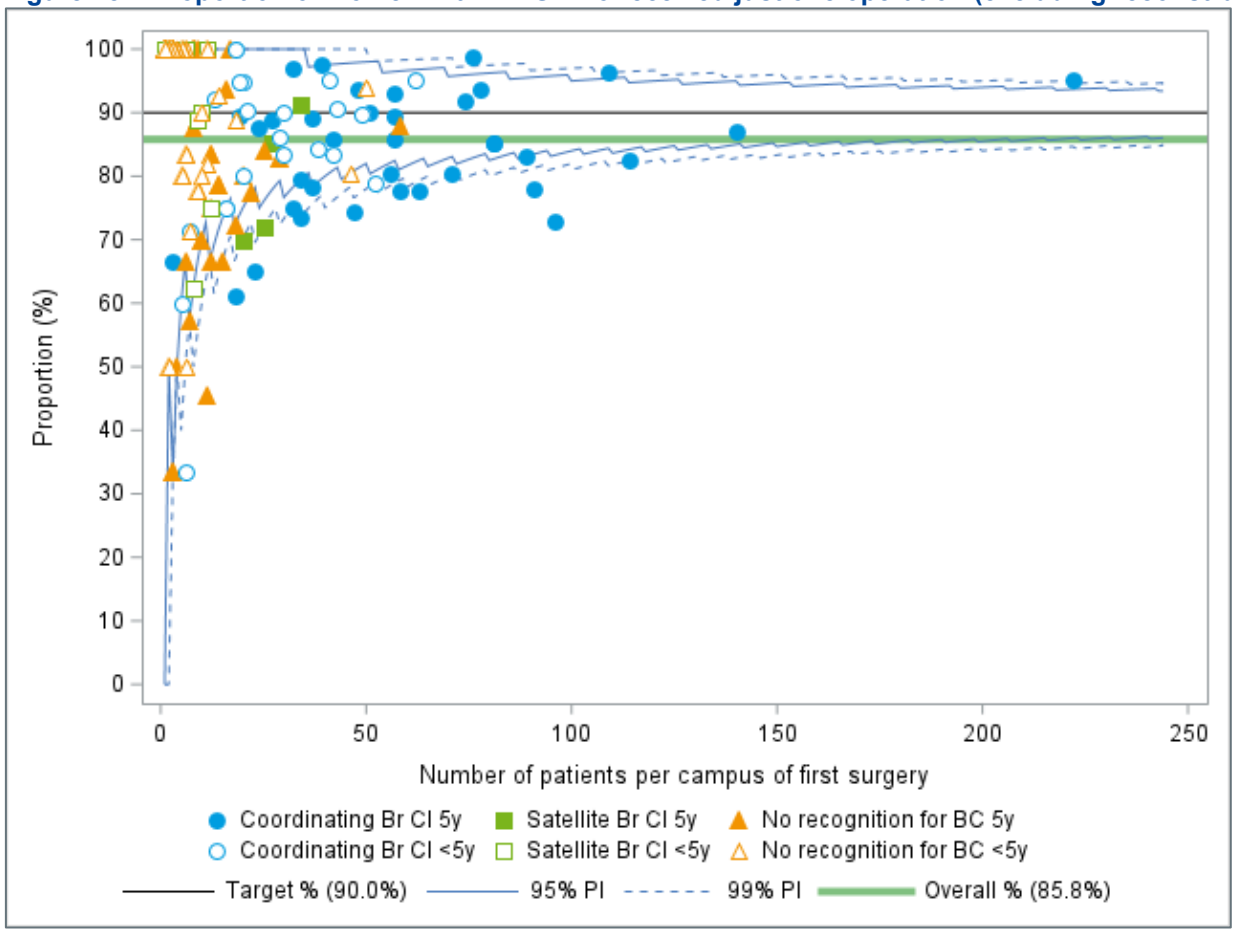
*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Table 152 – Association between recognition status for BC and campus volume, and the odds of receiving BCS in women with DCIS**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.503 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.84 | [0.52, 1.35] | |
| No recognition for BC | 1.11 | [0.84, 1.47] | |
| **Average annual campus volume** | | | 0.658 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.07 | [0.80, 1.42] | |
| <60 | 1.17 | [0.84, 1.63] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.399 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.17 | [0.81, 1.69] | |
| ***Satellite breast clinics*** | | | 0.633 |
| [60, 125[ | 1 | [reference] | |
| <60 | 0.79 | [0.31, 2.05] | |
| ***No recognition for BC*** | | | 0.747 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.81 | [0.33, 2.00] | |
| <60 | 1.00 | [0.43, 2.31] | |

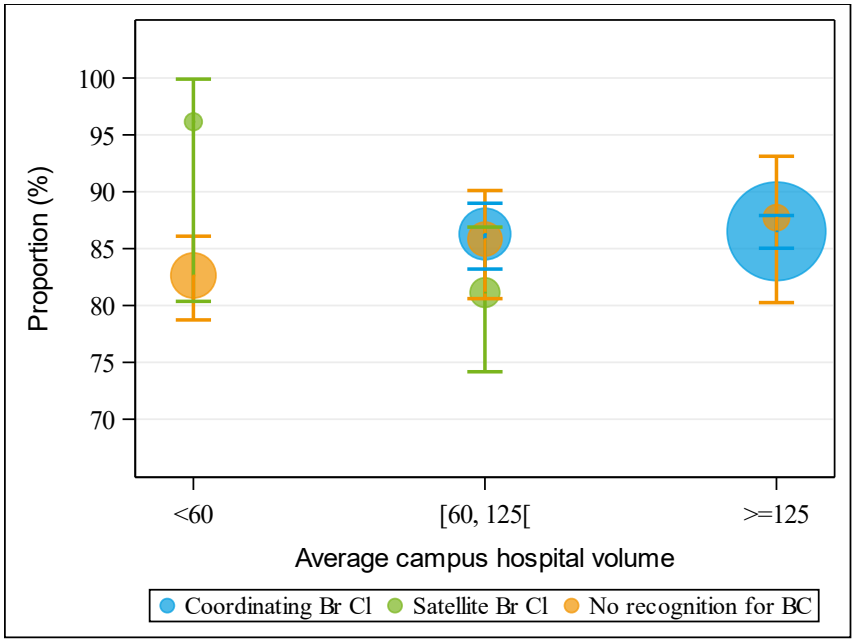
*DCIS: ductal carcinoma in situ; IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Figure 48 – Proportion of women with DCIS who received just one operation (excluding reconstruction), by campus of first surgery**



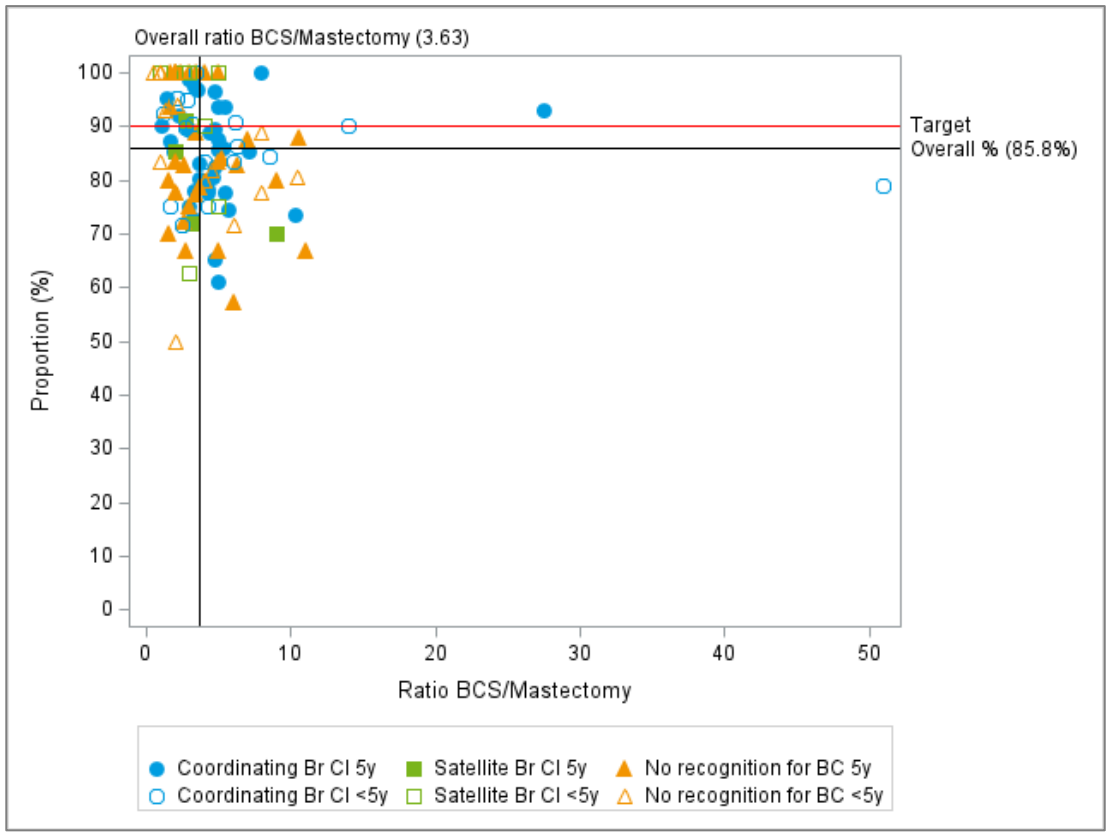

*DCIS: ductal carcinoma in situ; 155 units of analysis presented in the funnel plot, of which 65 units had less than ten patients in the denominator. Nine units were situated below the 99% prediction interval, while two were situated above that interval. An open plot symbol is used when the recognition status or the number of beds changed during the five year study period; five patients for whom the campus could not be identified, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

**Figure 49 – Bubble plot of the proportion of women with DCIS who received just one operation (excluding reconstruction), by average annual campus volume**




*DCIS: ductal carcinoma in situ; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 5 patients who could not be assigned to a campus, and 8 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Figure 50 – Proportion of women with DCIS who received just one operation (excluding reconstruction) versus BCS/mastectomy (left) and distribution of campuses over the four quadrants**




In Q1 = upper left (overall result > 85.8 and ratio < 3.63) - N=35 units of analysis

- Coordinating: 16 (active for 5 years: 9, active less than 5 years: 7)
- Satellite: 4 (5y: 1, <5y: 3)
- No recognition for BC: 15 (5y: 9, <5y: 6)

In Q2 = upper right (overall result > 85.8 and ratio > 3.63) - N=19 units of analysis

- Coordinating: 12 (5y: 9, <5y: 3)
- Satellite: 2 (5y: 0, <5y: 2)
- No recognition for BC: 5 (5y: 4, <5y: 1)

In Q3 = lower left (overall result < 85.8 and ratio < 3.63) - N=21 units of analysis

- Coordinating: 6 (5y: 4, <5y: 2)
- Satellite: 3 (5y: 2, <5y: 1)
- No recognition for BC: 12 (5y: 9, <5y: 3)

In Q4 = lower right (overall result < 85.8 and ratio > 3.63) - N=37 units of analysis

- Coordinating: 19 (5y: 14, <5y: 5)
- Satellite: 3 (5y: 1, <5y: 2)
- No recognition for BC: 15 (5y: 9, <5y: 6)

*DCIS: ductal carcinoma in situ; there are 112 units of analysis reported in the graph: 53 coordinating breast clinics (active for 5 years: 36, active less than 5 years: 17), 12 satellite breast clinics (active for 5 years: 4, active less than 5 years: 8), 47 campuses without recognition for BC (active for 5 years: 31, active less than 5 years: 16); this graph presents 43 units of analysis (218 patients) less than the funnel plot because in these units there were either no BCS or no mastectomies performed, making the calculation of a ratio impossible. An open plot symbol is used when the recognition status or the number of beds changed during the five year study period; five patients for whom the campus could not be identified, are not represented in the graph. The quadrants are defined by the overall QI result and the overall ratio BCS/mastectomy.*
*Source: BCR-IMA-HDD*

