Proportion of small cancers

Indicator for the Breast Cancer Screening Programme in Flanders

Marina Puddu, Cinthia Lemos, Jean Tafforeau
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Conceptual approach – Indicator for the Breast Cancer Screening Programme in Flanders

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TABLE OF CONTENTS

1. INTRODUCTION ..............................................................................................................................2
2. CONCEPTUAL FRAMEWORK ..........................................................................................................4
3. DEFINITION .......................................................................................................................................5
4. CALCULATION AND DATA SOURCES ..........................................................................................6
5. ADDITIONAL INFORMATION ..........................................................................................................7
   5.1. Relationship between tumour size and survival ................................................................. 7
   5.2. Relationship between tumour size and probability of tumour spread ............................... 8
   5.3. Relationship between tumour size and mortality ................................................................. 8
   5.4. Type of information provided ................................................................................................. 8
   5.5. Detecting early cancers ............................................................................................................ 9
   5.6. Data available in Belgium and other countries ................................................................. 10
6. OBJECTIVE, MINIMUM STANDARD AND TARGET .................................................................10
7. STRENGTHS AND LIMITATIONS .................................................................................................13
8. IMPORTANCE FOR THE DECISION MAKERS ........................................................................14
9. REFERENCES .....................................................................................................................................15

APPENDIX 1: COMPARISON OF PERFORMANCE INDICATORS FOR ORGANIZED BREAST
SCREENING PROGRAMMES IN DIFFERENT EUROPEAN AND NOT EUROPEAN COUNTRIES
..........................................................................................................................................................17
1. Introduction

The aim of the Flemish breast cancer screening programme is to reduce the mortality from breast cancer.

The progression of the breast cancer disease can be halted by early detection and treatment. This allows preventing a significant proportion of breast cancer deaths. The basic mechanism for the prevention of deaths by screening is the reduction in the incidence rate of advanced cancers and therefore in reducing mortality from advanced disease (1). The beneficial effect of screening is mediated by its effect in detecting early cancers, which are characterized by more favourable prognostic factors.

The prognostic factors related to breast cancer can be classified in two groups:

- Time-dependent factors: the tumour size, the extent of axillary lymph node involvement, the presence of metastases (tumour stage); all those factors are related to the duration since when the tumour exists.
- Biological factors: the histological type, the histological grade (malignancy grade); those factors are related to the intrinsic behaviour of the tumour.

Of these prognostic factors, tumour size, histological type, histological grade, lymph node status have been shown to be related to the clinical outcome. Survival and mortality are highly and directly correlated with these prognostic factors (2) (3) (4).

As the main cause of cancer mortality is due to metastatic dissemination, early detection of cancers increase the probability to treat the disease before the occurrence of the dissemination: this is while cancers respond better to treatment even if they have a high histological grade. As a result early detection improve survival and reduce morbidity and mortality.

The reduction in mortality from breast cancer is the necessary and sufficient indicator of the effectiveness of a screening programme. However, changes in mortality take too long to become evident after a few years. The mortality evolution is also influenced by factors outside the screening programme, such as the development of more effective treatments.

An attractive alternative to analyse breast cancer mortality is to identify early surrogate indicators and follow their development over time. These indicators make it possible to make predictions on the reduction of mortality and to evaluate the effectiveness of a screening programme without waiting for mortality results.

Some of the early indicators are based on the prognostic variables mentioned above. They are used to obtain an early estimate of the screening effect and to assess if the programme is operating as expected. In practice, one tries to predict the final reduction in breast cancer mortality that is likely to be achieved with the current level of screening performance. These indicators are also useful to monitor the breast cancer screening programme and to ascertain whether adjustments are required.

However, these early indicators are not sufficient and cannot as such be taken as a proof of effectiveness of the screening programme. Others indicators are needed as the cancer detection rate and the participation.
The Flemish health authorities in charge of the screening programme have identified operational objectives that can be used to monitor the management of the breast cancer screening programme and to measure its effectiveness in its early stages. These objectives are to a certain extent based on early indicators and surrogate outcome measures.
2. **Conceptual framework**

The development of the present indicator is part of the general framework of the breast cancer screening programme evaluation.

