Breast cancer standardized detection ratio (SDR)

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Conceptual approach – Breast cancer population-based screening programme indicators, Flanders 2006-2010

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1. Introduction

The main objective of the screening programme in Flanders, as in Belgium, is the reduction in breast cancer mortality (1). For the achievement of this objective the detection of small invasive cancer is generally recognised as being of major importance because it is likely to result in a reduction in breast cancer mortality (20). The detection of in situ carcinoma and larger invasive cancers is less important to achieve the expected mortality reduction.

The efficacy of the mammography as the breast cancer screen test had been proved by eight randomized controlled trials and through the evaluation of the screening programs. Following the Swedish two county trial results, the women invited to participate in the screening for breast cancer had a relative breast cancer mortality risk of 0.70 (p=0.0002) with 95% CI (0.58-0.85) (20). This result meaning that by screening the preventable fraction of breast cancer mortality is 30% or it is the reduction in mortality that can be expected when women aged 50-69 years old participate regularly in the screening program.

The reduction in mortality from breast cancer depends directly on the participation in the screening by the target population, and the capacity of the screening programme to detect...
invasive cancer. The screening programmes targets for the cancer detection rate should take into account the age range, background incidence, and different targets should be set for the first screen (prevalent cancers) and for the incident screens (subsequents).

The detection rate is conditioned by the underlying incidence and the inter-screening interval. In addition, the screening programme detection rate reflects the mean sojourn time and the screening sensitivity. The mean sojourn time is the average length of time that a tumour is detectable in the preclinical phase by the screening test or as well called pre-clinical detectable phase of the tumour (PCDP).

In relation to the detection rate, there is a well-established difference between prevalent and incident screening. In the prevalent screen, large prevalence pools of cancers are detected, always conditioned by the screening test sensitivity. Then, for the incident screening, many of the prevalent cancers have already been detected at the previous screen, so the detection rate at the incident screen may be smaller than at the prevalent screen (9).

In United Kingdom (UK) the targets for cancer detection rates have been set by using data from the Swedish two county randomised controlled trial, and applying the prevalence/incidence ratio to national incidence rates. The assumption under this targets definition was that if the screening programmes on average could reach the equivalent cancer detection rates as the Swedish two county trial, then the breast screening programmes would be able to achieve a comparable reduction in mortality from breast cancer (3).

2. Conceptual framework

The cancer detection rate concept

The detection rate is a frequently used quality standard for screening, either at prevalence (first) or incidence (subsequent) screens. In the European guidelines for quality assurance in mammography, the cancer detection rate is presented as a multiple of the background incidence (breast cancer incidence rate in absence of screening). The target is to detect at least three folds the background incidence at initial (prevalent) screen and one and half folds for the incident (subsequent) screens. Another way, to present the cancer detection rate is the number of cancers detected per 10,000 women screened (16).

An overall breast cancer detection rate represents the performance of screening programme but as well reflects the age structure of the population being screened. To provide a more sensitive measure of performance, the age-specific detection ratio per 5 years age groups is recommended. The age specific detection ratio has in the numerator the cancer detection rate by 5-year age groups and in the denominator the background expected incidence rate in the absence of screening.

\[
\text{Age specific detection ratio} = \frac{\text{Cancer detection rate in 5 - year age group}}{\text{Background expected incidence (5 y age group)}}
\]
The indirect standardisation by age

The distribution of the cancer detection rate at the prevalent screens varies within the target age groups, as the cancer detection rate is approximately twice as high for women aged 60-64 than those aged 50-54. In practice, a number of different methods can be used to allow different age distributions. The indirect standardization by age is indicated because there are main advantages over the other methods, such as direct standardisation or the calculation of age specific rates. The key advantages of indirect standardisation is that it is not affected by small numbers in individual categories and it does not require the knowledge of rates in individual age groups, which is not always available (3). Because of the different age distributions within the screened women, crude invasive cancer detection rates can be highly misleading (10).

The expected cancer detection rates

The expected cancer detection rate at the first (prevalent) screen is dependent on the background incidence rate and on the prevalence to incidence ratio, and takes into account the screening sensitivity. All these factors are age dependent (14).

