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Current Perspective

Overdiagnosis in breast cancer screening: The impact of study design and calculations

Elsebeth Lynge [a,*], Anna-Belle Beau [a], Peer Christiansen [b], My von Euler-Chelpin [a], Niels Kroman [c], Sisse Njor [d], Ilse Vejborg [c]

[a] Department of Public Health, University of Copenhagen, Øster Farimagsgade 5, DK 1014 København K, Denmark
[b] Plastic and Breast Surgery, Breast Surgery Unit, Aarhus University Hospital/Randers Regional Hospital, Norrebrogade 44, DK 8000 Aarhus C, Denmark
[c] Copenhagen University Hospital, Rigshospitalet, Copenhagen, Blegdamsvej 9, DK 2100 København K, Denmark
[d] Department of Clinical Epidemiology, Aarhus University, Olof Palmes Allé 43-45, DK 8200 Aarhus N, Denmark

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Abstract Overdiagnosis in breast cancer screening is an important issue. A recent study from Denmark concluded that one in three breast cancers diagnosed in screening areas in women aged 50–69 years were overdiagnosed. The purpose of this short communication was to disentangle the study's methodology in order to evaluate the soundness of this conclusion. We found that both the use of absolute differences as opposed to ratios; the sole focus on non-advanced tumours and the crude allocation of tumours and person-years by screening history for women aged 70–84 years, all contributed to the very high estimate of overdiagnosis. Screening affects cohorts of screened women. Danish registers allow very accurate mapping of the fate of every woman. We should be past the phase where studies of overdiagnosis are based on the fixed age groups from routine statistics.

1. Introduction

When it comes to evaluation of breast cancer screening, Denmark is in a particular position. A population-based screening program was offered to around 20% of Danish women up to 17 years before it was offered to the rest of Danish women. This allows for comparison of women exposed and women not exposed to screening. The

* Corresponding author.
E-mail address: elsebeth@sund.ku.dk (E. Lynge).

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screening program targeted women aged 50–69 years, and opportunistic screening was rare. On this basis, several studies have been undertaken on the impact of screening on breast cancer mortality [1–3], and overdiagnosis [4–6].

Recently, Jørgensen *et al.* [7] published a new Danish study on overdiagnosis. This study was based on the number of breast cancers divided into advanced (>20 mm in tumour diameter) and non-advanced cases. Person-years were estimated from the official Danish statistics. Incidence rates were calculated for women aged 35–49, 50–69 and 70–84 years and for two geographical areas (screening and non-screening area) and two periods (before and after screening started). The study concluded that 'one in every three women aged 50–69 years diagnosed with breast cancer was overdiagnosed in the screening area'.

If true, breast cancer screening in Denmark causes considerable harm and would be unjustified as a public health policy. It is therefore important to understand the analysis behind the conclusion by Jørgensen *et al.* With this purpose in mind, we looked into the details of the methodology. Jørgensen *et al.* estimated overdiagnosis in breast cancer screening in Denmark using two approaches, and we discussed them one by one.

2. Jørgensen approach 1

First, overdiagnosis was calculated based on absolute difference in changes of breast cancer incidence rates: (absolute difference between after and before in screening area)−(absolute difference between after and before in non-screening area) as numerator, and the incidence rate in the after period in the non-screening area as denominator. For women aged 50–84 years, this gave ([351.3−226.1]−[280−182.4])/280 = 0.099 or 9.9% (Jørgensen Table 3). All incidence rates were per 100,000, but for simplicity, we omitted the 'per 100,000' from both numerator and denominator.

However, the absolute difference in an outcome between an exposed and a non-exposed group cannot be used as a measure of the strength of the association between the exposure and the outcome. The size of the absolute difference depends not only on the changes over time but also on the levels before. Let us illustrate this with an example. In the data by Jørgensen *et al.*, (Jørgensen Table 3) for women aged 50–84 years, the incidence rate before screening was 226.1 in the screening area and 182.4 in the non-screening area. If both incidence rates increased by 10% they would become 248.7 and 200.6, respectively. The two areas had then undergone exactly the same changes over time, and the ratio of the rate ratios would be 1.00, but the absolute difference would be 4.4.

The actual impact of screening on breast cancer incidence would therefore be better measured with the ratio of rate ratios than with the absolute difference (Table 1). In the data by Jørgensen *et al.*, the ratio of the rate ratios was 1.01 (i.e. [351.3/226.1]/[280/182.4]) (Jørgensen Table 3). This would indicate an overdiagnosis of 1%, as compared with the overdiagnosis of 9.9%, Jørgensen *et al.* calculated from the absolute difference. Both calculations are, however, problematic due to limitations in the study design used by Jørgensen *et al.*, see in the following section.

3. Jørgensen approach 2

Second, overdiagnosis was calculated from the increase in non-advanced tumours in women aged 50–69 years. Advanced tumours were disregarded in the calculation for two reasons. The first reason was because the rate 'did not decrease in the screening area when incidence trends among women aged 35–49 years were accounted for'. For advanced tumours, the ratios of the rate ratios were 0.48, 0.66 and 0.69, respectively, for women aged 35–49, 50–69 and 70–84 years (Jørgensen Table 2). So, there was a decrease in all age groups, but the authors' argument seems to be that given a decrease in the rate in women below screening age, screening could not explain the decrease in the rate in women above screening age. The change in women below screening age is of course interesting but hardly tells about impact of screening.

The second reason for disregarding advanced tumours was because 'there was no compensatory decrease in the incidence of advanced tumours in older women'. Older women are here women aged 70–84 years. However, in older women, the ratio of the rate ratios for advanced tumours did in fact decrease more in screening than in non-screening areas; (154.8/124.0)/(162.2/89.7) = 0.69 (Jørgensen Table 2; 95% confidence interval 0.63–0.75, our calculation). It therefore seems strange that the authors found that overdiagnosis could be estimated based solely on data for non-advanced tumours.

In the second approach, the numerator was the absolute difference in changes of incidence rates in non-advanced breast cancer and the denominator was the incidence rate of advanced and non-advanced breast cancer in the non-screening area. For women aged

Table 1
Incidence rates of breast cancer per 100,000 person-years among women aged 50–84 years and changes over time calculated as a difference and as a ratio (data from Jørgensen, Table 3).

Area	Before	After	Difference	Ratio
Screening	226.1	351.3	125.2	1.55
Non-screening	182.4	280.0	97.6	1.54
Screening versus non-screening			27.6	1.01
Estimated overdiagnosis			9.9%[a] (i.e. [27.6/280] × 100)	1%

[a] The estimate of overdiagnosis by Jørgensen *et al.*