



Original Research

Advanced breast cancer rates in the epoch of service screening: The 400,000 women cohort study from Italy



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Received 4 October 2016; received in revised form 7 December 2016; accepted 20 December 2016

Available online 20 February 2017

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<http://dx.doi.org/10.1016/j.ejca.2016.12.030>

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KEYWORDS

Mammography screening;
Advanced breast cancer;
Screening attendance;
Self-selection bias;
Cohort study;
Screening effectiveness

Abstract Background: The objective of this study was to evaluate if mammography screening attendance is associated with a reduction in late-stage breast cancer incidence.

Methods: The cohort included over 400,000 Italian women who were first invited to participate in regional screening programmes during the 1990s and were followed for breast cancer incidence for 13 years. We obtained individual data on their exposure to screening and correlated this with total and stage-specific breast cancer incidence. Socio-economic status and pre-screening incidence data were used to assess the presence of self-selection bias.

Results: Overall, screening attendance was associated with a 10% excess risk of *in situ* and invasive breast cancer (IRR = 1.10; 95% confidence interval (CI): 1.06–1.14), which dropped to 5% for invasive cancers only (IRR = 1.05; 95% CI: 1.01–1.09). There were significant reductions among attenders for specific cancer stages; we observed a 39% reduction for T2 or larger (IRR = 0.61; 95% CI: 0.57–0.66), 19% for node positives (IRR = 0.81; 95% CI: 0.76–0.86) and 28% for stage II and higher (IRR = 0.72; 95% CI: 0.68–0.76). Our data suggest that the presence of self-selection bias is limited and, overall, invited women experienced a 17% reduction of advanced cancers compared with pre-screening rates.

Conclusions: Comparing attenders' and non-attenders' stage-specific breast cancer incidence, we have estimated that screening attendance is associated with a reduction of nearly 30% for stages II+.

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1. Introduction

Mammography screening has a potential to reduce breast cancer (BC) mortality, as confirmed by recent reviews of randomised screening trials and of observational studies of service screening in Europe [1,2]. In principle, the effect of mammography screening on BC mortality can occur only through the early detection of potentially life-threatening cancers before they metastasise, thus reducing the incidence of advanced cancers. For this reason, the incidence of advanced cancers in the target population can be considered an early surrogate of the effectiveness of a screening programme [3]. Moreover, since diagnosis is independent of treatment, monitoring advanced cancers helps to disentangle the effects of screening from improvements in treatment. This aspect has been raised as crucial to demonstrate the efficacy of mammography screening [4,5].

The study reported here is a development of the IMPACT project, an Italian national endeavour to evaluate the results of regional mammography screening programmes. The major IMPACT investigations have revealed a 25% decrease in BC mortality [6] and a 20–30% decrease in the incidence of pT2 or greater BC in the target population [7]. The latter study was designed as a temporal correlation study. To confirm that the observed association had not been a spurious one, we conducted a prospective cohort study of the more than 400,000 Italian women who were invited to participate in some regional screening programmes. We determined their exposure to screening using individual data and correlated it with total and stage-specific BC incidence.

2. Methods

In Italy, mammography screening programmes were generally introduced during the second half of the 1990s, offering high-quality mammography every two years to all resident women aged 50–69 years. Their annual performance measures are published by the National Centre for Screening Monitoring [8].

2.1. Definition of the cohort and screening exposure

Nine health care districts in central and northern Italy participated in this study. The cohort included all women 50–69 years old who were invited to the first round of their local mammography screening programme. The screening histories of all women in the cohort, including the dates of invitations and, if any, of screening tests following these invitations, were extracted from the local computerised screening databases.

The definition of exposure to screening was based on a woman's attendance at the first two screening rounds as follows: *attender*, if she responded to at least one of the two invitations; *non-attender*, if she responded to neither of them. For the women invited only to the first round ($n = 73,173$) because they were not eligible for the second (due to recent spontaneous presentation, reaching of upper age limit, migration, BC detection or death), screening exposure was defined as *attender* or *non-attender* on the basis of the attendance at the first round.

2.2. Statistical methods

All women were followed-up for BC incidence through links to local cancer registries, as recommended by the

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