

1.1.a.

Proportion of patients with invasive breast cancer in whom ER, PR and/or HER2 status assessment were performed

1.1.b.

Proportion of patients with invasive breast cancer in whom systemic treatment was performed in the absence of ER, PR and HER2 status assessment

1.1.c.

Proportion of patients with invasive breast cancer in whom ER, PR and/or HER2 status assessment were performed before any systemic treatment

1.2.a.

Proportion of patients with DCIS in whom ER/PR status assessment were performed

1.2.b.

Proportion of patients with DCIS in whom hormonal therapy was performed in the absence of ER/PR status assessment

1.2.c.

Proportion of patients with DCIS in whom ER/PR status assessment were performed before any hormonal therapy

Reference to:

- KCE report 150A: BC11 (concerning HER2 status) and BC12 (concerning ER and PR status)
- Selected QCI for Vlaamse Overheid: nr. 1
- EUSOMA-guidelines

Relation to quality:

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

Adjuvant hormonal therapy can be considered for patients with ER positive DCIS (1A evidence), however, the benefits and harms of endocrine therapy should be discussed with women with DCIS, and treatment decisions should be based on individual circumstances.

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

Type of indicator:

Process

Limitations concerning measurability:

- Before 2007, FISH HER2 was not reimbursed, and no nomenclature code existed before this moment. The first codes for HER2 assessment were introduced respectively on August 1st 2007 and July 1st 2009.
- The following nomenclature codes for ER/PR-assessment are not within the authorization of the BCR at this moment. Providing an approval of the additional authorization request, these nomenclature codes will not be available until 2013 at the earliest.

Code	Omschrijving	Creatiedatum
546416-546420	<i>Doseren van oestrogeen- en progesteronreceptoren in borsttumoren, ongeacht het aantal afnamen, met een immunologische methode (Maximum 1)(Cumulregel 66)</i>	01/07/1999

The pathology codes for immunohistological examination make up the larger part ($\pm 95\%$)¹ of the nomenclature used for ER/PR assessment. However, since these codes are not specific, nomenclature does not allow to distinguish between ER/PR assessment on one hand and other immunohistological examination on the other. In addition, a part of the codes for immunohistological examination might have been used for HER2 assessment, although a specific code for HER2 assessment exists since 01/08/2007. As a consequence, nomenclature does not allow to make a complete distinction between ER/PR assessment on one hand and HER2 assessment on the other.

Proposals agreed by experts:

- The ER/PR and +HER2 assessment is important to choose the more adapted systemic treatment and should preferably be performed in all patients. Therefore, a new proposal was made for the calculation of this indicator (see flow chart).
- Since DCIS is also mentioned in the guidelines for ER/PR assessment, we will calculate an indicator 1.1. and 1.2. for invasive breast cancer patients and DCIS patients respectively.

¹ KCE-rapport 150A: Kwaliteitsindicatoren in oncologie: borstkanker

Data bases and variables:

- BCR (ICD-10=C50, incidence date)
- IMA (nomenclature for ER/PR and HER2 assessment, CNK-codes for chemotherapy, hormonal therapy and Trastuzumab)

Nomenclature/CNK selection:

- ➔ See “Indicatorenfiches na bespreking 25 november 2011”
- ➔ See “Limitations concerning measurability” for ER/PR-assessment

Systemic treatment:

- Hormonal therapy
- Chemotherapy
- Trastuzumab

1.1. Invasive cancers:**a) Proportion of patients with invasive breast cancer in whom ER/PR and/or HER2 status assessment were performed****Numerator** (solid green box in flow chart 1):

All women diagnosed with invasive breast cancer undergoing ER/PR and/or HER2 status assessment within 3 months after incidence date.

Denominator (solid blue box in flow chart 1):

All women diagnosed with invasive breast cancer.

Expected range:

90-100%

b) Proportion of patients with invasive breast cancer in whom systemic treatment was performed in the absence of ER/PR and HER2 status assessment (within 3 months around incidence)**Numerator** (dotted green box in flow chart 1):

All women diagnosed with invasive breast cancer undergoing systemic treatment not preceded by ER/PR status assessment nor by HER2 status assessment (within 3 months around incidence date).

Denominator (dotted blue box in flow chart 1):

All women diagnosed with invasive breast cancer not undergoing ER/PR status assessment nor HER2 status assessment within 3 months around incidence date.

b.bis) Proportion of patients with invasive breast cancer in whom systemic treatment was performed in the absence of ER/PR and HER2 status assessment

Numerator (dotted green box in flow chart 2):

All women diagnosed with invasive breast cancer undergoing systemic treatment not preceded by ER/PR status assessment nor by HER2 status assessment.