The tumour size is an indicator of earlier detection and therefore a prognostic variable used to predict the outcome in terms of mortality (5). The tumour size is also a reliable determinant of survival (2).

It is used as an early surrogate indicator by which the effectiveness of a breast screening programme is assessed (6). A greater proportion of small cancers detected increases the likelihood that the anticipated reductions in morbidity and mortality from breast cancer will be achieved.

**Why the tumour size?**

Within the all possible indicators build on prognostic variables, tumour size is proposed as early indicator and surrogate measure to evaluate the Flemish programme for the following reasons:

1. **Availability:** tumour size is more frequently recorded than the other cancer features as the stage or the grade (10).
2. **Objectivity of the measure:** tumour size is more objectively measured than the histological grade. This last measure suffers from a much higher subjectivity than any other microscopic evaluation, as it is the sum of three different morphological features (tubule formation, nuclear polymorphism and mitotic counts).
3. **Quality of the information:** the quality of the information on tumour size is better than the information on stage. When using stage, comparisons over time may be biased by the increasing availability of techniques for staging, so cancers that might have been described as localized with less performing diagnostic techniques are now described as advanced. This phenomenon is known as “stage migration” (7). Tumour size is less subject to this bias than stage.
4. **Understanding:** tumour size is a feature easier to understand by a large public than stage or grade.
3. Definition

*Proportion of invasive small cancers*

The indicator proposed here measures the proportion of invasive small cancers detected among the eligible women invited and screened for breast cancer, expressed in percentage. A small cancer is defined as a cancer that the size is less than or equal to 10 mm in the maximum diameter according to the best data: from pathological, histological and radiological reports (8) (7).

Ideally, the tumour size should be assessed firstly in fresh or fixed resected pathological specimens and subsequently confirmed or amended after histological examination. If the two measurements are discrepant the histological examination should be preferred (5) (3). Histopathology remains indeed the universal basis of diagnosis; the addition of other elements only increase the precision of the prediction (9).

For the calculation of this indicator the *cancers in situ* are excluded. This has been done to focus better on the main aim of the programme: reduce the mortality from invasive breast cancer. As the natural history of the cancer in situ is uncertain and as he probably does not cause mortality, it falls outside of this scope (6). If however the cancers in situ were included in the indicator, the incidence rates would be higher\(^1\). Survival analysis could be also affected.

In order to analyse this indicator in function of the detection mode, all cancers have to be recorded regardless the detection method. Three detection ways are available: screening in the framework of an organized programme, opportunistic screening delivered outside the organized programmes and the medical diagnosis on the basis of complaints and symptoms.

*Other way to present this indicator: rate instead of proportion*

Another way to present this indicator is the use of rates per population screened instead of proportions.

The detection rate of small cancers is the number of women with small diameter (=10mm) invasive breast cancers detected among the women screened in the target age group, for every 1,000 or 10,000.

The denominator in the detection rate measures the number of women affected rather the number of cancers detected as seen in the proportion. In practice, when a woman presents more than one cancer by this way it is prevented that she’s counted more than once\(^2\).

Aged standardised detection rates\(^3\) are often used instead of crude cancer detection rate to make possible to compare the results between programmes of other countries and across time periods.

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\(^1\) Cancers in situ are not invasive cancers mainly diagnosed by screening. As result, screening will increase the incidence of cancer in situ and thus the incidence of breast cancer.

\(^2\) In this case, conventionally the record data reflect the cancer with the worst diagnosis or stage detected using the most invasive diagnostic technique (10). This convention is especially relevant when measuring the impact of screening on stage or size distribution.
In the UK a further measure used is the small cancer standardized detection ratio (SDR), which is the ratio of the observed number of invasive cancers <15 mm divided by the number expected from the Swedish Two-County (for more details see chapter on the indicator Standard Detection Ratio). Actually, the Swedish Two-County trial is considered as golden standard as it obtained the best results among all breast cancer screening randomised trials. In practice, a SDR of <1 indicate a possible under-performance of the programme under evaluation compared with the Swedish Two-County trial. The small cancer standardized detection ratio, after adjustment of the expected number of invasive cancers by the local background incidence, was used in the UK to evaluate the performance of regional screening programmes. When the screening programme data were merged with cancer registry data, it was also possible to compare the size distribution of cancers diagnosed inside and outside the screening programme (11).