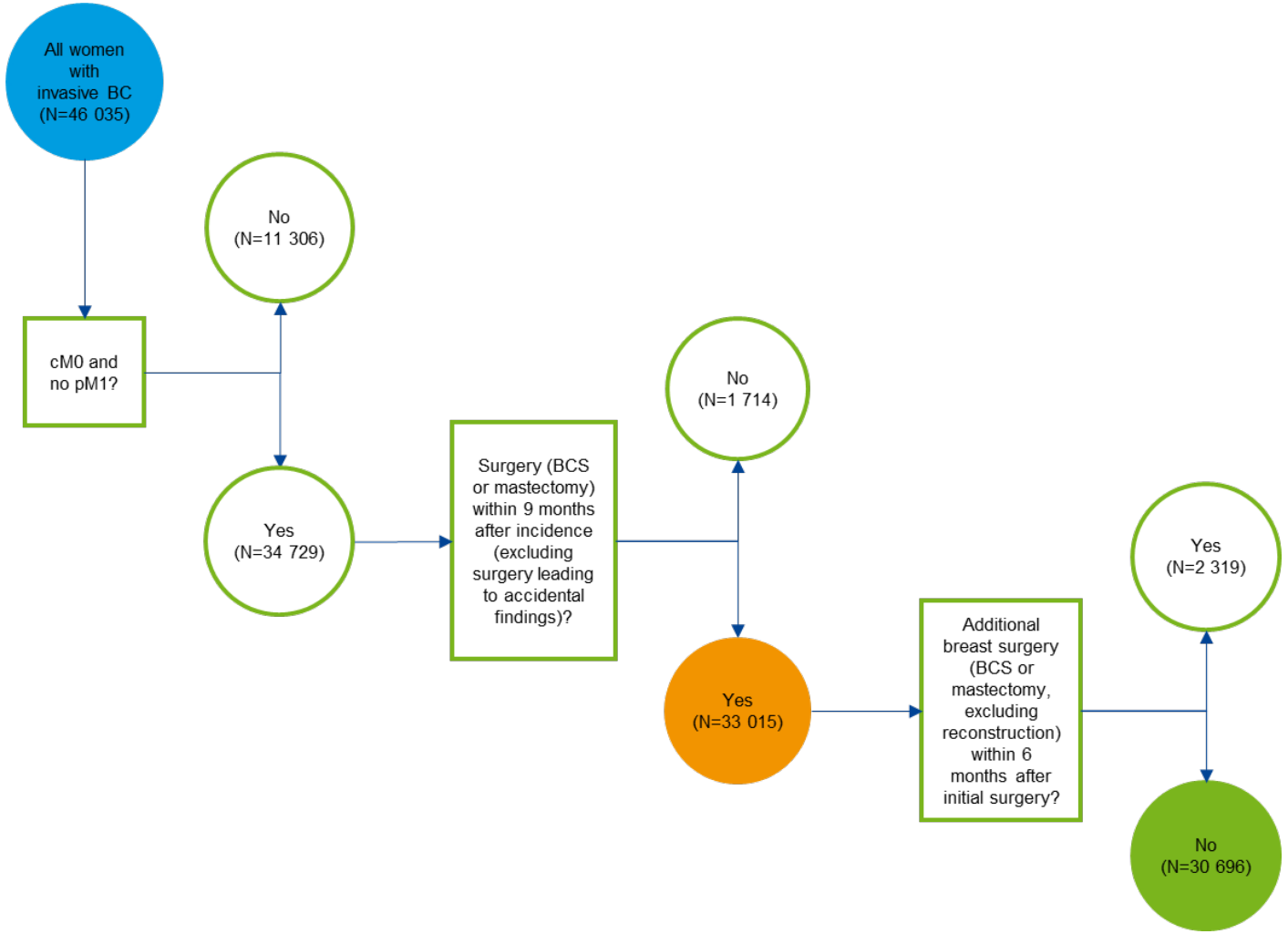
# APPENDIX 22. JUST ONE BREAST SURGERY IN IBC

## Appendix 22.1. Documentation sheet

| Title | Proportion of patients with IBC (M0) who received a single (breast) operation for the primary tumour (excluding reconstruction) |
|---|---|
| **Rationale** | There is significant variability of care for reoperation after initial wide excision for BC: rates of reoperation vary from less than 10% to more than 50%.[46] The financial, psychological, and cosmetic impact of these repeated surgeries is significant; they markedly increase the burden of BC therapy.[64] |
| **Type of QI** | Process |
| **Calculation** | Numerator: Number of women who did not receive a second breast surgery (which is not reconstruction surgery) within 6 months after initial surgery<br>Denominator: All women diagnosed with IBC (M0) who received surgery (BCS or mastectomy) within 9 months after incidence |
| **Target** | 90% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Breast surgery (BCS or mastectomy): for nomenclature codes, see Table 44, Table 45; nomenclature codes for surgery of benign breast lesions and excision biopsy (Table 46) were included in BCS.<br>M0 = cM0 and no pM1 (unknown clinical distant metastasis status i.e. cMx excluded; pMx is included) |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | The nomenclature codes do not provide any information on the laterality of procedures. Hence, in case of multiple surgical interventions identified for the same patient it cannot be revealed whether they were performed in the same breast or in the contralateral breast (e.g. preventive surgery). |
| **Subgroup analyses** | - Age at diagnosis<br>- Year of incidence<br>- Clinical/pathological/combined stage<br>- Type of initial surgery (BCS vs. mastectomy) |
| **Sensitivity analyses** | Incidence year 2009 - 2013 vs. 2014 - 2018<br>Excluding vs. including cases with missing clinical distant metastasis status (cMx) |
| **Benchmarking** | Centre of first surgery |
| **Level of benchmarking** | Campus level |

| Title | Proportion of patients with IBC (M0) who received a single (breast) operation for the primary tumour (excluding reconstruction) |
|---|---|
| **Comments** | In order to focus on surgery performed for BC, the nomenclature codes for surgery leading to accidental findings (i.e. breast reduction surgery) were not included in the analyses. |

## Appendix 22.2. Flowchart



## Appendix 22.3. Results

**Table 153 – Proportion of women with IBC who received just one operation (excluding reconstruction), by patient characteristics and type of first surgery**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 33 015 | 30 696 | 93.0 |
| **Age at diagnosis** | | | |
| <40 years | 1 813 | 1 672 | 92.2 |
| 40-49 years | 5 367 | 4 901 | 91.3 |
| 50-59 years | 8 319 | 7 670 | 92.2 |
| 60-69 years | 8 725 | 8 138 | 93.3 |
| 70-79 years | 5 712 | 5 362 | 93.9 |
| 80+ years | 3 079 | 2 953 | 95.9 |
| **Incidence year** | | | |
| 2014 | 5 994 | 5 581 | 93.1 |
| 2015 | 6 321 | 5 857 | 92.7 |
| 2016 | 6 508 | 6 100 | 93.7 |
| 2017 | 7 068 | 6 554 | 92.7 |
| 2018 | 7 124 | 6 604 | 92.7 |
| **Clinical stage** | | | |
| 0[$] | 424 | 348 | 82.1 |
| I | 16 108 | 14 937 | 92.7 |
| II | 13 175 | 12 347 | 93.7 |
| III | 2 139 | 2 057 | 96.2 |
| Unknown | 1 169 | 1 007 | 86.1 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **(y)Pathological stage** | | | |
| y0 | 988 | 972 | 98.4 |
| yis | 307 | 302 | 98.4 |
| (y)I | 15 794 | 14 757 | 93.4 |
| (y)II | 11 581 | 10 643 | 91.9 |
| (y)III | 3 440 | 3 160 | 91.9 |
| Unknown | 905 | 862 | 95.2 |
| **Combined stage** | | | |
| (y)0 | 994 | 978 | 98.4 |
| yis | 307 | 302 | 98.4 |
| (y)I | 15 977 | 14 926 | 93.4 |
| (y)II | 12 091 | 11 134 | 92.1 |
| (y)III | 3 626 | 3 338 | 92.1 |
| Unknown | 20 | 18 | 90.0 |
| **Type of first surgery** | | | |
| BCS | 22 952 | 20 815 | 90.7 |
| *BCS (stricto sensu[ss])* | *22 591* | *20 608* | *91.2* |
| *Excision biopsy* | *1* | *1* | *100.0* |
| *Surgery for benign breast lesions* | *360* | *206* | *57.2* |
| Mastectomy | 10 063 | 9 881 | 98.2 |

*IBC: invasive breast cancer; WHO: World Health Organization; BCS: breast conserving surgery; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis; $: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. These tumours were clinically assessed as in situ but appeared to be invasive after resection.*
*Source: BCR-IMA*

### Table 154 – Proportion of women with IBC who received breast surgery (excluding surgery leading to accidental findings), by type of first and second surgery (excluding breast reconstruction)

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **BCS as first surgery** | 22 952 | 20 815 | 90.7 |
| **More than one surgery$** | | 2 137 | |
| *BCS as second surgery** | | 1 243 | 58.2 |
| *Mastectomy as second surgery** | | 894 | 41.8 |
| **Mastectomy as first surgery** | 10 063 | 9 881 | 98.2 |
| **More than one surgery$** | | 182 | |
| *BCS as second surgery** | | 127 | 69.8 |
| *Mastectomy as second surgery** | | 55 | 30.2 |

*IBC: invasive breast cancer; BCS: Breast conserving surgery; $: as the nomenclature codes do not provide any information on the laterality of procedures, it cannot be revealed whether these patients underwent the second surgery in the same breast or in the contralateral breast (e.g. preventive surgery); *: denominator for these percentages is the number of patients having more than one surgery.*
*Source: BCR-IMA*

### Table 155 – Sensitivity analysis: Proportion of women with IBC who received just one operation (excluding reconstruction), by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 33 015 | 30 696 | 93.0 |
| **Comparison period (2009 - 2013)** | 28 652 | 26 083 | 91.0 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 156 – Sensitivity analysis: Proportion of women with IBC who received just one operation (excluding reconstruction), by in-/exclusion of cMx

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **2014 - 2018: cM0, pMx (Main quality indicator)** | 33 015 | 30 696 | 93.0 |
| **2014 - 2018: cM0/x, pMx** | 39 690 | 36 836 | 92.8 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Table 157 – Proportion of women with IBC who received just one operation (excluding reconstruction), by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 32 913 | 30 619 | 93.0 | [92.7, 93.3] | |
| **Recognition status for BC** | | | | | 0.022 |
| Coordinating breast clinic | 23 636 | 22 043 | 93.3 | [92.9, 93.6] | |
| Satellite breast clinic | 1 817 | 1 671 | 92.0 | [90.6, 93.2] | |
| No recognition for BC | 7 460 | 6 905 | 92.6 | [91.9, 93.1] | |
| **Average annual campus volume** | | | | | 0.001 |
| ≥125 | 19 859 | 18 557 | 93.4 | [93.1, 93.8] | |
| [60, 125[ | 8 271 | 7 644 | 92.4 | [91.8, 93.0] | |
| <60 | 4 783 | 4 418 | 92.4 | [91.6, 93.1] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.010 |
| ≥125 | 18 910 | 17 675 | 93.5 | [93.1, 93.8] | |
| [60, 125[ | 4 726 | 4 368 | 92.4 | [91.6, 93.2] | |
| ***Satellite breast clinics*** | | | | | 0.836 |
| [60, 125[ | 1 583 | 1 455 | 91.9 | [90.5, 93.2] | |
| <60 | 234 | 216 | 92.3 | [88.1, 95.4] | |
| ***No recognition for BC*** | | | | | 0.735 |
| ≥125 | 949 | 882 | 92.9 | [91.1, 94.5] | |
| [60, 125[ | 1 962 | 1 821 | 92.8 | [91.6, 93.9] | |
| <60 | 4 549 | 4 202 | 92.4 | [91.6, 93.1] | |

*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Table 158 – Association between recognition status for BC and campus volume, and the odds of receiving just one operation (excluding reconstruction) in women with IBC, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.583 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 0.87 | [0.60, 1.24] | |
| No recognition for BC | 0.91 | [0.74, 1.12] | |
| **Average annual campus volume*** | | | 0.582 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.96 | [0.75, 1.23] | |
| <60 | 0.88 | [0.69, 1.13] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.953 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.99 | [0.71, 1.38] | |
| ***Satellite breast clinics*** | | | 0.753 |
| [60, 125[ | 1 | [reference] | |
| <60 | 0.88 | [0.39, 1.98] | |
| ***No recognition for BC*** | | | 0.872 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 1.02 | [0.53, 1.98] | |
| <60 | 0.94 | [0.51, 1.73] | |

*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Table 159 – Proportion of women with IBC who received BCS, by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 32 913 | 22 879 | 69.5 | [69.0, 70.0] | |
| **Recognition status for BC** | | | | | <0.0001 |
| Coordinating breast clinic | 23 636 | 16 254 | 68.8 | [68.2, 69.4] | |
| Satellite breast clinic | 1 817 | 1 376 | 75.7 | [73.7, 77.7] | |
| No recognition for BC | 7 460 | 5 249 | 70.4 | [69.3, 71.4] | |
| **Average annual campus volume** | | | | | 0.016 |
| ≥125 | 19 859 | 13 733 | 69.2 | [68.5, 69.8] | |
| [60, 125[ | 8 271 | 5 853 | 70.8 | [69.8, 71.7] | |
| <60 | 4 783 | 3 293 | 68.8 | [67.5, 70.2] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.343 |
| ≥125 | 18 910 | 12 977 | 68.6 | [68.0, 69.3] | |
| [60, 125[ | 4 726 | 3 277 | 69.3 | [68.0, 70.7] | |
| ***Satellite breast clinics*** | | | | | 0.770 |
| [60, 125[ | 1 583 | 1 197 | 75.6 | [73.4, 77.7] | |
| <60 | 234 | 179 | 76.5 | [70.5, 81.8] | |
| ***No recognition for BC*** | | | | | <0.0001 |
| ≥125 | 949 | 756 | 79.7 | [77.0, 82.2] | |
| [60, 125[ | 1 962 | 1 379 | 70.3 | [68.2, 72.3] | |
| <60 | 4 549 | 3 114 | 68.5 | [67.1, 69.8] | |