The background incidence rate is used to derive the expected rate for invasive cancer, which can be obtained by extrapolation of trends in incidence observed before the start of the screening programme.

The trends in breast cancer incidence can be estimated by poisson regression (Breslow and Day, 1987), in which the logarithms of the age-specific incidence rates are assumed to increase linearly over calendar time (9).

For the period after the introduction of the screening programme, the background incidence estimation can be done by extrapolation of the incidence rate by linear and log-linear modelling. This later correction is necessary because screening itself will cause an increase in incidence rates (3).

An approximate estimate of the prevalence/incidence ratio at a given age can be calculated by modelling the log of the prevalence to incidence ratio, with the midpoint age of the three age groups (50-54, 55-59, 60-64). The expected cancer detection rate for the screening programme at any age can be calculated by multiplying the prevalence/incidence ratio by the estimated background incidence at that age. The data from the Swedish Two county (STC) study have been used in the UK screening programme for the estimation of the prevalence/incidence ratio, as presented in table 1.

Table 1 - Prevalence to incidence (P/I) ratio for invasive cancers by age group (data from Swedish two county study)

<table>
<thead>
<tr>
<th>Age group</th>
<th>P/I ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-54</td>
<td>2.21</td>
</tr>
<tr>
<td>55-59</td>
<td>2.86</td>
</tr>
<tr>
<td>60-64</td>
<td>3.67</td>
</tr>
</tbody>
</table>
The prevalence at first screen to incidence ratio will be approximately equal to the sensitivity of screening multiplied by the mean sojourn time. The sojourn time is the length of time a preclinical breast cancer lesion is detectable by the screening test.

\[
P/I \text{ ratio} = \frac{\text{Prevalence at first screening}}{\text{Expected incidence rate}} = \text{sensitivity} \times \text{mean sojourn time}
\]

The estimated reduction in breast cancer mortality based on participation rates and cancer detection rate

Cancer detection rates are the first indicator of screening performance and, if monitored on an annual basis, give the earliest information on achievable mortality reduction. Correction actions can be taken early, rather than waiting for other indicators, such as interval cancer rates, which can be measured only several years later.

If we want to estimate the expected reduction of mortality, we need first to calculate the programme uptake. The programme uptake is the comparison of the programme participation to the reference participation in the STC trial, which was in average 90%. As example, if we have a programme with an average participation rate of 70%, the estimated uptake will be 0.7/0.9 or 0.78.

Further, to estimate the expected reduction in mortality, the programme uptake is multiplied by the STC estimated reduction in mortality of 30%. In the same example, 0.78*0.30 = 23%, meaning that the mammography screening programme can prevent 23% of the breast cancer mortality.

The best estimate of the breast cancer mortality reduction takes into account the screening programme standardised cancer detection ratio (SDR). By this method, the breast cancer mortality reduction is estimated by the product of the programme uptake, the standardised detection rate and the STC expected breast cancer reduction. As example, taking the UK screening programme 1993-1994 round, when the SDR was 0.83, the expected reduction in mortality could be estimated as \((0.70/0.90) \times 0.83 \times 30\% = 19.4\%\). Further on time, in the screening round 1999-2000, assuming constant participation (70%), but with an improvement in cancer detection, the SDR became 1.14, producing an increase in the expected reduction in mortality as: \((70/90) \times 1.14 \times 30\% = 26.6\%\).

**Figure 1 – Observed and expected numbers of invasive cancers in women aged 50—64 in UK and the modelled mortality reduction, 1993-2000.**