4. Calculation and data sources

The proportion of small screen-cancers detected is expressed as the number of screen-detected cancers measuring =10 mm divided by the total number of invasive screen-detected cancers as shown in the formula below (8):

\[
\frac{N_{\text{small}}}{N_{\text{total}}} \times 100 = P_{\text{small}}
\]

- \(N_{\text{small}}\): number of invasive screen-detected cancers =10 mm
- \(N_{\text{total}}\): total number of invasive screen-detected cancers
- \(P_{\text{small}}\): % invasive cancers ≤10 mm

To notice that in the scientific literature the small cancers measuring =10 mm are indicating with the acronym \(pT1a\).

In the Flemish database of the breast cancer screening programme the indicator could be calculated from the variable AT field 46: “Result of further assessment”, where the information on the tumour size of the cancers detected within the programme is encoded.

The information on the tumour size could be obtained from:

1. The feedback of the women’s physician
2. By deriving the information directly from the pathology reports
3. Through record linkage with the Flemish Cancer Register

The record linkage with the cancer registry allows improving the validity of the information on tumour size and its completeness (percentage of cases without the information about the size).

Moreover, it allows to complete the information on the other features of the detected cancers and to ensure the exhaustiveness of the database.

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3 Age standardised rates enable comparisons to be made between populations that have different age structures.
4 MVG, Administratie Gezondheidszorg, dataset, 11/4/2005
5 Vlaams Kankerregistratienetwerk (VKR) www.vlaamsetegenkanker.be
6 Validity refers to the extent to which the information recorded on the variable (size) is true, accurate
5. Additional information

5.1. Relationship between tumour size and survival

Tumour size is a time-dependent prognostic factor that correlate directly with survival (3).

It has been shown consistently in many studies that tumour size influence prognosis (2) (12) (13). Patients with smaller cancers have better long-term survival than those with large tumours.

That is partly explained by the fact that small cancers are more likely to be lymph node negative. Actually the lymph node status has a greater effect on the survival than the tumour size: women with lymph node metastases had poorer survival than those with lymph node negative no matter the size of the tumour.

Furthermore, in behalf of the histological grade, it has been noticed that the tumours with the higher grade of malignancy (grade III) had better prognosis if they were small.

Moreover, the Swedish two-county trial data (14) (2) indicate that survival is improved with reduction in tumours size, independently from the treatment or the age of the patient. A 16-year survival rate of > 90% was reported for tumours measuring 6-10 mm and >95% for tumours of 1-5 mm, while for large tumours (20-50mm) barely a survival rate of 20% was reported (figure 1).

Figure 1: Cumulative survival by tumour size (2)

Further in the Swedish two-county became clear that the effect of early detection is not mediated purely by a reduction in tumour size but also by the mode of detection. When one compare clinically detected tumours (palpable) with screen-detected tumours (nonpalpable), for each size category the survival is better in the screen-detected group. For instance in the Swedish two-county trial the 16-year survival rate by mode of detection for tumours measuring 6-10 mm clinically detected was 85% while she was 89% for those screen-detected (2).

To explain the good survival of the screen detected cancers the effect of other prognostic factors such as lymph node status and the histological grade should be also considered. It has been shown that screen detected cancers present a smaller proportion of lymph node invasion and also have more favourable histological grade, indicating earliness of diagnosis among screened cancers (15) (16).
5.2. **Relationship between tumour size and probability of tumour spread**

An interesting model was built to study the natural history, enrolling 4,000 breast cancer patients with a follow-up ranging from 20 to 35 years. The aim was to study the relationship between tumour size and the probability of metastatic dissemination. The study results have shown that the time interval between cancer treatment and the emergence of clinical metastases is related to the tumour size. The proportion of patients with metastases after 20 years follow-up was significantly lower in patients with a small cancer (5).