Denominator (solid blue box in flow chart 2):

All women diagnosed with invasive breast cancer undergoing systemic treatment.

Remark: if indicator b is calculated according to flow chart 1, patients with systemic treatment in the absence of ER/PR and/or HER2 assessment might be overestimated. For example: if a patient has an ER/PR and/or HER2 assessment on the 4 month after incidence, then it is not included in the first YES-group. If for this patient systemic treatment was started up on the 5th month after incidence, then this patient will be wrongfully included in the second YES-group. This overestimation can be circumvented when using flow chart 2 for calculation of indicator b. Here we look at all ER/PR and/or HER2 assessments that took place between incidence date (-1 month) and date of systemic treatment (included).

Expected range:

0%

c) Proportion of patients with invasive breast cancer in whom ER/PR and/or HER2 status assessment were performed before any systemic treatment

Numerator (solid green box in flow chart 2):

All women diagnosed with invasive breast cancer undergoing ER/PR and/or HER2 status assessment before any systemic treatment.

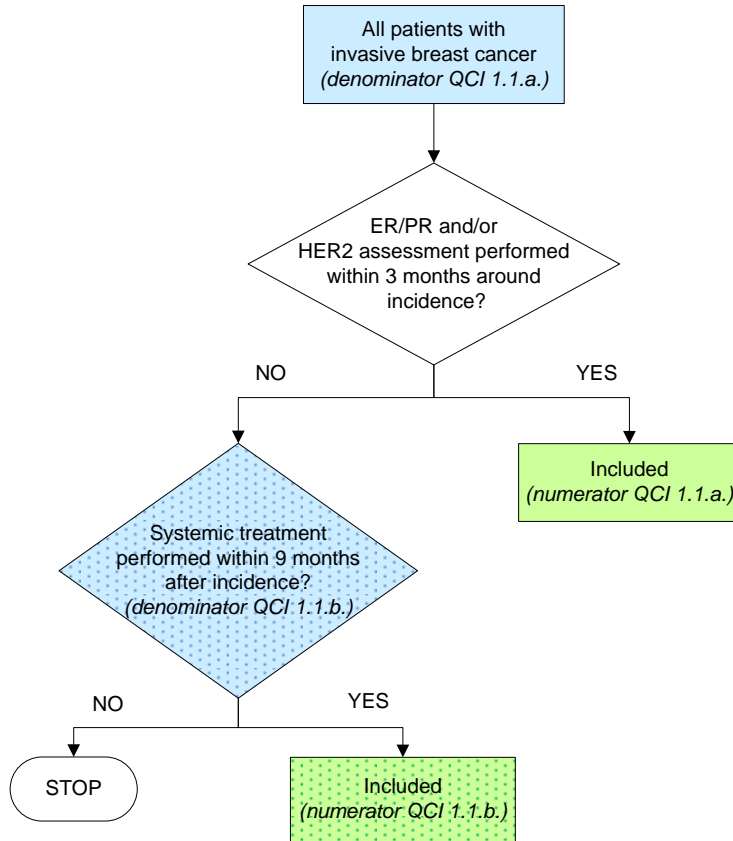
Denominator (solid blue box in flow chart 2):

All women diagnosed with invasive breast cancer undergoing systemic treatment.

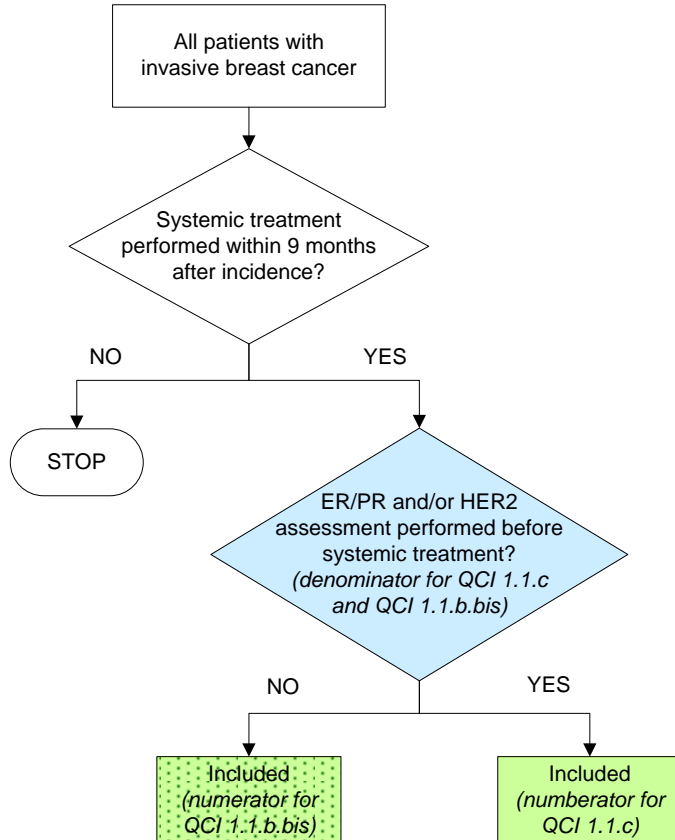
Expected range:

90-100%

Flow chart 1 (NEW PROPOSAL):



Flow chart 2 (NEW PROPOSAL):



Time frames (convention: 1 month = 30 days):

Flow chart 1:

- Suggestion for ER, PR and HER2 assessment:
 - Work with time frame of [-3,+3] months around incidence date
- Suggestion for systemic treatment:
 - Work with time frame of [-1;+9] months around incidence date.
 - Inclusion of chemotherapy, hormonal therapy and Trastuzumab. Since HER2 assessment is performed to decide on treatment with Trastuzumab, this product was included in the definition of systemic treatment for this indicator.

Flow chart 2:

- Suggestion for systemic treatment:
 - Work with time frame of [-1;+9] months around incidence date
- Suggestion for ER, PR and HER2 assessment:
 - Closest ER/PR/HER2 assessment to systemic treatment within the time frame of incidence-1month and date of systemic treatment (included).

1.2. DCIS:

a) Proportion of patients with DCIS in whom ER/PR status assessment was performed

Numerator (solid green in flow chart 3):

All women diagnosed with DCIS undergoing ER/PR assessment within 3 months after incidence date.

Denominator (solid blue in flow chart 3):

All women diagnosed with DCIS.

b) Proportion of patients with DCIS in whom hormonal treatment was performed in the absence of ER/PR status assessment

Numerator (dotted green in flow chart 3):

All women diagnosed with DCIS undergoing hormonal treatment not preceded by ER/PR status assessment.

Denominator (dotted blue in flow chart 3):

All women diagnosed with DCIS not undergoing ER/PR status assessment within 3 months after incidence date.

b.bis) Proportion of patients with DCIS in whom hormonal treatment was performed in the absence of ER/PR status assessment

Numerator (dotted green box in flow chart 4):

All women diagnosed with DCIS undergoing hormonal treatment not preceded by ER/PR status assessment.

Denominator (solid blue box in flow chart 4):

All women diagnosed with DCIS undergoing hormonal treatment.

Remark: if indicator b is calculated according to flow chart 1, patients with hormonal therapy in the absence of ER/PR status assessment might be overestimated.

For example: if a patient has an ER/PR assessment on the 4 month after incidence, then it is not included in the first YES-group. If for this patient hormonal therapy was started up on the 5th month after incidence, then this patient will be wrongfully included in the second YES-group. This overestimation can be circumvented when using flow chart 2 for calculation of indicator b. Here, we look at all ER/PR HER2 assessments that took place between incidence date (-1 month) and date of hormonal therapy (included).

c) Proportion of patients with DCIS in whom ER/PR status assessment was performed before any hormonal therapy