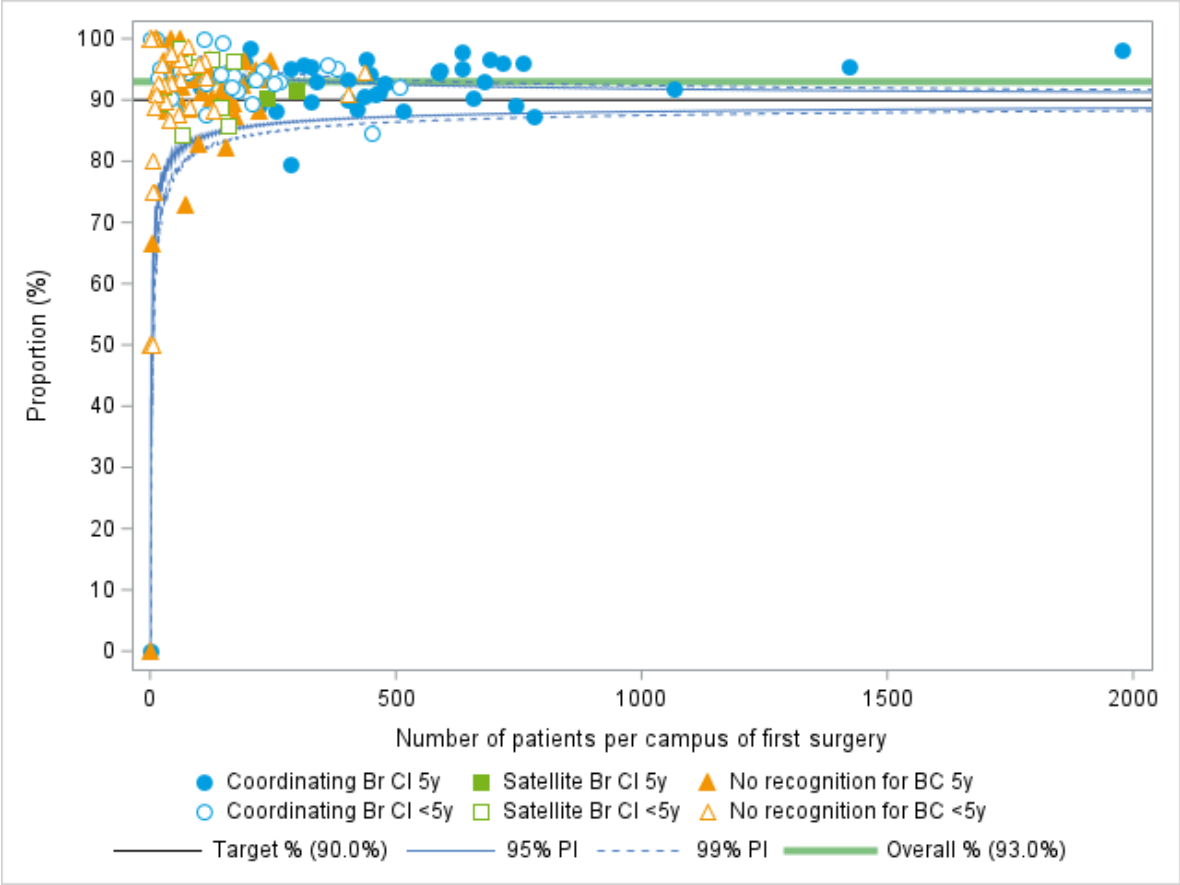
*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a campus, hence patients with DCIS or IBC, but also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Table 160 – Association between recognition status for BC and campus volume, and the odds of receiving BCS in women with IBC**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] |
|---|---|---|---|
| **Recognition status for BC** | | | 0.047 |
| Coordinating breast clinic | 1 | [reference] | |
| Satellite breast clinic | 1.29 | [1.01, 1.64] | |
| No recognition for BC | 0.94 | [0.82, 1.09] | |
| **Average annual campus volume*** | | | 0.250 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.96 | [0.81, 1.13] | |
| <60 | 0.87 | [0.74, 1.03] | |
| **Volume groups per recognition status** | | | |
| ***Coordinating breast clinics*** | | | 0.499 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.93 | [0.75, 1.15] | |
| ***Satellite breast clinics*** | | | 0.703 |
| [60, 125[ | 1 | [reference] | |
| <60 | 1.11 | [0.65, 1.87] | |
| ***No recognition for BC*** | | | 0.027 |
| ≥125 | 1 | [reference] | |
| [60, 125[ | 0.60 | [0.38, 0.95] | |
| <60 | 0.56 | [0.37, 0.86] | |

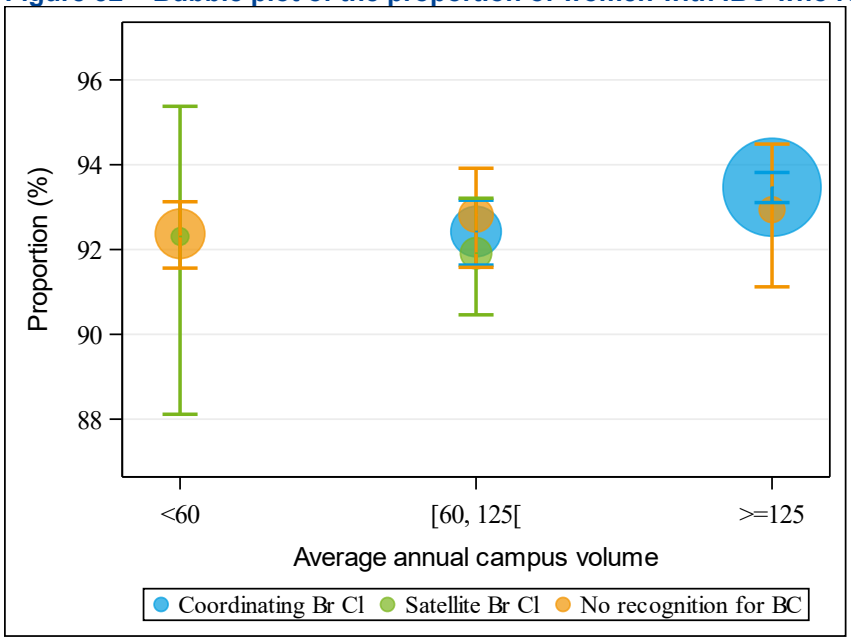
*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into campuses (i.e. centre of first surgery) was taken into account; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Figure 51 – Proportion of women with IBC who received just one operation (excluding reconstruction), by campus of first surgery**



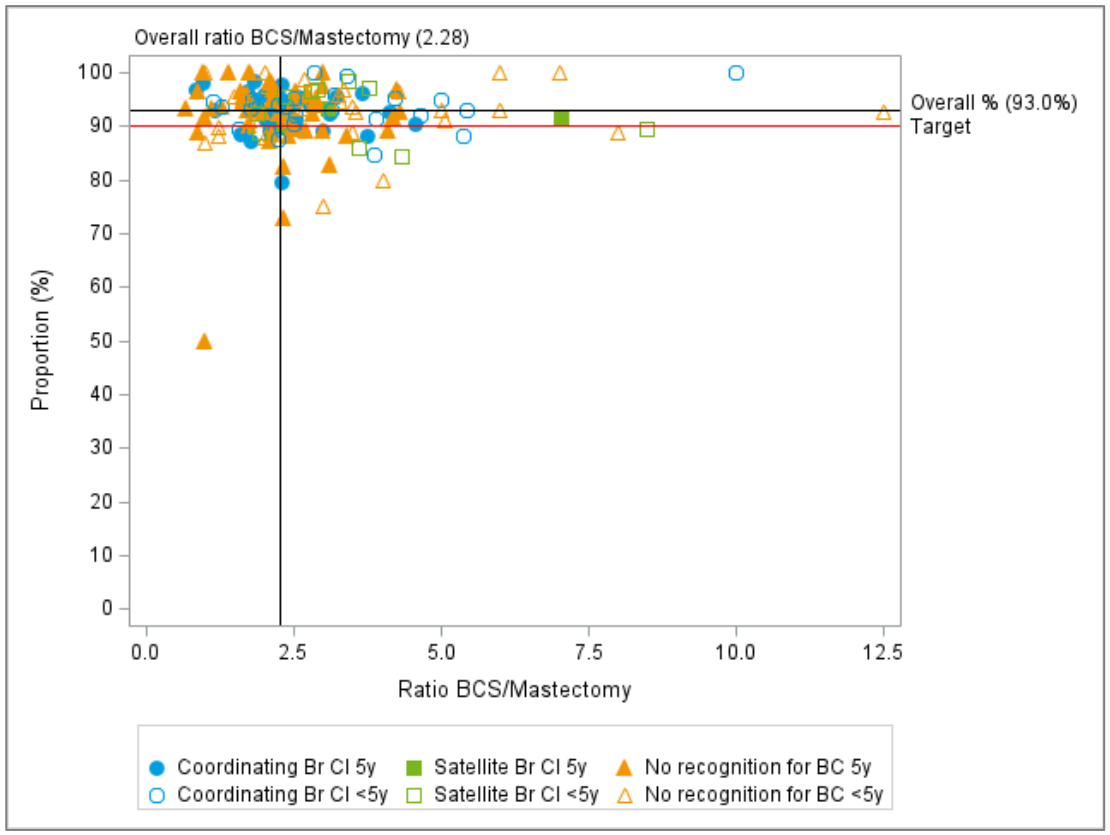

*IBC: invasive breast cancer; There were 167 units of analysis reported in the funnel plot, of which twenty units had less than ten patients in the denominator. Four units were situated below the 99% prediction interval, while 28 were situated above that interval. An open plot symbol is used when the recognition status or the number of beds changed during the five year study period; 42 patients for whom the campus could not be identified, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

**Figure 52 – Bubble plot of the proportion of women with IBC who received just one operation (excluding reconstruction), by campus volume***




*IBC: invasive breast cancer; *: the average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 42 patients who could not be assigned to a campus, and 60 patients assigned to a coordinating breast clinic in volume group < 60 patients/year, were excluded.*
*Source: BCR-IMA-HDD*

**Figure 53 – Proportion of women with IBC who received just one operation (excluding reconstruction) versus BCS/mastectomy (left) and distribution of campuses over the four quadrants**




In Q1 = upper left (overall result > 85.8 and ratio < 3.63) - N=40 units of analysis

- Coordinating: 16 (active for 5 years: 10, active less than 5 years: 6)
- Satellite: 0
- No recognition for BC: 24 (5y: 17, <5y: 7)

In Q2 = upper right (overall result > 85.8 and ratio > 3.63) - N=40 units of analysis

- Coordinating: 15 (5y: 7, <5y: 8)
- Satellite: 6 (5y: 1, <5y: 5)
- No recognition for BC: 19 (5y: 10, <5y: 9)

In Q3 = lower left (overall result < 85.8 and ratio < 3.63) - N=27 units of analysis

- Coordinating: 10 (5y: 8, <5y: 2)
- Satellite: 2 (5y: 0, <5y: 2)
- No recognition for BC: 15 (5y: 10, <5y: 5)

In Q4 = lower right (overall result < 85.8 and ratio > 3.63) - N=48 units of analysis

- Coordinating: 19 (5y: 11, <5y: 8)
- Satellite: 6 (5y: 3, <5y: 3)
- No recognition for BC: 23 (5y: 14, <5y: 9)

*IBC: invasive breast cancer; there are 155 units of analysis reported in the graph: 60 coordinating breast clinics (active for 5 years: 36, active less than 5 years: 24), 14 satellite breast clinics (active for 5 years: 4, active less than 5 years: 10), 81 campuses without recognition for BC (active for 5 years: 51, active less than 5 years: 30); this graph present twelve units (21 patients) less than the funnel plot because in these units there were either no BCS or no mastectomies performed, making the calculation of a ratio impossible. An open plot symbol is used when the recognition status or the number of beds changed during the five year study period; 42 patients for whom the campus could not be identified, are not represented in the funnel plot.*
*Source: BCR-IMA-HDD*