5.3. **Relationship between tumour size and mortality**

Randomised control trials on mammographic screening have shown that detection of early cancers by mammography can result in fewer deaths from breast cancer. The level of this reduction varied from 32% (latest follow-up of 20 years of the Swedish Two-county trial) to 13% (latest follow-up of 14 years of the Edinburgh trial) (17) (18).

Particularly, in the Swedish Two-county trial where a reduction of 32% of breast cancer mortality was observed the percentage of small cancer was higher in the group of screened women than in the control group (respectively 18% vs. 7% for cancers measuring 1-9mm).

The results found in the randomised trials were also reproduced in organised screening programmes.

An example is given by the screening programme carried out as public health intervention in Finland. In the Finnish programme, Hakama et al. (16) compared the size, the nodal status and the histological type of breast cancers in women screened as opposed to those diagnosed outside the national organised screening programme. They found that almost 70% of the invasive cancers detected in screened population had a good clinically prognosis (the cancers were small without positive lymph nodes). This percentage was higher than among controls. Consequently, these early surrogate indicators predict a breast cancer mortality reduction due to the screening programme in Finland.

5.4. **Type of information provided**

The percentage of small cancers is an indicator that estimates the potential reduction in breast cancer mortality on the basis of one of the prognostic factors: the size of screening-detected tumours.

It indicates the ability of screening programmes to advance the diagnosis of breast cancer to an earlier stage.

It is clearly related to the main objective of the screening programme, the reduction of breast cancer mortality.

As the size of tumours is an indicator of earlier detection and result in earlier diagnosis, which can affect mortality, one can consider the size of tumours as a surrogate outcome measure for mortality reduction.

Poor performance of this indicator indicates that corrective action of the cancer screening programme is required (improve participation, improve radiologist’s performance and quality of equipments, reconsider the interval screening…..).
When the rate of small cancers is used as measure of the efficacy of breast cancer screening, one must be aware of the fact that high rates may reflect overdiagnosis through screening and thus overestimate the actual efficacy of the screening process. Overdiagnosis will also have an impact on incidence and survival rates, resulting in artificially high survival rates particularly for early stage cancers (6).

Tumour size is also an important quality assurance measure for breast screening programmes (19) and can be used in part to judge the ability of radiologists to detect small, impalpable invasive cancers via mammography. In addition when the pathologists measure the tumour diameter the measurement should be done as accurately as possible. It is known that when the size decreases, the risk of measurements errors increases (20).

5.5. Detecting early cancers

Find breast cancer early by screening means increasing the chance to detect cancers in an early phase of the disease (early-stage cancers). That means to detect invasive cancers before they attain the characteristics that indicate poor prognosis, and the aforementioned results indicate that this means detecting them when they are small.

Actually small invasive screen-detected tumours are likely to be early stage cancers characterized by better prognosis. They are generally small (less than 10 of 15 mm), not spread (loco-regional disease without lymph node metastases) and with a low histological grade.

It should be kept in mind that detection of an early-stage breast cancer differs from “early detection” of breast cancer. Discovering an early-stage breast cancer is fortunate. Early discovery of a small but late stage breast cancer makes less difference, as the breast cancer screening programmes are intended to find cancers that are smaller and in the preclinical phase.

A small cancer is not necessarily a cancer at an early stage. Although size is definitely one of the most important factors, far more important is whether the cancer has or not metastasis. If cancers have disseminated it is a late-stage cancer no matter how small it is. No matter the size, a cancer that contains poorly differentiated cells (grade III) is a later cancer than the one that has more differentiated cells.

However even if histological grade is an independent prognostic variable it was noted that the grade increases with the size of the tumour, this suggests a histological progression of the tumours during their growth (5).