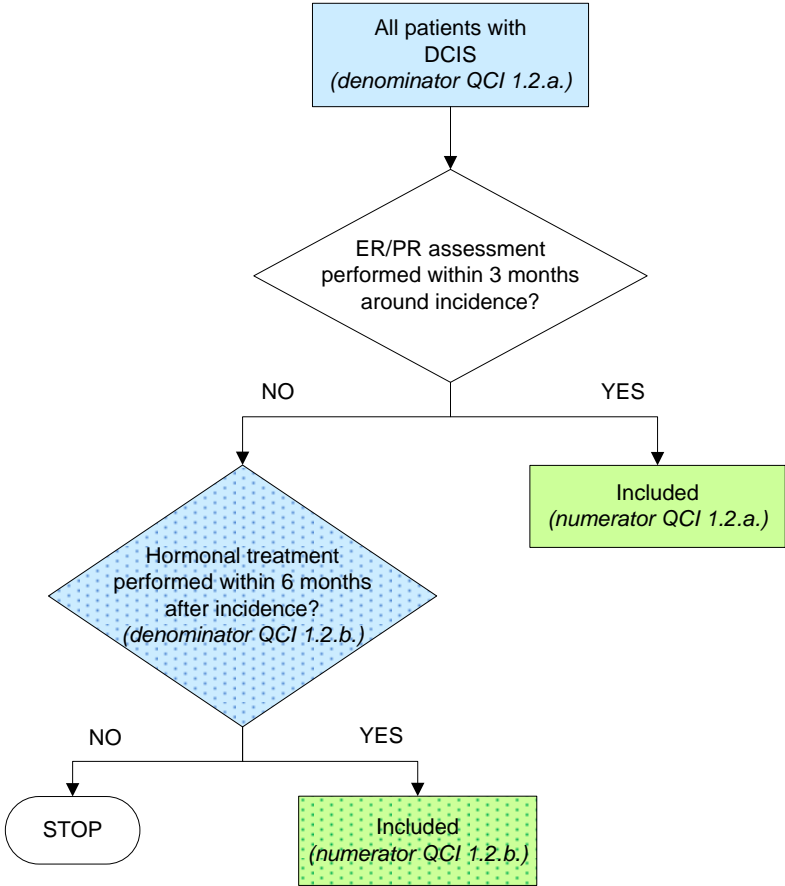
Numerator (solid green box in flow chart 4):

All women diagnosed with DCIS undergoing ER/PR status assessment 3 months before any hormonal therapy.

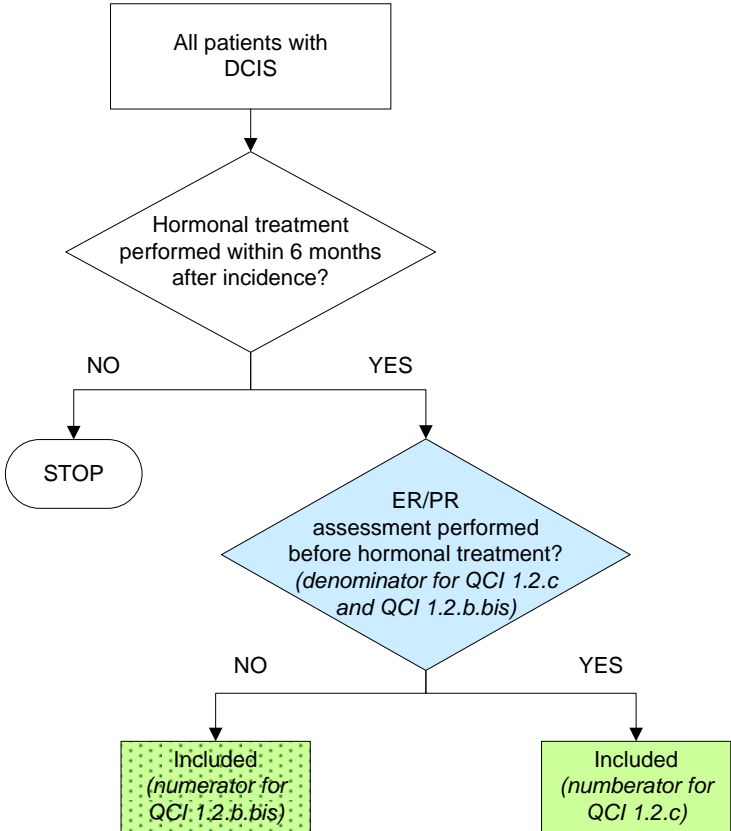
Denominator (solid blue box in flow chart 4):

All women diagnosed with DCIS undergoing hormonal therapy.

Flow chart 3 (NEW PROPOSAL):



Flow chart 4 (NEW PROPOSAL):



Time frames (convention: 1 month = 30 days):

Flow chart 3:

- Suggestion for ER/PR:
 - Work with time frame of [-3,+3] months around incidence date
- Suggestion for hormonal therapy:
 - Work with time frame of [-1;+6] months around incidence date.

Flow chart 4:

- Suggestion for hormonal therapy:
 - Work with time frame of [-1;+6] months around incidence date
- Suggestion for ER/PR:
 - Closest ER/PR assessment to hormonal therapy within the time frame of incidence-1month and date of hormonal treatment (included).