# APPENDIX 23. POST-OPERATIVE RADIOTHERAPY IN WOMEN WITH IBC

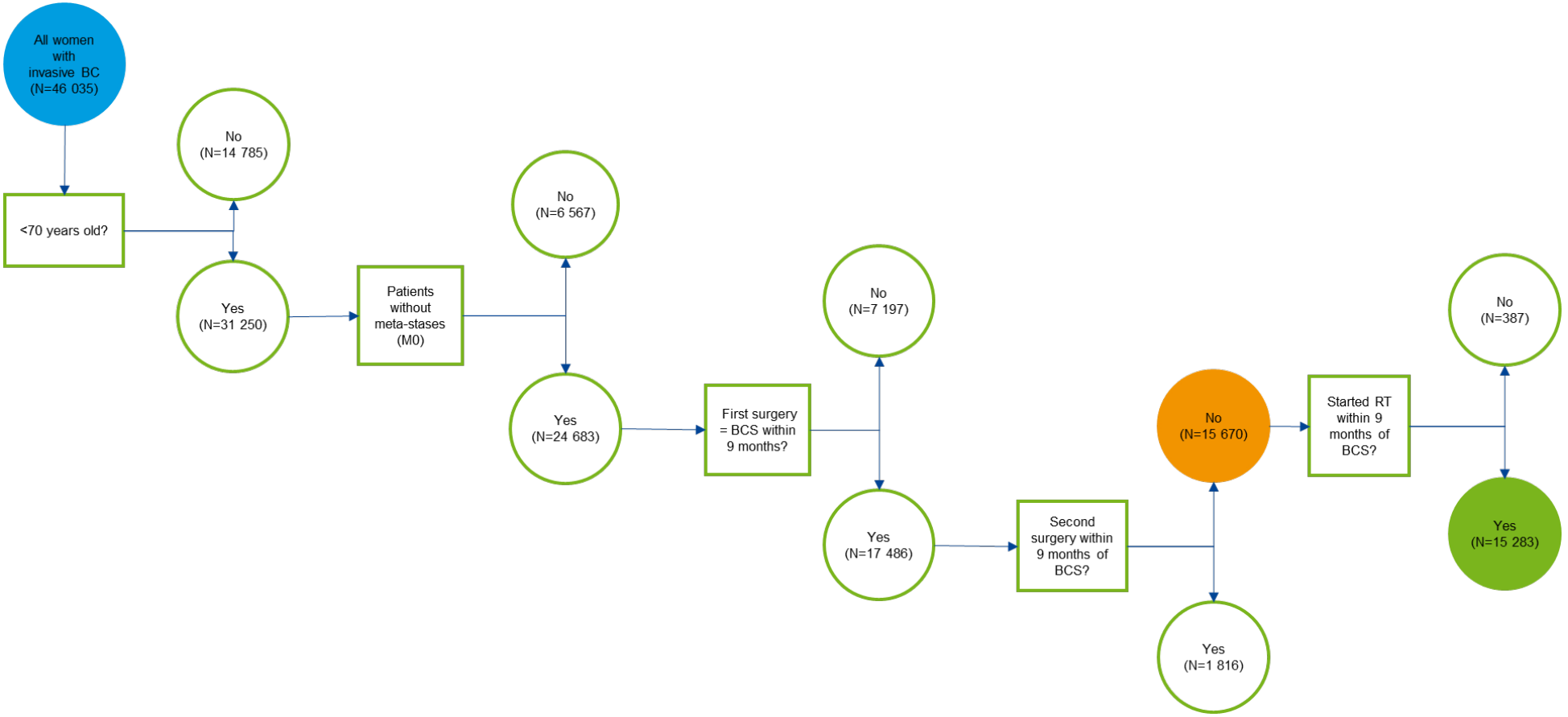
## Appendix 23.1. Documentation sheet

| Title | Proportion of women <70 years old with IBC (M0) who started radiotherapy within nine months after breast conserving surgery |
|---|---|
| **Rationale** | The Early Breast Cancer Trialists' Collaborative Group (EBCTCG) meta-analysis, which comprised information from 10 801 women included in 17 trials indicated that radiotherapy (RT) after breast conserving surgery (BCS) not only substantially reduces the risk of recurrence but also moderately reduces the risk of death from BC.[135]<br>Patients with a low-risk BC and/or a short life expectancy (based on performance status, comorbidity and age) and who take adjuvant endocrine therapy, have limited benefit from RT in terms of local control, and no benefit in terms of overall survival. The results for these patients are similar if they receive adjuvant endocrine therapy or postoperative RT, making the choice between these treatment modalities part of the shared decision making process.[46] Therefore, after discussion with the clinical experts, this quality indicator was focused on women younger than seventy years. |
| **Selection** | This QI was selected by 82% of experts who completed the online survey in spring 2020. |
| **Type of QI** | Process |
| **Calculation**[jjj] | Numerator: All women in whom RT started within 9 months after breast conserving surgery (BCS)<br>Denominator: All women <70 years old diagnosed with IBC (M0) who underwent breast conserving surgery within 9 months after incidence, without any other surgical intervention within 9 months after the breast conserving surgery |
| **Target** | 95% (EUSOMA[46]) |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>M0 = cM0 and no pM1<br>Incidence date as registered at BCR (= date of first histopathological confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Surgery, for nomenclature codes, see Table 44, Table 45, Table 46, Table 47<br>Radiotherapy, for nomenclature codes, see Table 49<br>Chemotherapy, for ATC codes, see Table 50<br>Endocrine therapy, for ATC codes, see Table 52 |
| **Risk adjustment** | None (process indicator) |

[jjj] Note: In the ECIBC documents, this indicator is phrased differently ('Proportion of surgically treated women with primary M0 invasive breast cancer, who underwent adjuvant radiotherapy, and who started undergoing radiotherapy ≤ 8 weeks after the date of surgery or the date of the last cycle of adjuvant chemotherapy.'), with a target set at 80%.[45] This may be informative for future QI projects.

| Title | Proportion of women <70 years old with IBC (M0) who started radiotherapy within nine months after breast conserving surgery |
|---|---|
| **Limitations** | - Based on the RIZIV – INAMI licensing codes mentioned in the IMA – AIM data, the distinction between a main and an associated radiotherapy unit cannot be made.<br>- The start date of radiotherapy is not always available in the IMA – AIM database; for these cases the start date of radiotherapy was estimated based on the simulation date. If also the simulation date was not available, the start date was estimated based on the end date and duration of the series of similar patients for whom the start date was available in the IMA-database.<br>- Another limitation is that it was impossible to distinguish patients who completed the whole RT scheme from patients who stopped their treatment before it was completed; when an RT scheme is stopped, the fee for the whole scheme is billed, even when not all fractions were given. |
| **Subgroup analyses** | - Age at diagnosis<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Year of incidence<br>- Pathological and combined stage<br>- With/without adjuvant endocrine therapy |
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs. 2014 - 2018<br>- Radiotherapy started within 3 and 6 months after BCS (in patients who had adjuvant chemotherapy vs. those who did not have adjuvant chemotherapy)<br>- Patients ≥ 70 years with/without adjuvant endocrine therapy<br>- Type of radiotherapy |
| **Benchmarking** | Main treatment centre |
| **Level of benchmarking** | Hospital level |
| **Comments** | |

## Appendix 23.2. Flowchart



## Appendix 23.3. Results

**Table 161 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by patient, tumour and treatment characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 15 670 | 15 283 | 97.5 |
| **Age at diagnosis** | | | |
| <40 years | 845 | 813 | 96.2 |
| 40-49 years | 3 156 | 3 079 | 97.6 |
| 50-59 years | 5 614 | 5 486 | 97.7 |
| 60-69 years | 6 055 | 5 905 | 97.5 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 10 625 | 10 378 | 97.7 |
| 1 – Symptomatic but completely ambulatory | 4 272 | 4 152 | 97.2 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 31 | 29 | 93.5 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 10 | 7 | 70.0 |
| 4 – Completely disabled; totally confined to bed or chair | 6 | 6 | 100.0 |
| Missing | 726 | 711 | 97.9 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 12 448 | 12 142 | 97.5 |
| 1-5 days | 2 585 | 2 534 | 98.0 |
| 6-15 days | 465 | 447 | 96.1 |
| >15 days | 172 | 160 | 93.0 |
| **Number of comorbidities** | | | |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| 0 | 10 364 | 10 095 | 97.4 |
| 1 | 4 197 | 4 108 | 97.9 |
| 2 | 1 038 | 1 010 | 97.3 |
| 3 | 71 | 70 | 98.6 |
| **Cardiovascular disease** | | | |
| Absent | 11 135 | 10 841 | 97.4 |
| Present | 4 535 | 4 442 | 97.9 |
| **Respiratory disease** | | | |
| Absent | 14 776 | 14 420 | 97.6 |
| Present | 894 | 863 | 96.5 |
| **Diabetes** | | | |
| Absent | 14 613 | 14 250 | 97.5 |
| Present | 1 057 | 1 033 | 97.7 |
| **Incidence year** | | | |
| 2014 | 2 858 | 2 792 | 97.7 |
| 2015 | 2 992 | 2 926 | 97.8 |
| 2016 | 3 114 | 3 050 | 97.9 |
| 2017 | 3 362 | 3 297 | 98.1 |
| 2018 | 3 344 | 3 218 | 96.2 |
| **(y)Pathological stage** | | | |
| y0 | 544 | 535 | 98.3 |
| yis | 152 | 147 | 96.7 |
| (y)I | 9 771 | 9 571 | 98.0 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| (y)II | 4 157 | 4 028 | 96.9 |
| (y)III | 632 | 604 | 95.6 |
| Unknown | 414 | 398 | 96.1 |
| **Combined stage** | | | |
| (y)0 | 549 | 539 | 98.2 |
| yis | 152 | 147 | 96.7 |
| (y)I | 9 883 | 9 678 | 97.9 |
| (y)II | 4 408 | 4 274 | 97.0 |
| (y)III | 667 | 638 | 95.7 |
| Unknown | 11 | 7 | 63.6 |
| **Endocrine therapy within 9 months after surgery** | | | |
| No | 2 745 | 2 563 | 93.4 |
| Yes | 12 925 | 12 720 | 98.4 |
| **Endocrine therapy within 12 months after surgery** | | | |
| No | 2 487 | 2 324 | 93.4 |
| Yes | 13 183 | 12 959 | 98.3 |

*IBC: invasive breast cancer; WHO: World Health Organization; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis.*
*Source: BCR-IMA*

**Table 162 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by time period**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 15 670 | 15 283 | 97.5 |
| **Comparison period (2009 - 2013)** | 13 297 | 13 025 | 98.0 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

**Table 163 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine, six, and three months after breast conserving surgery**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Radiotherapy within 9 months of first surgery (main quality indicator)** | 15 670 | 15 283 | 97.5 |
| **Radiotherapy within 6 months of first surgery** (confined to patients who did not have adjuvant chemotherapy within 9 months after surgery) | 10 867 | 10 638 | 97.9 |
| **Radiotherapy within 3 months of first surgery** (confined to patients who did not have adjuvant chemotherapy within 9 months after surgery) | 10 867 | 10 573 | 97.3 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

**Table 164 – Sensitivity analysis: Proportion of women <70 years old with IBC (M0) who started radiation therapy within nine months after breast conserving surgery, by type of radiotherapy**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| IORT only | 15 283 | 362 | 2.4 |
| IORT + adjuvant series | 15 283 | 384 | 2.5 |
| Adjuvant series only | 15 283 | 14 537 | 95.1 |