<table>
<thead>
<tr>
<th>Screening year</th>
<th>Participation (%)</th>
<th>Observed</th>
<th>Expected (%)</th>
<th>SDR</th>
<th>Mortality reduction (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1993-1994</td>
<td>77.40</td>
<td>4447</td>
<td>5344,6</td>
<td>0.83</td>
<td>19.40</td>
</tr>
<tr>
<td>1994-1995</td>
<td>76.00</td>
<td>4452</td>
<td>4952,5</td>
<td>0.90</td>
<td>21.00</td>
</tr>
<tr>
<td>1995-1996</td>
<td>76.00</td>
<td>4486</td>
<td>4725,5</td>
<td>0.95</td>
<td>22.20</td>
</tr>
<tr>
<td>1996-1997</td>
<td>75.30</td>
<td>4833</td>
<td>4799,7</td>
<td>1.01</td>
<td>23.6</td>
</tr>
<tr>
<td>1997-1998</td>
<td>75.30</td>
<td>5187</td>
<td>4964,2</td>
<td>1.04</td>
<td>24.3</td>
</tr>
<tr>
<td>1998-1999</td>
<td>76.00</td>
<td>5744</td>
<td>5064,2</td>
<td>1.13</td>
<td>26.4</td>
</tr>
<tr>
<td>1999-2000</td>
<td>78.60</td>
<td>5795</td>
<td>5076,6</td>
<td>1.14</td>
<td>26.6</td>
</tr>
</tbody>
</table>
As we can see, by the SDR values, the invasive cancers detection rate was inadequate in the early years of the UK programme, as it was confirmed by the high rates of interval cancers. This low rate was not perceived earlier partly because of high rate of detection of ductal carcinoma in situ (DCIS), which contributed to achievement of what was considered to be an “adequate cancer detection rate”.

3. Definition

The SDR is defined as the observed number of screen detected invasive cancers divided by the expected number invasive cancers. A breast invasive cancer is considered as a cancer that the cells have disseminated beyond the basal membrane of the galactophore or lobule of the breast.

The SDR measures the ratio of screen detected invasive cancers to the number expected, if the individual screening programmes was detecting invasive cancers at a similar rate as achieved by the Swedish two county randomised controlled trial.

An SDR of 1 would indicate that the observed number of invasive cancers is the same as that expected, greater than 1 would indicate higher, and less than 1 lower than the Swedish two county study. A standardized detection ratio of less than 0.75 was taken to indicate a possible under-performance and the need for a visit by quality assurance staff (13).

4. Calculation and data sources

For the monitoring of the screening programmes performance, Blanks in 1996 introduced the method to calculate the standardised detection ratio, as:

\[
SDR = \frac{\sum I_i}{\sum S_i R_i}
\]

Where
- \(I_i\) = number of screen detected invasive cancers in each age stratum,
- \(S_i\) = the number of women of each age stratum screened
- \(R_i\) = the expected rate, for each age stratum.

The \(I_i\), the screen detected invasive cancers can be provided by the screening programmes or by means of data linkage with the cancer registry and represents the observed or screening-detected invasive cancers.

The women screened per age stratum are the participants per screening round, information available in the records of each screening programme for prevalent and incident screens.

The breast cancer background incidence rate is used to estimate the expected cancer detection rate (\(R_i\)). The incidence rates, prior to 2001 available at the cancer registry, could be used to develop the model to estimate the background incidence before the organised screening started in Belgium.

Geographical variation of breast cancer incidence
Another important aspect in the estimation of the background incidence rate is the possible geographical variation of the breast cancer incidence between different individual screening programmes. The spatial coverage of the screening programmes can be different, being: urban, rural or a combination of both.

The UK NHS breast cancer evaluation unit developed a method to introduce background correction factors to improve the accuracy of either crude invasive cancer detection rates or the standardised detection ratio (SDR)(4).

Following this method, the SDR can be corrected for the background risk by multiplying the expected number of cancer by the background correction factor. To produce the correction factor for a screening programme, the catchment area must be characterised. These estimates can be achieved by using population statistics to weight the geographical unity (commune, province, region) relative risk and the catchment areas figures. When the background incidence analysis for individual programmes in the UK was done after the application of correction factors, the changes in the SDR values had varied of maximum of 15%.

5. Additional information

5.1. Type of information provided

This indicator measures the sensitivity of the screening programme, how many of the expected cancers are being actually detected by the programme (screening performance).

It is a useful instrument for timely estimates of screening performance and can result in rapid implementation of quality assurance checks, if the resulting ratio is found to be lower than 1.

By achieving equivalent cancer detection and interval cancer rates to those in the Swedish Two County trial, the equivalent mortality reduction should also be achieved (2) (3) (10).