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7 Overdiagnosis means here the diagnosis (and recording) of a cancer, which would not have emerged clinically in the absence of screening. There are 3 possible source of overdiagnosis: one is the diagnosis of slow-growing disease, which would note have progressed to clinical significance in the person’s lifetime (evidence for this source of overdiagnosis comes from autopsy studies). A second source is the inclusion of non-progressive disease (clinically benign) amongst the cancer cases. Diagnosis of a proportion of benign cases as malignant will affect incidence rates (but not mortality). The third source is the diagnosis of in situ cancers.

8 The establishment of a threshold of the size of small cancers is a crucial point. Some authors propose 9 or less, others 10 mm and even others 15mm, on the basis of the results of their studies. This lack of uniformity in definition causes problems in the interpretation and comparison of data from different studies.
More in general to evaluate screening programmes the other prognostic factors (node status and histological grade) should be also considered (21).

5.6 Data available in Belgium and other countries

Tumour size is frequently included in the evaluation of the screening programmes. It could be expressed in three different ways:

1. The proportion of small cancers (Europe, Canada, Sweden)
2. Small cancer detection rate (UK, Australia)

In most of countries small cancers are considered to be those measuring less than 10 mm. However in Sweden and in the UK the cut-off for small cancers is <15 mm; this definition has been established on the basis of the results of the Swedish Two-County study, which showed excellent survival rates for tumours measuring 10-14 mm (14).

Appendix 1 is providing an overview of the situation of some performance indicators for organized breast cancer screening programmes in different European and not European countries.

6. Objective, Minimum standard and Target

The results of randomised trials are usually used to define targets for national screening programme, as they have produced significant reductions in breast cancer mortality. After the adaptation of the parameters of these trials for local conditions this indicator is allowing to predict the eventual reduction in breast cancer mortality likely to be achieved in a national programme (1).

Other countries

The target value for the proportion of small invasive cancers varies in accordance to the way the indicator is expressed. As example in Sweden, where the proportion is used, the target is 50% of invasive cancers measuring less than 15 mm (14) while in the countries where the rate is used, as example in UK, the minimum standard and the target for rate of invasive cancers less than 15 mm is =1,5-1,7/1.000 for prevalent screen and =2-2,3/1.000 for incident screen (22).

In Australia the target rate to be achieved for of invasive cancers measuring less or equal to 10 mm is =8/10.000 (23).

In Table 1 an overview of the targets of some organized screening programmes.
Table 1: Overview of the targets of some organized breast cancer screening programme

<table>
<thead>
<tr>
<th>Country</th>
<th>Prevalent screen</th>
<th>Incident screen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>=25% =10 mm</td>
<td>=30% =10 mm at initial screening</td>
</tr>
<tr>
<td>Sweden</td>
<td>&gt;50% &lt;15 mm</td>
<td>&gt;50% &lt;15 mm</td>
</tr>
<tr>
<td>United Kingdom</td>
<td>2,0 per 1.000&lt;15 mm</td>
<td>2,3 per 1.000 &lt;15 mm</td>
</tr>
<tr>
<td>Australia</td>
<td>&gt;8 per 10.000&lt;10 mm</td>
<td>&gt;8 per 10.000 (=10 mm)*</td>
</tr>
<tr>
<td>Canada</td>
<td>=25% =10 mm</td>
<td>=25% =10 mm*</td>
</tr>
</tbody>
</table>

*Not reported separately for initial and subsequent screening examinations

**Flanders**

**Objective:** The aim of the Flemish programme is to maximise the early detection of breast cancers by increasing the number of small invasive cancers detected.

The minimum standards proposed for Flanders are in agreement with the deliverable levels required for this indicator by the European guidelines (8). The following are thus proposed:

**Minimum standard:**
- =25% =10 mm at initial screening (prevalent screen)
- =30% =10 mm at subsequent screening (incident screen)

The targets here proposed are based partly on the current results of screening programmes in some European and not European countries (see Appendix 1) and partly on the results obtained from the European Breast Cancer Network (EBCN), (see Table 2).

**Target:**
- =35% =10 mm at initial screening (prevalent screen)
- =40% =10 mm at subsequent screening (incident screen)

The EBCN network is composed of 17 pilot projects. Out of the 17 projects involved, 10 projects from 6 European countries provided aggregated data on screening examinations and features of breast cancers detected over the period 1998-2000.