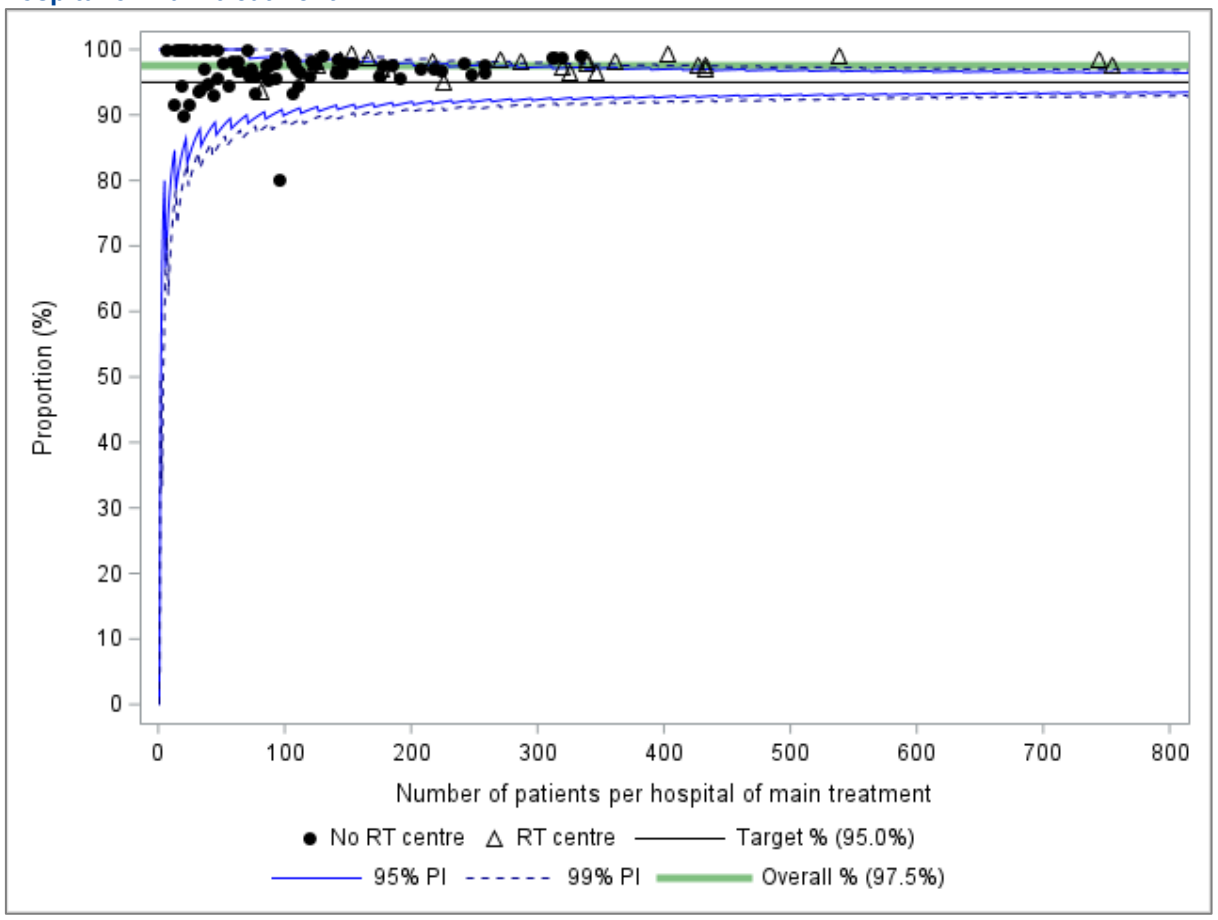
*IBC: invasive breast cancer;* IORT: intraoperative radiotherapy
*Source: BCR-IMA*

**Table 165 – Sensitivity analysis: Proportion of women ≥70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, treated with or without adjuvant endocrine therapy**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Radiotherapy in women ≥70 years, overall** | 5 040 | 4 605 | 91.4 |
| Adjuvant endocrine therapy within 9 months after BCS | | | |
| No | 710 | 575 | 81.0 |
| Yes | 4 330 | 4 030 | 93.1 |
| Adjuvant endocrine therapy within 12 months after BCS | | | |
| No | 682 | 551 | 80.8 |
| Yes | 4 358 | 4 054 | 93.0 |

*IBC: invasive breast cancer*
*Source: BCR-IMA*

**Figure 54 – Proportion of women <70 years old with IBC (M0) who started radiation therapy within 9 months after breast conserving surgery, by hospital of main treatment**




*IBC: invasive breast cancer; there were 98 hospitals reported in the funnel plot, one of them having less than ten patients in the denominator; 1 out of 100 hospitals was situated below the 99% prediction interval, while sixteen were situated above the 99% prediction interval; 25 hospitals are recognised as RT centre.*
*Source: BCR-IMA*

# APPENDIX 24. ADJUVANT CHEMOTHERAPY AND/OR ENDOCRINE THERAPY IN PATIENTS <70 YEARS WITH M0 IBC

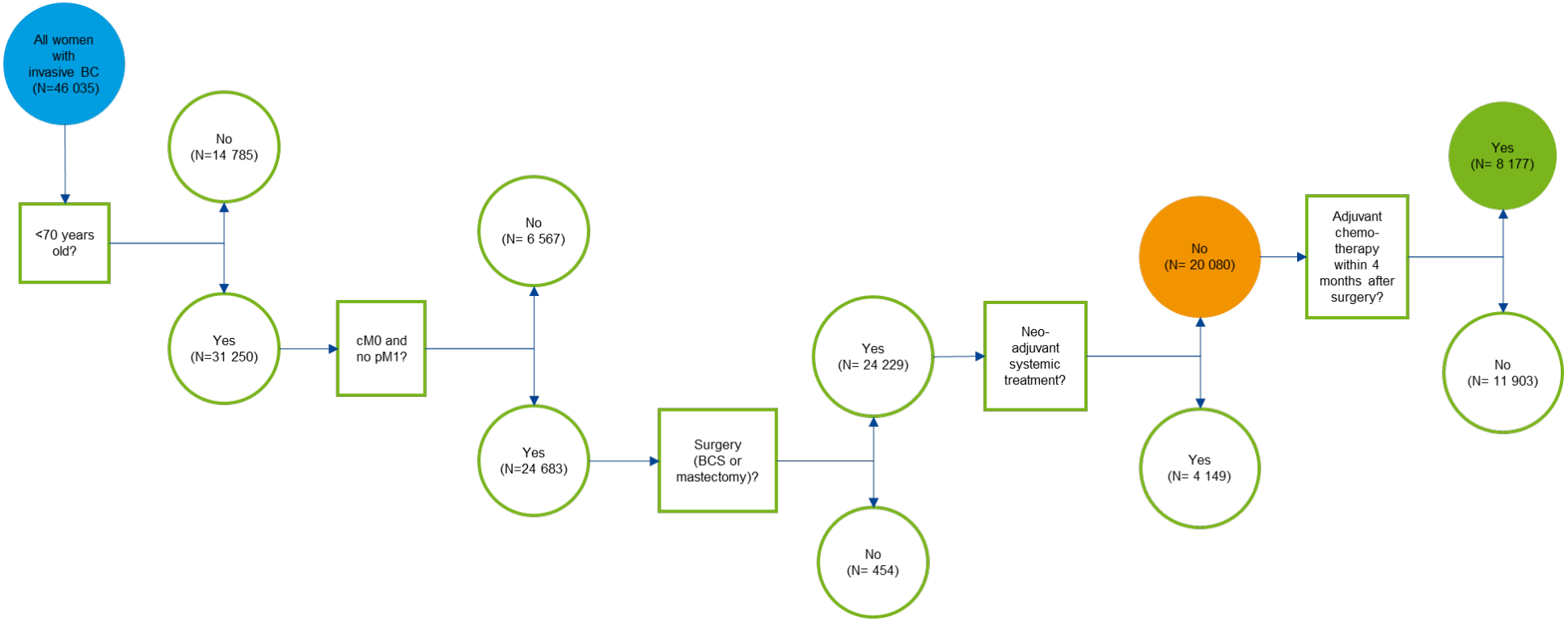
## Appendix 24.1. Documentation sheet

| Title | Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy and/or endocrine therapy |
|---|---|
| **Rationale** | The choice of adjuvant systemic treatment for IBC should be driven by the hormonal sensitivity, risk profile of the tumour, age, menopausal status and comorbidities of the patient.[85] As the concordance of the test results for hormonal status (oestrogen and progestogen) and HER 2 receptor status (in the BCR database) with the data available in the medical files (based on which medical treatment is based) was below par according to the clinical experts, several quality indicators on systemic treatment could not be calculated. Therefore, this indicator was elaborated as a descriptive indicator, illustrating the type of systemic treatment that is delivered to women with M0 IBC. In other words, no target was set and the variability between the hospitals is illustrated in a scatter plot. |
| **Type of QI** | Process |
| **Calculation** | Numerator for indicator A: All women who received adjuvant chemotherapy (from the day of surgery until 4 months after surgery), regardless of any endocrine or targeted therapy<br>Numerator for indicator B: All women who received adjuvant endocrine therapy (from the day of surgery until 9 months after surgery), regardless of any chemotherapy or targeted therapy<br>Denominator: All women <70 years old diagnosed with M0 IBC who had surgery (BCS or mastectomy) within 1 month before to 9 months after incidence but no neoadjuvant systemic treatment (regardless of RT) |
| **Target** | None – descriptive indicator |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Surgery, for nomenclature codes, see Table 44, Table 45, Table 46, Table 47<br>Radiotherapy, for nomenclature codes, see Table 49<br>Chemotherapy, for ATC codes, see Table 50 |

| Title | Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy and/or endocrine therapy |
|---|---|
| | Endocrine therapy, for ATC codes, see Table 52<br>Non-metastatic patients: M0 = cM0 and no pM1 (unknown clinical distant metastasis status i.e. cMx excluded; pMx is included) |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | - Trial drugs are not routinely registered and included in the administrative database. Therefore an underestimation of this indicator is possible. |
| **Subgroup analyses** | - Age at diagnosis<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Year of incidence<br>- Clinical, pathological, combined stage<br>- Treatment scheme |
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs. 2014 - 2018<br>- Excluding vs. including cases with missing clinical distant metastasis status (cMx)<br>- By type of adjuvant systemic therapy |
| **Benchmarking** | Centre of main treatment |
| **Level of benchmarking** | Campus level |
| **Comments** | |

# Appendix 24.2. Indicator A - Adjuvant chemotherapy in M0 IBC

## *Appendix 24.2.1. Flowchart*



## *Appendix 24.2.2. Results*

**Table 166 – Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by patient, tumour and treatment characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 20 080 | 8 177 | 40.7 |
| **Age at diagnosis** | | | |
| <40 years | 1 023 | 783 | 76.5 |
| 40-49 years | 4 244 | 2 139 | 50.4 |
| 50-59 years | 7 066 | 2 756 | 39.0 |
| 60-69 years | 7 747 | 2 499 | 32.3 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 13 278 | 5 036 | 37.9 |
| 1 – Symptomatic but completely ambulatory | 5 674 | 2 734 | 48.2 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 50 | 20 | 40.0 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 10 | 4 | 40.0 |
| 4 – Completely disabled; totally confined to bed or chair | 12 | 2 | 16.7 |
| Missing | 1 056 | 381 | 36.1 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 15 948 | 6 597 | 41.4 |
| 1-5 days | 3 327 | 1 297 | 39.0 |
| 6-15 days | 577 | 199 | 34.5 |
| >15 days | 228 | 84 | 36.8 |
| **Number of comorbidities** | | | |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| 0 | 13 309 | 5 675 | 42.6 |
| 1 | 5 366 | 1 976 | 36.8 |
| 2 | 1 309 | 487 | 37.2 |
| 3 | 96 | 39 | 40.6 |
| **Cardiovascular disease** | | | |
| Absent | 14 311 | 6 079 | 42.5 |
| Present | 5 769 | 2 098 | 36.4 |
| **Respiratory disease** | | | |
| Absent | 18 901 | 7 724 | 40.9 |
| Present | 1 179 | 453 | 38.4 |
| **Diabetes** | | | |
| Absent | 18 756 | 7 661 | 40.8 |
| Present | 1 324 | 516 | 39.0 |
| **Incidence year** | | | |
| 2014 | 3 838 | 1 680 | 43.8 |
| 2015 | 3 923 | 1 717 | 43.8 |
| 2016 | 3 953 | 1 642 | 41.5 |
| 2017 | 4 231 | 1 622 | 38.3 |
| 2018 | 4 135 | 1 516 | 36.7 |
| **Clinical stage** | | | |
| 0[$] | 357 | 90 | 25.2 |
| I | 12 053 | 3 362 | 27.9 |
| II | 6 433 | 4 084 | 63.5 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| III | 355 | 302 | 85.1 |
| Unknown | 882 | 339 | 38.4 |
| **(y)Pathological stage** | | | |
| y0 | 0 | 0 | 0.0 |
| yis | 0 | 0 | 0.0 |
| (y)I | 11 467 | 2 481 | 21.6 |
| (y)II | 6 754 | 4 095 | 60.6 |
| (y)III | 1 671 | 1 547 | 92.6 |
| Unknown | 188 | 54 | 28.7 |
| **Combined stage** | | | |
| (y)0 | 6 | 0 | 0.0 |
| yis | 0 | 0 | 0.0 |
| (y)I | 11 555 | 2 500 | 21.6 |
| (y)II | 6 825 | 4 125 | 60.4 |
| (y)III | 1 680 | 1 552 | 92.4 |
| Unknown | 14 | 0 | 0.0 |
| **Treatment scheme** | | | |
| Surgery < adjuvant systemic Tx | 2 408 | 935 | 38.8 |
| Surgery < adjuvant RT + systemic Tx | 17 133 | 7 242 | 42.3 |

*IBC: invasive breast cancer; WHO: World Health Organization; BCS: breast conserving surgery; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis; $: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; Tx: treatment.*
*Source: BCR-IMA*

### Table 167 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 20 080 | 8 177 | 40.7 |
| **Comparison period (2009 - 2013)** | 19 157 | 8 945 | 46.7 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 168 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by in-/exclusion of cMx