Further the SDR was used on the setting of cancers detection standards related to the size of the invasive tumours. Like this, the NHS breast-screening programme has established a target for: a SDR (SIC) for small invasive cancers and a SDR (LIC) for large invasive cancers was established (6). Further information can be obtained in the chapter on the proportion of invasive small cancers.

The measurement of the invasive cancer detection rate is important because in the early years of the screening programmes an unexpected high detection of non-invasive cancers (ductal carcinoma in situ) had been previously described (7).

Further, the use of crude rates rather than standardized rates might lead to falsely reassuring cancer detection rates, which can mask a low sensitivity for small invasive cancers (5).

5.2. Data available from other countries

The National Health Services (NHS) in United Kingdom used the SDR to monitor the performance of different programmes, and to reorient the quality assurance programme to
increase the detection of small invasive cancers. It was defined to assess the capacity of the screening programme to reach the target of 25% reduction of breast cancer mortality (4). During the screening round, 1998/1999, the SDR was 1.11, ranging from 0.61-1.63, 76(80%) of the 95 individual screening programmes achieved an SDR above 1(5).

When the cancer detection trend was studied in the UK, the results have shown an increase of 36% in the SDR, going from 0.83 to 1.13 over the period of 1993/94 to 1998/99 (5).

During the evaluation of 1999-2000 in the New Zealand screening programme, the cancer detection rate was 6/1.000 women screened, the expected incidence among these women in absence of screening was 2.4/1.000 and the SDR was 0.90(0.81-0.99) for 2000(17).

5.3. Situation in Flanders

If we take as example the participation in the screening in Flanders during 2002-2003, we could estimate the reduction in mortality when the programme had a 33% participation rate. If the uptake will be 0.37 (0.33/0.90), the reduction of mortality that can be attributed to screening mammography will be equal to: 0.37*30%=11%. In this case we considered a SDR equal to one, or that the screening programmes in Flanders are achieving the same cancer detection rate as the Swedish two county trial.

6. Objective and target

The objective is to reach a 30% breast cancer mortality reduction by increasing the invasive cancer detection rate until the standardized detection ratio (SDR) reaches the target value of 1.

7. Strengths and Limitations

**Strengths**

- A surrogate indicator used for the estimation of the likely final reduction in breast cancer mortality by screening (19)
- Determines the performance of the screening programme, incorporating age standardization and cancer detection targets for the screening programmes in reference to the Swedish two county study (STC) (3).
- It allows for geographical differences in breast cancer rates, which might reflect different incidence rates or the completeness of cancer registration in different regions.

**Limitations**

- Depends on the accuracy of the expected rates, which is dependent of the knowledge of the background incidence in the absence of screening (3)
- It is difficult to estimate the exact contribution of screening towards reduction in breast cancer mortality, because other factors contribute as well towards the decrease in mortality. Other factors influencing the mortality trends include breast cancer awareness, use of screening before mass programmes were available, improved therapies, specially the systematic adjuvant therapy (introduced in the
1980) and cohort effects(18). The cohort effect is the study of the mortality by birth cohorts. When Arbyn et al, studied the Belgium breast cancer mortality trend, it was found that the breast cancer mortality increased for all cohorts until those born in 1940, and onwards the tendency was towards reduction (2).

- Sophisticated calculation which request the preliminary measurement of the screening programmes performance indicators (participation rate, cancer detection rate, background incidence rate, sensitivity, screening interval)

8. Importance for the decision makers

**Screening programme project cycle**

Another aspect of the SDR calculation is the expected contribution for the screening programme performance evaluation. After an initial phase when the individual screening programmes were organised, and the participation rate was the main indicator of programme performance. The next step, following the programme cycle, is the implementation of the monitoring to assure the screening quality that can be expressed as the cancer detection rate or the programme sensitivity.

The SDR calculation, as the measure of the individual programmes capacity to detect invasive cancers, requires that the screening programmes and the screening centres must be able to define the complete set of performance indicators: participation rate, cancer detection rate, background incidence rate, sensitivity, screening interval.

