



Position statement

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This position statement has been endorsed by the Australian Health Ministers' Advisory Council Standing Committee on Screening, Cancer Council Australia and the Royal Australian and New Zealand College of Radiologists, and is supported by the Cancer Australia Advisory Council.

Context

National Breast and Ovarian Cancer Centre* first released a position statement on overdiagnosis from mammographic screening in 2008, followed by an update in 2010. The present statement is a further update by Cancer Australia. This update was based on a review of the published scientific literature and incorporation of input from international and national experts in the field.

Cancer Australia position statements address significant clinical issues, emerging issues in cancer control and issues of ongoing interest, using the best available evidence. The purpose of this position statement is to provide evidence-based information on overdiagnosis from population-based mammographic screening for breast cancer. The intended audiences are cancer organisations, health professionals, medical colleges, media, and policy makers.

Definition

“Overdiagnosis” from breast screening does not refer to error or misdiagnosis, but rather refers to breast cancer diagnosed by screening that would not otherwise have been diagnosed during a woman’s lifetime.

“Overdiagnosis” includes all instances where cancers detected through screening (ductal carcinoma in situ or invasive breast cancer) might never have progressed to become symptomatic during a woman’s life, i.e., cancer that would not have been detected in the absence of screening. It is not possible to precisely predict at diagnosis, to which cancers overdiagnosis would apply.

Summary

- Cancer Australia supports the importance of mammographic screening in reducing breast cancer mortality.
- The national BreastScreen Australia Evaluation indicated a reduction in breast cancer mortality for the age group of 50-69 years of approximately 21-28% at the participation level of 56%.
- Participation in the BreastScreen Australia Program would result in around 8 deaths prevented for every 1000 women screened every two years from age 50 to age 74.
- A majority of breast cancers found through screening would be progressive and would become symptomatic within a woman’s lifetime if left untreated.
- It is likely that some screen-detected breast cancers (ductal carcinoma in situ or invasive breast cancer) might never have progressed to become symptomatic in a woman’s lifetime. Detection of these cancers is sometimes referred to as “overdiagnosis”.
- It is not possible to precisely predict at diagnosis, to which cancers overdiagnosis would apply.
- Estimates of overdiagnosis vary widely. Based on UK and European reviews, it is estimated that for every 1000 women in Australia who are screened every two years from age 50 to age 74, around 8 (between 2 and 21) breast cancers may be found and treated that would not have been found in a woman’s lifetime.
- Research is needed, including molecular and genomic research, to find means of identifying cancers



- that would be of minimal risk of progression and therefore could be managed more conservatively.
- Information about the benefits of mammographic screening as well as the risks, including overdiagnosis, can assist women to make informed decisions about screening participation.

Evidence for mammographic screening

Mammographic screening has been shown from randomised trials to reduce death rates from breast cancer.¹⁻¹² In 2002, the reduction was estimated by an Expert Group of the International Agency for Research on Cancer (IARC) to approximate 35% in 50-69 year old women who participated in regular screening. Since then, for screening participants of all ages, lower breast cancer reduction (25%) was estimated in a meta-analysis of trial data.¹³ From trial data¹³⁻¹⁵ for women invited to screening compared with women not invited, reductions of around 20% were estimated.

Evaluation of mammographic screening from observational studies in Australia has provided broadly consistent results that point to a higher reduction in breast cancer mortality in percentage terms¹⁷ from screening participation, than in the randomised trials. Studies from South Australia¹⁷ and Western Australia¹⁸ of screening participants compared to non-participants indicated a reduction in breast cancer mortality for 50-69 years ranging from 47-52%. A population study from New South Wales¹⁸ indicated a breast cancer mortality reduction for 50-69 years of 32% for a 70% participation rate. The national BreastScreen Australia Evaluation indicated a reduction in breast cancer mortality at a population level for the target age group of 50-69 years of approximately 21-28% at the participation level of 56%.^{19,20} Based on these studies, it is estimated that about 8 deaths would be prevented per 1000 women screened from age 50 through to 74 years, with the estimate ranging with the data source from 6 to 10.¹⁶⁻²⁰

Collective results from other countries are also broadly consistent with the 35% reduction estimated by the IARC Expert Group for screening participants in trials,²¹⁻⁴³ although with individual results varying from little or no benefit to reductions of up to 76%.

A recent review of screening service evaluations in Europe presented similar findings to the Australian results, indicating breast cancer mortality reductions in screening participants that were higher than estimated from the trial data.^{16-20,22,32,33,38,43}

The higher reduction in breast cancer mortality from observational studies than that estimated from randomised trial data may reflect advances in screening technology, but it is also probable that estimates were affected by self-selection to screening. Self-selection to screening may have resulted in an uneven distribution between screened and unscreened women, e.g., due to positive family histories of breast cancer, use of hormone replacement therapy, history of benign breast disease and other risk factors.