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **2014 - 2018: cM0, pMx (main quality indicator)** | 20 080 | 8 177 | 40.7 |
| **2014 - 2018: cM0/x, pMx** | 24 084 | 9 489 | 39.4 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 169 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by type of adjuvant systemic therapy

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Chemotherapy (regardless other systemic therapies) (main QI)** | 20 080 | 8 177 | 40.7 |
| **Chemotherapy only** | 20 080 | 7 830 | 39.0 |
| **Chemotherapy and endocrine therapy** | 20 080 | 347 | 1.7 |
| **Chemotherapy and targeted therapy** | 20 080 | 0 | 0.0 |
| **Chemotherapy, endocrine therapy and targeted therapy** | 20 080 | 0 | 0.0 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

**Table 170 – Proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value |
|---|---|---|---|---|---|
| **Overall** | 20 028 | 8 162 | 40.8 | [40.1, 41.4] | |
| **Recognition status for BC** | | | | | 0.208 |
| Coordinating breast clinic | 14 407 | 5 854 | 40.6 | [39.8, 41.4] | |
| Satellite breast clinic | 1 075 | 417 | 38.8 | [35.9, 41.8] | |
| No recognition for BC | 4 546 | 1 891 | 41.6 | [40.2, 43.0] | |
| **Average annual campus volume*** | | | | | 0.451 |
| ≥125 | 12 232 | 5 015 | 41.0 | [40.1, 41.9] | |
| [60, 125[ | 4 986 | 1 994 | 40.0 | [38.6, 41.4] | |
| <60 | 2 810 | 1 153 | 41.0 | [39.2, 42.9] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.115 |
| ≥125 | 11 592 | 4 747 | 41.0 | [40.1, 41.9] | |
| [60, 125[ | 2 815 | 1 107 | 39.3 | [37.5, 41.2] | |
| ***Satellite breast clinics*** | | | | | 0.168 |
| [60, 125[ | 927 | 352 | 38.0 | [34.8, 41.2] | |
| <60 | 148 | 65 | 43.9 | [35.8, 52.3] | |
| ***No recognition for BC*** | | | | | 0.446 |
| ≥125 | 640 | 268 | 41.9 | [38.0, 45.8] | |
| [60, 125[ | 1 244 | 535 | 43.0 | [40.2, 45.8] | |
| <60 | 2 662 | 1 088 | 40.9 | [39.0, 42.8] | |

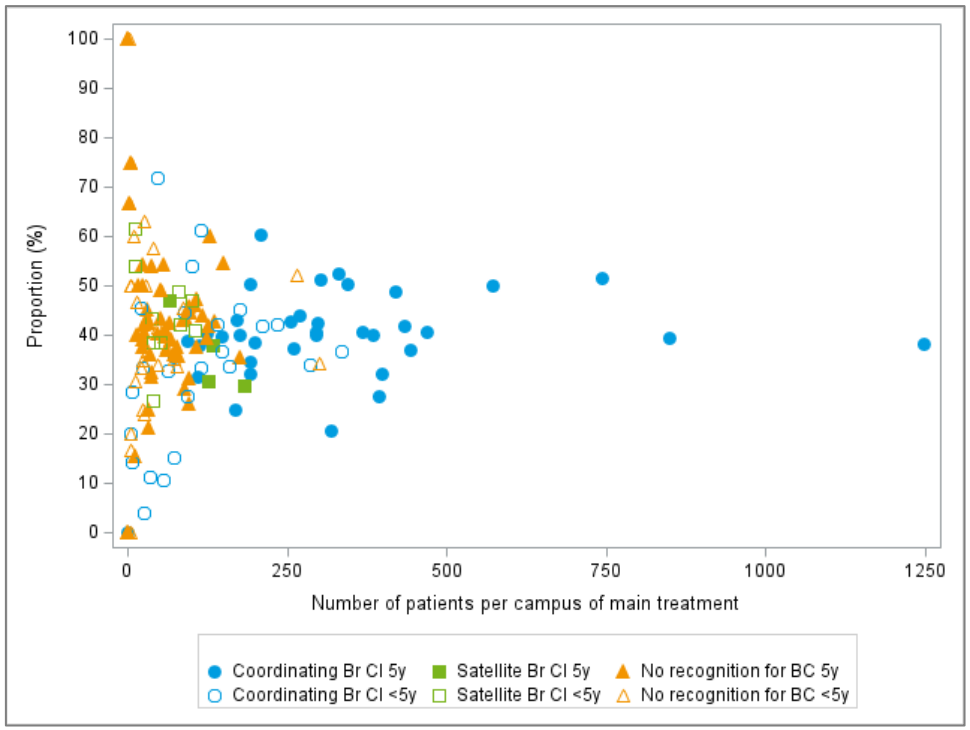
*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded.*
*Source: BCR-IMA-HDD*

**Table 171 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant chemotherapy within 4 months after surgery in women <70 years old with M0 IBC, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III[$] | Adjusted** OR | 95% CI | P-value, type III[$] |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.476 | | | 0.099 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 1.05 | [0.82, 1.34] | | 1.09 | [0.75, 1.59] | |
| No recognition for BC | 1.09 | [0.95, 1.26] | | 1.27 | [1.02, 1.58] | |
| **Average annual campus volume*** | | | 0.727 | | | 0.506 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 1.01 | [0.86, 1.19] | | 1.13 | [0.87, 1.46] | |
| <60 | 1.07 | [0.90, 1.26] | | 1.15 | [0.89, 1.49] | |
| **Volume groups per recognition status** | | | | | | |
| ***Coordinating breast clinics*** | | | 0.792 | | | 0.732 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.97 | [0.75, 1.25] | | 1.07 | [0.74, 1.54] | |
| ***Satellite breast clinics*** | | | 0.275 | | | |
| [60, 125[ | 1 | [reference] | | 1 | [reference] | 0.748 |
| <60 | 1.30 | [0.81, 2.07] | | 0.87 | [0.38, 1.99] | |
| ***No recognition for BC*** | | | 0.707 | | | 0.435 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 1.07 | [0.74, 1.56] | | 0.81 | [0.42, 1.53] | |
| <60 | 0.98 | [0.70, 1.39] | | 0.71 | [0.39, 1.29] | |

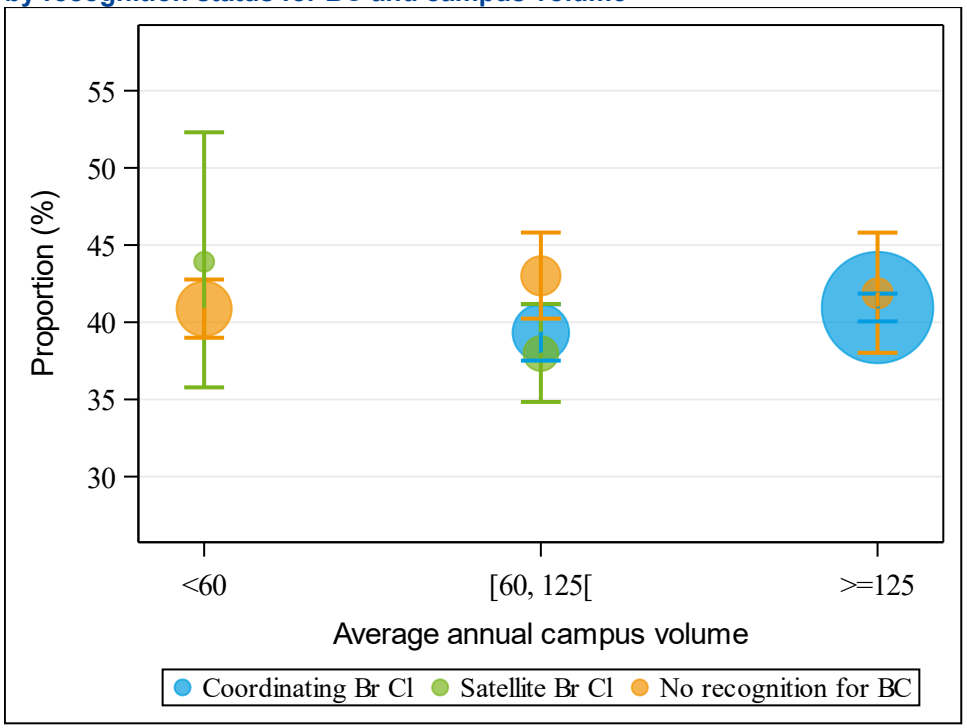
*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; **: adjusted for age at diagnosis, combined stage, tumour differentiation grade, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiac and respiratory diseases, and diabetes); $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into hospital campuses (i.e. centre of surgery) was taken into account; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded; 14 observations with combined stage X had to be deleted from the multivariable model.*
*Source: BCR-IMA-HDD*

**Figure 55 – Scatter plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by campus of main treatment**




*IBC: invasive breast cancer; there were 162 units of analysis presented in the scatter plot, of which 23 units had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 22 patients for whom the campus could not be identified, are not represented in the scatter plot.*
*Source: BCR-IMA-HDD*

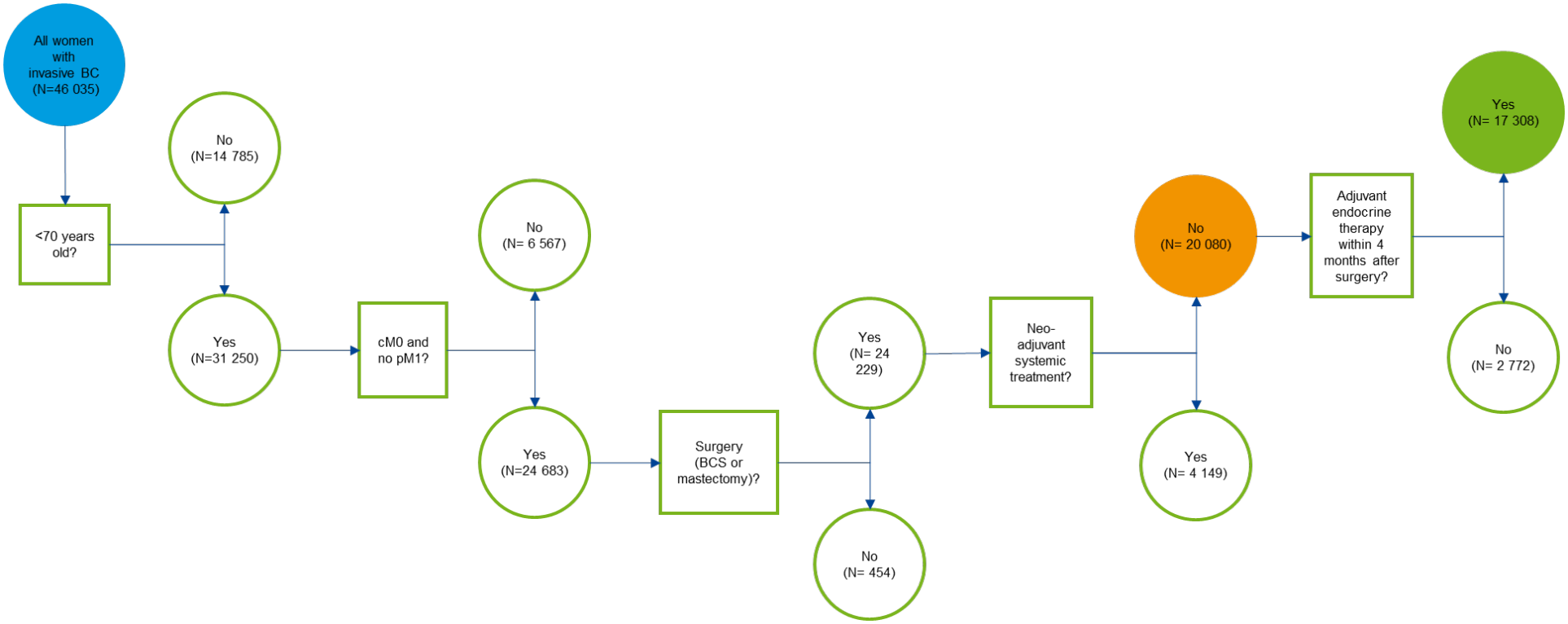
**Figure 56 – Bubble plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume***




*IBC: invasive breast cancer; *: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded.*
*Source: BCR-IMA-HDD*