The results of a study analysing the early performance indicators of the screening projects within the EBCN were summarized separately for projects in centralized (Denmark, Italy, 9 Standardized detection rate
10 Small cancer detection rate
11 In countries with a centralized health care system, supported mainly by the national government, primary health care is delivered through salaried physicians, and the search for medical care at primary, secondary and tertiary levels follow strict rules. Screening is usually centrally organized and distinct from the delivery of general health care. As a consequence the units as well as the professionals involved are dedicated to screening activities. In a decentralised (or liberal) health care system, as in Belgium, France and Luxembourg, most physicians are paid on fee-for-service basis, and patients may attend the physician or the hospital of their choice. Screening is implemented mainly through the use of existing health care facilities. This implies the involvement of many (screening) units and numerous professionals many of whom are less committed to screening; consequently, the co-ordinating centre in a centralized health care system must assume an active role in order to ensure a successful high-quality screening programme. This includes organizing, supervising and monitoring all screening activities and setting up a rigorous evaluation system (24).
Spain) versus decentralized health care systems (Belgium, France, Luxembourg) (25), (see Table 2):

Table 2: Comparison of performance indicators for centralized and decentralized projects within EBCN, adapted from (25)

<table>
<thead>
<tr>
<th>Performance indicator</th>
<th>EBCN (mean, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calendar period</td>
<td>1989-2000</td>
</tr>
<tr>
<td>Age group</td>
<td>50-64</td>
</tr>
<tr>
<td></td>
<td>Centralized</td>
</tr>
<tr>
<td><strong>Initial screening</strong></td>
<td></td>
</tr>
<tr>
<td>PT1ab (%)*</td>
<td>34 (27-41)</td>
</tr>
<tr>
<td><strong>Subsequent screening</strong></td>
<td></td>
</tr>
<tr>
<td>PT1ab (%)</td>
<td>37 (28-44)</td>
</tr>
</tbody>
</table>

*PT1ab = tumour =10 mm in the greatest dimension
7. **Strengths and Limitations**

**Strengths**

- Tumour size is a surrogate outcome measure that predict the results of the screening programme (6). The advantage of using surrogate outcome measures is that the results become available much more quickly, than if it is necessary to wait for the long term results (mortality reduction).

- Tumour size is probably the most relevant early indicators of the effectiveness of breast cancer screening available in most cases. Tumour size is already collected in the Flemish breast cancer screening programme database and could thus be easily studied. It is also frequently present in cancer registries (when absent there are often clear indications that the tumour is larger, inoperable and advanced). In addition, for cancers small enough to be stage I the information on tumour size is only rarely absent (1).

- Tumour size could be used as a surrogate for stage since:
  1. Tumour size is of strong prognostic value in its own (1)
  2. The proportion of cases with positive nodes is strongly related to tumour size; this relation is the same in screen detected as in clinically detected cases (14). This point suggests that a shift towards smaller size due to early detection also will increase the probability that the breast cancer is not disseminated (2).

- Tumour size is less subject to bias than stage. Actually when using stage, comparisons over time may be biased by the increasing availability of techniques for staging, so that cancers that might have been previously described as localized with less performing diagnostic techniques are now described as advanced. This phenomenon is known as “stage migration” (7).

- Small cancers are more likely to be well differentiated (grade I). It was noted that the grade increases with the size of the tumour what suggests a histological progression of the tumours during their growth (5).

- Tumour size is a reliable determinant of survival. It is highly associated with tumour size and the improvement of survival associated with reduction in tumour size is greater than it could be achieved by differences in therapy (2).

- Understanding: tumour size is a feature easier to understand than stage or grade by a large public and for policy makers not specialised in the field.

- Tumour size is a notion that could easily be used by information or education programmes.
Limitations

- Depends on the accuracy of the measurement.
- Size is not in itself sufficient to demonstrate a reduction of mortality. Nodal status and grade should be also reported (2).
- To allow comparisons between different populations, rates should be presented as standardized rates per population screened to adjust for differences in the age-structure (7).
- Availability of a cancer registry of good quality and the possibility to merge the screening database with the cancer registry.