**Cost benefit analysis**

When few years ago the decision was taken to implement the breast cancer-screening programme, the basic assumption was to adopt of a cost-effective public health intervention that could reduce at least 30% of the breast cancer mortality of women aged 50-69 years old in Flanders.

The key information to orient the resources allocation by decision makers and public health managers is the amount of funds expends to implement a public health intervention by the expected benefit. When the cost-benefit analysis takes into account a cancer-screening programme, the balance will be between the budget allocated and the number of lives saved.

By the calculation of the standardised detection rate by individual screening centre and at the level of the Flanders community, the expected reduction in breast cancer mortality could be estimated. As consequence, we could predict the estimated number of lives saved per women invited and/or screened in Flanders.

**Example of messages that could be used to orient decision makers or public health managers:**

The Finish screening programme, proposed the following estimations to orient decision makers and public health managers: (11)

- The number of cancer deaths prevented per screen (estimated to be 4 deaths per 10,000 screens)
- Life span gained per breast cancer death prevented (estimated to be 15 years)
- Life span gained per patient with breast cancer detected by screening (estimated to be 1.5 years)
- Life span gained per screen (estimated to be 2.2 days, which can be compared with the estimated half day spent by a women attending for screening)
- Life span gained per invitation to screening, per member of the target population of women (estimated to 1.9 days)

In a new analysis of the STC trial, Tabar et al, found that to save one life from breast cancer is necessary to screen 465 women on average of three times over seven years period or presented in a more easy way, the estimated number of mammography examinations needed to save one life was therefore 1.499 (95% CI 1.046 – 2.642)(21).

When the evidence about the breast cancer screening was evaluated in a meta-analysis of eight randomized trials, by the U.S. preventive services task force, the combined relative risk reduction found was 0.81 (95% CI 0.73 - 0.89), and the number of women 50-69 years old needed to invite to screening was 1.008 (95% CI 531-2.128)(12).

9. Annex: Another method to calculate the expected cancer detection rate at prevalent and incident screens

In 2005, during the process of setting the new targets for the cancer detection in the UK NHS breast cancer screening programme, a more advanced method was applied to estimate the expected cancer detection rates (9).

The expected detection rate at prevalent screens (P)

The following formula was used to calculate the expected detection rate at prevalent screens (P):

\[ P = IMS \]

Where:

\( I \) = background incidence  
\( M \) = mean sojourn time (MST)  
\( S \) = screening test sensitivity

The expected detection rate can be estimated per age group when we assume that within each stratum the incidence and MST are roughly homogeneous. Tabar et al found the mean sojourn time (MST) of 3.7 and 4.2 years for the age groups 50-59 and 60-69 years, respectively. In the age group 50-64 years, typical estimates of the MST are around 3-4 years and sensitivity is generally high, between 85-90%.(15).
The size of the cancers detected at prevalent screen (prevalence pool) will be equal to the incidence (I) multiplied by the average time the tumours spent in the preclinical detectable phase (M). The (S) sensitivity will be the proportion of these tumours detectable at first screen.

The proportional detection rate will be equal to the mean sojourn time times the screening test sensitivity.

\[ P_s = MS \]

At incidence screens, the estimation of the expected detection rate is more complicated. Assuming a steady-state incidence screening, the programme sensitivity, is the proportion of tumours diagnosed within the programme that are screen-detected, calculated by

\[ S_p = \frac{S}{\lambda r (1 - e^{-\lambda r})} \]

Where:
- \( r \) = screening interval in years
- \( \lambda = 1/M \), or the rate of transition from preclinical to clinical disease phase (sojourn time)

If \( Q \) is the expected detection rate of tumours at an incidence screen, we have

\[ Q = IrS_p \]
Therefore,

\[
Q = S \left(1 - e^{\frac{\lambda_i}{1-(1-S)^{\lambda_i}}}\right)
\]

To obtain the proportional detection rate at incident screens, we divide by the background incidence rate (I)

\[
Q = S \frac{(1 - e^{\frac{\lambda_i}{\lambda}})}{\left(1 - e^{\frac{\lambda_i}{\lambda}}\right)}
\]
10. References