# Appendix 24.3. Indicator B - Adjuvant endocrine therapy in M0 IBC

## *Appendix 24.3.1. Flowchart*



## *Appendix 24.3.2. Results*

**Table 172 – Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by patient, tumour and treatment characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 20 080 | 17 308 | 86.2 |
| **Age at diagnosis** | | | |
| <40 years | 1 023 | 746 | 72.9 |
| 40-49 years | 4 244 | 3 574 | 84.2 |
| 50-59 years | 7 066 | 6 147 | 87.0 |
| 60-69 years | 7 747 | 6 841 | 88.3 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 13 278 | 11 508 | 86.7 |
| 1 – Symptomatic but completely ambulatory | 5 674 | 4 833 | 85.2 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 50 | 40 | 80.0 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 10 | 8 | 80.0 |
| 4 – Completely disabled; totally confined to bed or chair | 12 | 9 | 75.0 |
| Missing | 1 056 | 910 | 86.2 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 15 948 | 13 759 | 86.3 |
| 1-5 days | 3 327 | 2 858 | 85.9 |
| 6-15 days | 577 | 499 | 86.5 |
| >15 days | 228 | 192 | 84.2 |
| **Number of comorbidities** | | | |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| 0 | 13 309 | 11 367 | 85.4 |
| 1 | 5 366 | 4 713 | 87.8 |
| 2 | 1 309 | 1 143 | 87.3 |
| 3 | 96 | 85 | 88.5 |
| **Cardiovascular disease** | | | |
| Absent | 14 311 | 12 226 | 85.4 |
| Present | 5 769 | 5 082 | 88.1 |
| **Respiratory disease** | | | |
| Absent | 18 901 | 16 275 | 86.1 |
| Present | 1 179 | 1 033 | 87.6 |
| **Diabetes** | | | |
| Absent | 18 756 | 16 169 | 86.2 |
| Present | 1 324 | 1 139 | 86.0 |
| **Incidence year** | | | |
| 2014 | 3 838 | 3 299 | 86.0 |
| 2015 | 3 923 | 3 331 | 84.9 |
| 2016 | 3 953 | 3 430 | 86.8 |
| 2017 | 4 231 | 3 682 | 87.0 |
| 2018 | 4 135 | 3 566 | 86.2 |
| **Clinical stage** | | | |
| 0[$] | 357 | 263 | 73.7 |
| I | 12 053 | 10 740 | 89.1 |
| II | 6 433 | 5 282 | 82.1 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| III | 355 | 283 | 79.7 |
| Unknown | 882 | 740 | 83.9 |
| **(y)Pathological stage** | | | |
| y0 | 0 | 0 | 0.0 |
| yis | 0 | 0 | 0.0 |
| (y)I | 11 467 | 10 181 | 88.8 |
| (y)II | 6 754 | 5 618 | 83.2 |
| (y)III | 1 671 | 1 369 | 81.9 |
| Unknown | 188 | 140 | 74.5 |
| **Combined stage** | | | |
| (y)0 | 6 | 2 | 33.3 |
| yis | 0 | 0 | 0.0 |
| (y)I | 11 555 | 10 253 | 88.7 |
| (y)II | 6 825 | 5 667 | 83.0 |
| (y)III | 1 680 | 1 375 | 81.8 |
| Unknown | 14 | 11 | 78.6 |
| **Treatment modality** | | | |
| Surgery < adjuvant systemic Tx | 2 408 | 2 017 | 83.8 |
| Surgery < adjuvant RT + systemic Tx | 17 133 | 15 291 | 89.2 |

*WHO: World Health Organization; BCS: breast conserving surgery; combined stage: combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis; $: in correspondence with TNM 7th & 8th edition, cTis cN0 cM0 tumours are categorized as cStage 0. For IBC, these tumours were clinically assessed as in situ but appeared to be invasive after resection; Tx: treatment; <: followed by.*
*Source: BCR-IMA*

**Table 173 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine within 9 months after surgery, by time period**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 20 080 | 17 308 | 86.2 |
| **Comparison period (2009 - 2013)** | 19 157 | 15 763 | 82.3 |

*Source: BCR-IMA*

**Table 174 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by in-/exclusion of cMx**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **2014 - 2018: cM0, pMx (main quality indicator)** | 20 080 | 17 308 | 86.2 |
| **2014 - 2018: cM0/x, pMx** | 24 084 | 20 734 | 86.1 |

*Source: BCR-IMA*

**Table 175 – Sensitivity analysis: Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by type of adjuvant systemic therapy**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Endocrine therapy (regardless other systemic therapies) (main QI)** | 20 080 | 17 308 | 86.2 |
| **Endocrine therapy only** | 20 080 | 11 324 | 56.4 |
| **Endocrine therapy + chemotherapy (no targeted)** | 20 080 | 4 456 | 22.2 |
| **Endocrine therapy + targeted therapy (no chemotherapy)** | 20 080 | 11 | 0.1 |
| **Endocrine therapy + chemotherapy + targeted therapy** | 20 080 | 1 517 | 7.6 |

*Source: BCR-IMA*

**Table 176 – Proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by recognition status for BC and campus volume**

| Characteristic | N | n | n/N (%) | 95% CI | P-value[$] |
|---|---|---|---|---|---|
| **Overall** | 20 028 | 17 264 | 86.2 | [85.7, 86.7] | |
| **Recognition status for BC** | | | | | 0.044 |
| Coordinating breast clinic | 14 407 | 12 462 | 86.5 | [85.9, 87.1] | |
| Satellite breast clinic | 1 075 | 934 | 86.9 | [84.7, 88.8] | |
| No recognition for BC | 4 546 | 3 868 | 85.1 | [84.0, 86.1] | |
| **Average annual campus volume*** | | | | | 0.058 |
| ≥125 | 12 232 | 10 578 | 86.5 | [85.9, 87.1] | |
| [60, 125[ | 4 986 | 4 304 | 86.3 | [85.3, 87.3] | |
| <60 | 2 810 | 2 382 | 84.8 | [83.4, 86.1] | |
| **Volume groups per recognition status** | | | | | |
| ***Coordinating breast clinics*** | | | | | 0.904 |
| ≥125 | 11 592 | 10 029 | 86.5 | [85.9, 87.1] | |
| [60, 125[ | 2 815 | 2 433 | 86.4 | [85.1, 87.7] | |
| ***Satellite breast clinics*** | | | | | 0.229 |
| [60, 125[ | 927 | 810 | 87.4 | [85.1, 89.4] | |
| <60 | 148 | 124 | 83.8 | [76.8, 89.3] | |
| ***No recognition for BC*** | | | | | 0.807 |
| ≥125 | 640 | 549 | 85.8 | [82.8, 88.4] | |
| [60, 125[ | 1 244 | 1 061 | 85.3 | [83.2, 87.2] | |
| <60 | 2 662 | 2 258 | 84.8 | [83.4, 86.2] | |

**: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; $: p-value from Pearson chi² test; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded.*
*Source: BCR-IMA-HDD*

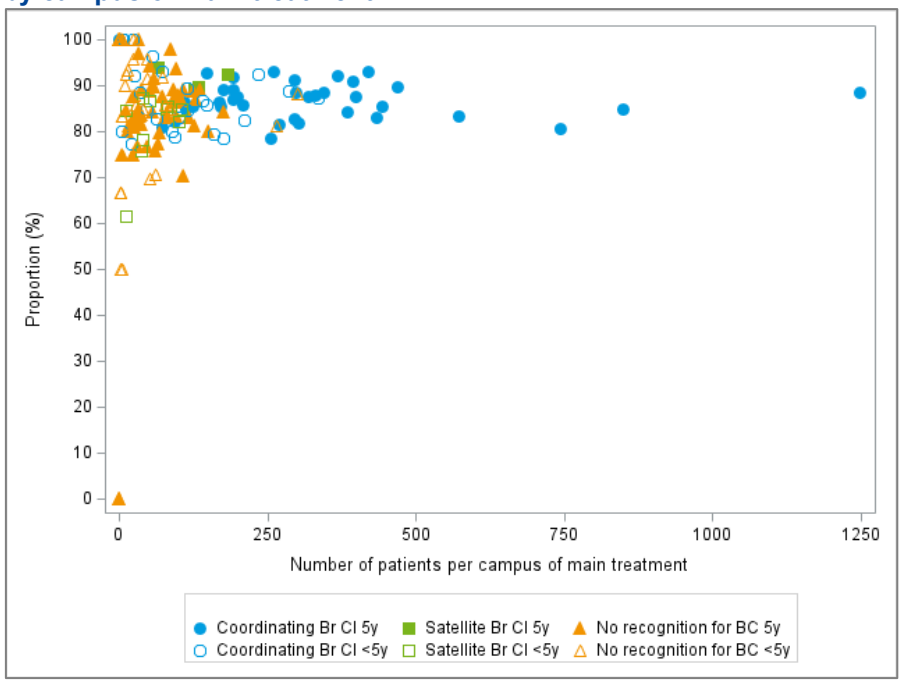
**Table 177 – Association between recognition status for BC and campus volume, and the odds of receiving adjuvant endocrine therapy within 9 months after surgery in women <70 years old with M0 IBC, including volume analyses by recognition status**

| Characteristic | Unadjusted OR | 95% CI | P-value, type III$ | Adjusted** OR | 95% CI | P-value, type III$ |
|---|---|---|---|---|---|---|
| **Recognition status for BC** | | | 0.278 | | | 0.183 |
| Coordinating breast clinic | 1 | [reference] | | 1 | [reference] | |
| Satellite breast clinic | 0.95 | [0.72, 1.24] | | 0.97 | [0.70, 1.36] | |
| No recognition for BC | 0.88 | [0.76, 1.03] | | 0.84 | [0.69, 1.02] | |
| **Average annual campus volume*** | | | 0.174 | | | 0.227 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.96 | [0.81, 1.14] | | 0.93 | [0.74, 1.16] | |
| <60 | 0.84 | [0.71, 1.01] | | 0.82 | [0.65, 1.03] | |
| **Volume groups per recognition status** | | | | | | |
| ***Coordinating breast clinics*** | | | 0.790 | | | 0.437 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.97 | [0.79, 1.20] | | 0.90 | [0.68, 1.18] | |
| ***Satellite breast clinics*** | | | 0.344 | | | 0.723 |
| [60, 125[ | 1 | [reference] | | 1 | [reference] | |
| <60 | 0.74 | [0.39, 1.39] | | 0.88 | [0.43, 1.79] | |
| ***No recognition for BC*** | | | 0.780 | | | 0.632 |
| ≥125 | 1 | [reference] | | 1 | [reference] | |
| [60, 125[ | 0.92 | [0.53, 1.59] | | 1.22 | [0.59, 2.52] | |
| <60 | 0.86 | [0.52, 1.42] | | 1.01 | [0.51, 2.00] | |

**: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; **: adjusted for age at diagnosis, combined stage, tumour differentiation grade, WHO performance status, the number of inpatient bed days the year preceding the incidence year and comorbidities (cardiac and respiratory diseases, and diabetes); $: p-value for the composite null hypothesis that there are no differences in the average QI result over the volume/recognition groups; clustering of patients into hospital campuses (i.e. centre of surgery) was taken into account; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded; 14 observations with combined stage X had to be deleted for the multivariable model.*

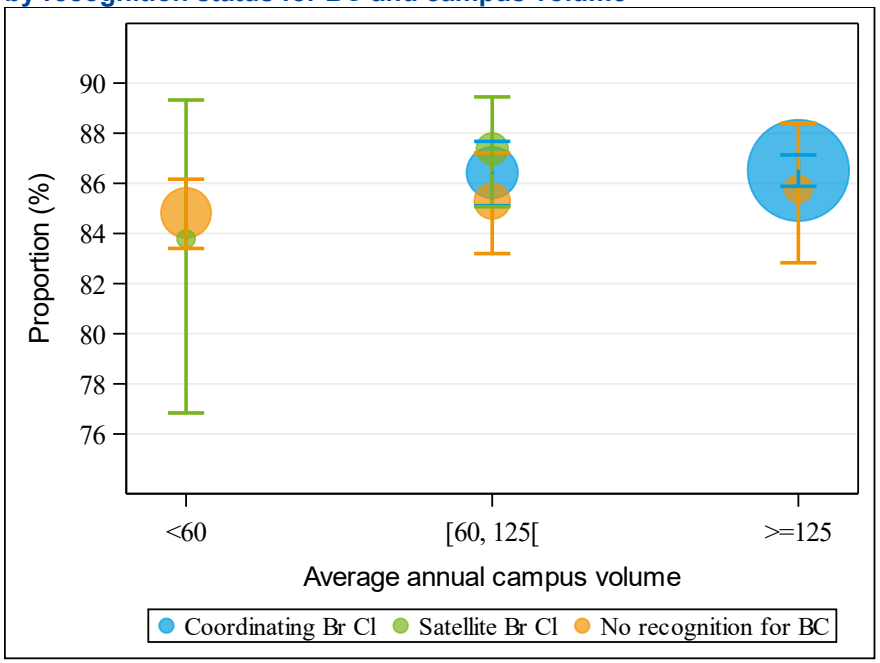
*Source: BCR-IMA-HDD*

**Figure 57 – Scatter plot of the proportion of women <70 years old with M0 IBC who received adjuvant endocrine therapy within 9 months after surgery, by campus of main treatment**