8. Importance for the decision makers

The indicator proportion of invasive small cancers expresses the capacity of the programme to detect early cancers, which means cancers with a good prognostic in term of morbidity, survival and mortality. Increasing the proportion of small cancers is of cardinal importance for the better quality of life of the woman as early detection of breast cancer results in most cases, in increased survival, reduction in morbidity and mortality (5).

The scientific data show us that survival is excellent in tumours less or equal to 10 mm, irrespective of the kind of treatment and the age of the woman. That means that nine women in ten will survive over a 16 years period of time an invasive breast cancer if the tumour is less than 10 mm. Unlike, in case of large tumours (20-50 mm) barely two women in ten will survive over the same period of time (2).

Besides this important aspect, early cancers respond better to treatment increasing the chance of women to recover from breast cancer. In addition, in case of early cancers less extensive surgery will be required. As result, women who have cancer detected early may suffer less the morbidity associated to breast cancer (15). Data from many studies have shown that women who are found to have small invasive cancers are less likely to undergo a mastectomy than those with larger tumours. Women with smaller cancers are able to have more choice in terms of breast conserving surgery versus mastectomy, with similar survival rates. Women diagnosed with these small cancers are less likely to have positive axillary nodes and less likely to have more aggressive adjuvant treatments.

Last but not least increasing the detection of small cancers save lives. The mortality reduction from breast cancer of about 30% shown by the randomized controlled studies on breast cancer screening has been possible above all thanks to a higher detection of small cancers (16) (18).

From a financial point of view detecting breast cancers at an early stage is profitable as they are less expensive to treat than the advanced ones (26). Furthermore, when the tumours are in the more favourable stages it is possible to save the treatment costs for palliative care.
9. References


(22) Standards for the NHS Breast Screening Programme. 1-34. 2005. Sheffield, NHS Cancer Screening Programmes.
Ref Type: Report

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# Appendix 1: Comparison of performance indicators for organized breast screening programmes in different European and not European countries

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<td>Age group</td>
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<td><strong>Initial</strong></td>
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<td></td>
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<tr>
<td>Participation (%)</td>
<td>79*</td>
<td>74</td>
<td>43*</td>
<td>87</td>
<td>54*</td>
<td>30,2*</td>
<td>30-59*</td>
<td>24,3</td>
<td>23</td>
<td></td>
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<tr>
<td>Detection rate (%)</td>
<td>6,5</td>
<td>6,8</td>
<td>5,6</td>
<td>4,8</td>
<td>5,9</td>
<td>4,8</td>
<td>8,3</td>
<td>5,8</td>
<td>8,1</td>
<td></td>
</tr>
<tr>
<td>PT1ab (%)</td>
<td>27</td>
<td>22 (50-54)</td>
<td>35</td>
<td>11</td>
<td>37*</td>
<td>38*</td>
<td>30</td>
<td>40</td>
<td>36</td>
<td>30,2</td>
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<tr>
<td><strong>Subsequent</strong></td>
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<tr>
<td>Participation (%)</td>
<td>79*</td>
<td>87</td>
<td>43*</td>
<td>78</td>
<td>54*</td>
<td>30,2*</td>
<td>30-59*</td>
<td></td>
<td></td>
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<tr>
<td>Detection rate (%)</td>
<td>3,6</td>
<td>5,3</td>
<td>4,2</td>
<td>4,8</td>
<td>3,6</td>
<td>3,4</td>
<td>5,9</td>
<td>5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT1ab (%)**</td>
<td>31</td>
<td>25 (50-54)</td>
<td>37</td>
<td>21</td>
<td>37*</td>
<td>38*</td>
<td>32</td>
<td>33</td>
<td>30</td>
<td></td>
</tr>
</tbody>
</table>

*Not reported separately for initial and subsequent screening examinations

** PT1ab = tumour ≥10 mm in greatest dimension