There has been international debate and differing conclusions about the contributions of screening and improvements in treatment to reductions over time in breast cancer mortality. One recent analysis interpreted breast cancer mortality trends by age to indicate that these reductions were mostly a result of treatment rather than screening.⁴⁴ However, statistical modelling analyses of national US data, using seven independent statistical models, gave a combined estimate that around half the mortality reduction was attributable to screening and half to treatment.⁴⁵ Analysis of data from one region in the UK provided similar estimates.⁴⁶

Mammographic screening and overdiagnosis

Mammographic screening reduces numbers of breast cancer deaths by bringing forward the date of diagnosis of breast cancers to improve outcomes and reduce mortality. However, some breast cancers detected through screening might never have progressed to become symptomatic during a woman's lifetime, a consequence of





which would be overdiagnosis and potentially overtreatment. Examples would include women with screen-detected cancers who die prematurely from accidents or other acute events, or from heart disease or other chronic diseases. In addition, there would be screen-detected cancers that may not progress for many years because of their biology.^{1,25,42,47,48} Rarely, cancers might regress without treatment, if left, although this would generally be regarded as an unlikely event.^{25,47,49,50}

Overdiagnosis is a statistical inference at the population level. Such inferences have a measure of uncertainty and can vary substantially, depending on underlying statistical assumptions and choice of research design.^{1,14} Overdiagnosis is not a visually identifiable clinical entity at the individual level. It is not possible to precisely predict at diagnosis, to which cancers overdiagnosis would apply. Therefore, the challenge for ongoing research is not whether the diagnosis is cancer, but whether we can identify which cancers may not require treatment.

Estimates of overdiagnosis

Differences in study design, methodology and assumptions bring different strengths and weaknesses that are open to debate and result in estimates of overdiagnosis that differ widely.

Researchers have interpreted data from the original mammographic screening trials differently,⁵¹⁻⁵⁸ with estimates of overdiagnosis varying widely.^{13,48,58-68} Estimates of overdiagnosis also come from studies outside trial settings and from simulation studies.^{46,69-113} Estimates from these sources also vary widely, depending on methodology and research assumptions, from near zero to as high as one lesion in every three.^{46,69,113}

Reasons why overdiagnosis estimates vary widely include:^{18,59,61,85,100}

- whether ductal carcinoma in situ (DCIS) is included with invasive breast cancer in the calculations;
- study design, whether randomised trial, observational study or modelling study;
- whether results apply to populations offered breast screening or only to individual women invited to breast screening, screening participants, regular screening participants or just screen-detected lesions;
- the age range of women screened and whether account is taken of any changes in incidence, independent of screening;
- whether adjustments are made for differences in breast cancer risk factors between screened and unscreened women and what estimates are used when making these adjustments;
- the duration for which women are followed after screening cessation;
- the estimates used for lead-time effects (i.e., the time diagnosis was brought forward through screening);
- whether account is taken of non-diagnostic mammography outside the screening program and how this is done;
- death rates from other diseases and hence variations in life expectancy at time of screening;
- screening quality; different screening policies and protocols, including policies for recall for assessment of women with screen-detected abnormalities, and extent of adherence of practice to these different policies.

While a range of 5-13% of all breast carcinomas (invasive and DCIS) was cited as a plausible estimate of extent of overdiagnosis in the first position statement of the former National Breast and Ovarian Cancer Centre, research publications since then have presented widely divergent estimates. Recent modelling studies confirm earlier results that higher levels of overdiagnosis would apply to DCIS than invasive breast cancers.^{74,101,113} A review of over 50 individual studies, reviews and evidence commentaries cited since 2010, indicated overdiagnosis estimates ranging from near zero to 35% of diagnosed lesions (invasive and DCIS). While the median figure was in the 5-9% range, irrespective of whether studies included only invasive cancers or DCIS as well, this figure masked a widely divergent bimodal range of estimates,^{46,69-113} including estimates from an Australian study that were at the high end of the range.⁸⁸

A recent landmark UK review confirmed a lack of reliable data and considerable uncertainty around the extent of





overdiagnosis and indicated that any estimate will be, at best, provisional.¹⁵ The provisional estimate of overdiagnosis from the UK Panel is in the range of 11-19%, expressed as a proportion of diagnosed cancers in women invited for screening. Another European review, including data from 7 countries, estimated overdiagnosis in the range of 1-10%, after adjusting for breast cancer risk and lead time.⁹⁷ Based on the UK and European reviews,^{15,97} it is estimated that for every 1000 women in Australia who are screened every two years from age 50 to age 74, around 8 breast cancers are found and treated that would not have been found in a woman's lifetime. This estimate of around 8 (between 2 and 21) breast cancers has been confirmed by results from cohort studies, including two cohort studies subsequently published in 2013.^{76,98,114}

Conclusion

Mammographic screening has been shown from randomised trials and from observational studies to reduce mortality from breast cancer.¹⁻¹² Evaluations of mammographic screening from observational studies in Australia and Europe have provided broadly consistent results and have indicated breast cancer reductions in screening participants higher than that estimated from trial data. The national BreastScreen Australia Evaluation indicated a reduction in breast cancer mortality at a population level for the target age group of 50-69 years of approximately 21-28% at the participation level of 56%.

“Overdiagnosis” from breast screening does not refer to error or misdiagnosis, but rather refers to breast cancer diagnosed by screening that might never have progressed to become symptomatic in a woman's lifetime. It is likely that despite uncertainties about the extent of overdiagnosis, there would be a subset of screen-detected invasive and pre-invasive cancers that would progress very slowly if at all. If distinguishing features could be identified for such cancers, it may be possible to determine subsets of cancers that may be treated more conservatively, if at all. Molecular and genomic research is needed to find means of identifying, with enough certainty, which cancers are at minimal risk of progression and therefore could be managed more conservatively.¹¹⁵⁻¹²⁷

Access to information about the benefits of mammographic screening as well as the risks, including overdiagnosis, can assist women to make informed decisions about screening participation.

Information about mammographic screening for women is available online: [BreastScreen and You](#).

*On 30 June 2011, National Breast and Ovarian Cancer Centre (NBOCC) amalgamated with Cancer Australia to form a single national agency, Cancer Australia, to provide leadership in cancer control and improve outcomes for Australians affected by cancer.

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