*Note: There were 162 units of analysis presented in the scatter plot, of which 23 units had less than 10 patients in the denominator. An open plot symbol is used when the recognition status or the number of beds changed during the 5 year study period; 22 patients for whom the campus could not be identified, are not represented in the scatter plot.*
*Source: BCR-IMA-HDD*

**Figure 58 – Bubble plot of the proportion of women <70 years old with M0 IBC who received adjuvant chemotherapy within 4 months after surgery, by recognition status for BC and campus volume***




**: The average annual campus volume refers to the main treatment volume of a hospital campus, also taking into account patients with multiple tumours, sarcoma, Paget's disease, etc. and male patients; 22 patients who could not be assigned to a campus and 30 patients assigned to a coordinating breast clinic in volume group <60/year were excluded.*
*Source: BCR-IMA-HDD*

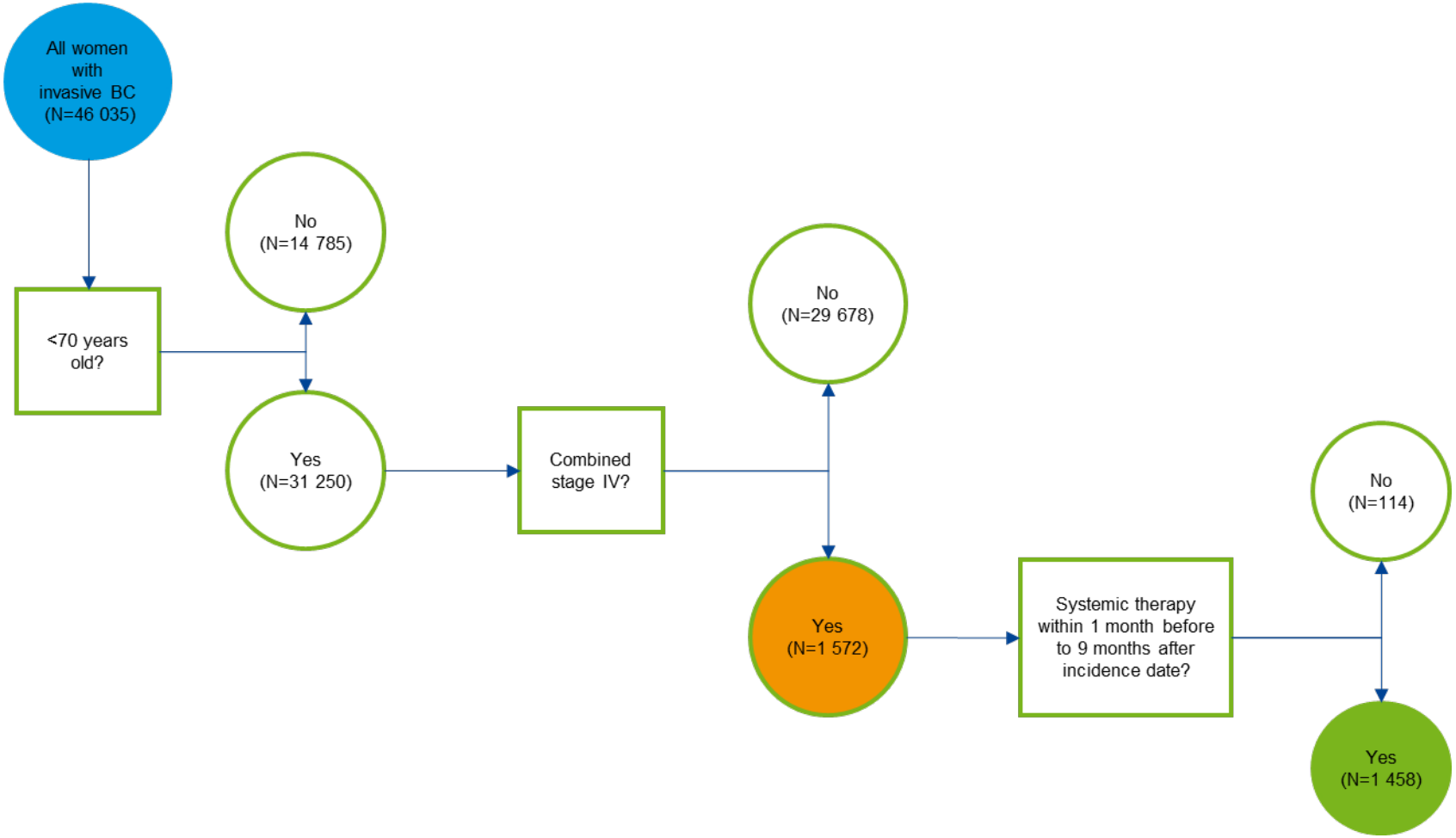
# APPENDIX 25. ADJUVANT SYSTEMIC THERAPY IN PATIENTS <70 YEARS WITH M1 IBC

## Appendix 25.1. Documentation sheet

| Title | Proportion of women <70 years old with metastatic BC who received systemic therapy |
|---|---|
| **Type of QI** | Process |
| **Calculation** | Numerator: All women who received systemic therapy within 1 month before to 9 months after incidence date<br>Denominator: All women <70 years diagnosed with combined stage IV BC (regardless of any treatment) |
| **Target** | None – descriptive indicator |
| **Data sources** | • Belgian Cancer Registry (BCR): incidence years 2014 – 2018<br>• IMA – AIM data: 2013 – 2020 (Q2) |
| **Technical definitions** | Women diagnosed with IBC (ICD-10: C50; for ICD-O-3 morphology codes see Table 26)<br>Incidence date as registered at BCR (= date of first microscopic (cytological/histological) confirmation of malignancy, if not available, the incidence date is determined in decreasing priority by 1) first hospitalization for cancer, 2) first consultation because of malignancy, 3) initial clinical or technical diagnosis, 4) start of treatment for cancer and 5) death)<br>Systemic therapy includes:<br>• Chemotherapy: for ATC codes, see Table 50<br>• Endocrine therapy: for ATC codes, see Table 52<br>• Targeted therapy: for ATC codes, see Table 51<br>Metastatic patients: combined stage IV (i.e. inclusion of cM1 and/or pM1) |
| **Risk adjustment** | None (process indicator) |
| **Limitations** | - Trial drugs are not routinely registered and included in the administrative database. Therefore an underestimation of this indicator is possible. |
| **Subgroup analyses** | - Age at diagnosis<br>- WHO performance status at time of diagnosis<br>- Number of inpatient bed days the year preceding the incidence date<br>- Number and type of comorbidities<br>- Year of incidence<br>- Treatment scheme |

| Title | Proportion of women <70 years old with metastatic BC who received systemic therapy |
|---|---|
| **Sensitivity analyses** | - Incidence year 2009 - 2013 vs. 2014 - 2018<br>- Women < 70 years old vs. ≥70 years old<br>- Chemotherapy only vs. endocrine only vs. targeted only vs. chemotherapy + endocrine (no targeted) vs. chemotherapy + targeted (no endocrine) vs. targeted + endocrine (no chemotherapy) vs. chemotherapy + endocrine + targeted |
| **Benchmarking** | Centre of main treatment |
| **Level of benchmarking** | Campus level |
| **Comments** | This indicator was elaborated as a descriptive indicator, illustrating the type of systemic treatment that is delivered to women with M0 IBC. In other words, no target was set and the variability between the hospitals is illustrated in a scatter plot. |

## Appendix 25.2. Flowchart



## Appendix 25.3. Results

**Table 178 – Proportion of women <70 year with metastatic BC who received systemic therapy, by patient and treatment characteristics**

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall** | 1 572 | 1 458 | 92.7 |
| **Age at diagnosis** | | | |
| <40 years | 122 | 120 | 98.4 |
| 40-49 years | 274 | 260 | 94.9 |
| 50-59 years | 490 | 464 | 94.7 |
| 60-69 years | 686 | 614 | 89.5 |
| **WHO performance status at time of diagnosis** | | | |
| 0 – Asymptomatic | 498 | 464 | 93.2 |
| 1 – Symptomatic but completely ambulatory | 815 | 768 | 94.2 |
| 2 – Symptomatic, up and about more than 50% of waking hours | 90 | 84 | 93.3 |
| 3 – Symptomatic, confined to bed or chair more than 50% of waking hours | 40 | 30 | 75.0 |
| 4 – Completely disabled; totally confined to bed or chair | 15 | 9 | 60.0 |
| Missing | 114 | 103 | 90.4 |
| **Number of inpatient bed days in year prior to incidence** | | | |
| 0 days | 1 057 | 1 000 | 94.6 |
| 1-5 days | 363 | 321 | 88.4 |
| 6-15 days | 117 | 105 | 89.7 |
| >15 days | 35 | 32 | 91.4 |
| **Number of comorbidities** | | | |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| 0 | 955 | 889 | 93.1 |
| 1 | 471 | 436 | 92.6 |
| 2 | 135 | 123 | 91.1 |
| 3 | 11 | 10 | 90.9 |
| **Cardiovascular disease** | | | |
| Absent | 1 051 | 977 | 93.0 |
| Present | 521 | 481 | 92.3 |
| **Respiratory disease** | | | |
| Absent | 1 463 | 1 357 | 92.8 |
| Present | 109 | 101 | 92.7 |
| **Diabetes** | | | |
| Absent | 1 428 | 1 328 | 93.0 |
| Present | 144 | 130 | 90.3 |
| **Incidence year** | | | |
| 2014 | 277 | 259 | 93.5 |
| 2015 | 286 | 270 | 94.4 |
| 2016 | 322 | 297 | 92.2 |
| 2017 | 326 | 290 | 89.0 |
| 2018 | 361 | 342 | 94.7 |
| **Treatment modality** | | | |
| Surgery < adjuvant RT | 1 | 0 | 0.0 |
| Surgery < adjuvant systemic Tx | 35 | 35 | 100.0 |
| Surgery < adjuvant RT + systemic Tx | 73 | 73 | 100.0 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| Neoadjuvant Tx < Surgery (< adjuvant Tx) | 230 | 230 | 100.0 |
| Surgery only | 3 | 0 | 0.0 |
| Primary systemic and/or radiotherapy (no surgery) | 1 144 | 1 120 | 97.9 |
| No oncological treatment | 86 | 0 | 0.0 |

*IBC: invasive breast cancer; WHO: World Health Organization; BCS: breast conserving surgery; Tx: treatment; <: followed by.*
*Source: BCR-IMA*

### Table 179 – Sensitivity analysis: Proportion of women <70 year with metastatic BC who received systemic therapy, by time period

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Overall (Main quality indicator; 2014 - 2018)** | 1 572 | 1 458 | 92.7 |
| **Comparison period (2009 - 2013)** | 1 354 | 1 280 | 94.5 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 180 – Sensitivity analysis: Proportion of women with metastatic BC who received systemic therapy, by age category

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **< 70 years (Main QI)** | 1 572 | 1 458 | 92.7 |
| **≥ 70 years** | 1 437 | 1 235 | 85.9 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

### Table 181 – Sensitivity analysis: Proportion of women <70 year with metastatic BC who received systemic therapy, by treatment type

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Endocrine therapy only** | 1 572 | 353 | 22.5 |
| **Chemotherapy only** | 1 572 | 204 | 13.0 |

| | IBC | | |
|---|---|---|---|
| | Denominator | Numerator | Proportion (%) |
| **Targeted therapy only** | 1 572 | a5 | 0.3 |
| **Chemotherapy + targeted therapy (no endocrine)** | 1 572 | 261 | 16.6 |
| **Chemotherapy + endocrine therapy (no targeted)** | 1 572 | 251 | 16.0 |
| **Chemotherapy + endocrine therapy + targeted therapy** | 1 572 | 214 | 13.6 |
| **Targeted therapy + endocrine therapy (no chemotherapy)** | 1 572 | 170 | 10.8 |

*IBC: invasive breast cancer.*
*Source: BCR-IMA*

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Volksgezondheid, de Stichting Kankerregister en het Federaal Kenniscentrum (KCE) in het kader van een studie over de kwaliteit van de zorg in de borstklinieken en in de ziekenhuizen / Délibération n° 21/194 du 7 décembre 2021 portant sur le traitement de données à caractère personnel relatives à la santé pseudonymisées par le SPF Santé publique, la Fondation Registre du cancer et le Centre fédéral d'expertise (KCE) dans le cadre d'une étude sur la qualité des soins dans les cliniques du sein et les hôpitaux. [Web page].2021 [cited 9 Nov 2022]. Available from: https://www.ehealth.fgov.be/ehealthplatform/file/view/AX20Se69QQaZnRgXjFTD?filename=21-194-f374-qualit%C3%A9%20des%20soins%20dans%20les%20cliniques%20du%20sein-Registre%20du%20Cancer.pdf

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