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Analysis of breast cancer outcomes and screening behaviour for BreastScreen Australia

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Analysis of breast cancer outcomes and screening behaviour for BreastScreen Australia

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Data for the National Death Index are provided to the Australian Institute of Health and Welfare by the state and territory registries of births, deaths and marriages and the National Coronial Information System (managed by the Victorian Department of Justice) and include cause of death coded by the Australian Bureau of Statistics.

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Abbreviations

ABS	Australian Bureau of Statistics
ACD	Australian Cancer Database
ACT	Australian Capital Territory
AIHW	Australian Institute of Health and Welfare
CCPHPC	Community Care and Population Health Principal Committee
CI	confidence interval
DCIS	ductal carcinoma in situ
HPV	human papillomavirus
HR	hazard ratio
IARC	International Agency for Research on Cancer
ICD-10	International Statistical Classification of Diseases and Related Health Problems, Tenth Revision
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
iFOBT	Immunochemical Faecal Occult Blood Test
NBCSP	National Bowel Cancer Screening Program
NCSP	National Cervical Screening Program
NDI	National Death Index
NHVPR	National HPV Vaccination Program Register
NSW	New South Wales
NT	Northern Territory
PPV	positive predictive value
Qld	Queensland
SA	South Australia
Tas	Tasmania
VCS	Victorian Cytology Service Foundation
Vic	Victoria
WA	Western Australia
WHO	World Health Organization

Symbols

χ^2	chi-square statistic
—	nil or rounded to zero
. .	not applicable
<	less than
>	greater than
≤	less than or equal to
≥	greater than or equal to
%	per cent
±	plus or minus
p	The probability that the observed difference or association could have occurred by chance alone. If that probability is less than 5% (0.05), it is conventionally held that the observed difference is unlikely enough to be due to chance that it is evidence of a true difference or association.

Summary

This is the second report from an Australian-first project, combining data from BreastScreen Australia, the National Cervical Screening Program, the National Bowel Cancer Screening Program, the Australian Cancer Database, the National Death Index, and the National HPV (human papillomavirus) Vaccination Program Register.

While the first report (AIHW 2018a) presented primary cancer outcomes for the target age groups for all three cancer screening programs, as well as examining screening behaviour across the three cancer screening programs, this report focuses on breast cancer outcomes and screening behaviour that are relevant to BreastScreen Australia.

Building on breast cancer outcomes for women in the BreastScreen Australia target age group of 50–69, these results also include age groups eligible to attend, but outside the target age group (note that the current target age group of 50–74 was not applicable to this project). Additionally, these results include outcomes using different correction factors for lead-time bias and screening selection bias that may be more appropriate for these Australian data. Screening behaviour analyses focus on key areas identified to be of particular interest and value to BreastScreen Australia.

The following analyses compare survival outcomes of breast cancers detected through BreastScreen Australia with breast cancers diagnosed in women who had never screened through BreastScreen Australia. For the years of data included, women aged 50–69 were targeted for screening, but were eligible to screen when aged 40–49 or 70 or over.

Breast cancers diagnosed in women targeted by BreastScreen Australia

Of the 73,440 breast cancers diagnosed in women aged 50–69 in 2002–2012:

- 31,968 (44%) were detected through BreastScreen Australia
- 20,245 (28%) were diagnosed in women who had never screened.

Breast cancers detected through BreastScreen Australia had a 69% lower risk of causing death before 31 December 2015 (the end of follow-up) than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

After correcting for lead-time bias (where an earlier diagnosis may not affect date of death, yet give a seemingly longer survival time) and screening selection bias (where women who participate in screening may have a different risk of death than those who do not) using lead times and correction factors deemed most appropriate for Australian women aged 50–69, breast cancers detected through BreastScreen Australia had a 54% to 63% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

This indicates that it is beneficial for a breast cancer to be detected through screening mammography rather than due to the breast cancer being symptomatic. This may be due to breast cancers detected through BreastScreen Australia being at an earlier stage than breast cancers that have become symptomatic.

Although it was not possible to know the stage of the breast cancers diagnosed in this study, tumour size (one of the three factors that determine stage, along with lymph node involvement and presence of distant metastases) was recorded for most breast cancers.

In this study, 55.3% of breast cancers detected through BreastScreen Australia were found to be small, compared with 27.6% of breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Breast cancers diagnosed in women eligible to attend, but not targeted by BreastScreen Australia

Of the 26,463 breast cancers diagnosed in women aged 40–49 in 2002–2012:

- 3,461 (13%) were detected through BreastScreen Australia
- 18,059 (68%) were diagnosed in women who had never screened.

Breast cancers detected through BreastScreen Australia had a 55% lower risk of causing death before 31 December 2015 (the end of follow-up) than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

After correcting for lead-time and screening selection bias using lead times and correction factors deemed most appropriate for Australian women aged 40–49, breast cancers detected through BreastScreen Australia had a 34% to 51% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Of the 37,568 breast cancers diagnosed in women aged 70 and over in 2002–2012:

- 6,893 (18%) were detected through BreastScreen Australia
- 20,627 (55%) were diagnosed in women who had never screened.

Breast cancers detected through BreastScreen Australia had a 64% lower risk of causing death before 31 December 2015 (the end of follow-up) than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

After correcting for lead-time and screening selection bias using lead times and correction factors deemed most appropriate for Australian women aged 70 and over, breast cancers detected through BreastScreen Australia had a 55% to 62% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Association between cervical screening participation and participation in BreastScreen Australia

Women who were regular participants in cervical screening were more likely to participate in, and become regular screeners in, BreastScreen Australia. This effect was strongest at the age of 50—the age at which women are first invited to screen through BreastScreen Australia.

Women already participating in cervical screening began participating in BreastScreen Australia earlier than those who were not. Cervical screening participants had a mean commencement age in BreastScreen Australia of about 50, while non-participants had a mean commencement age in BreastScreen Australia that was 5 to 10 years later than this.

Rescreening behaviour in BreastScreen Australia

Rescreening within 27 months (considered to be within the recommended screening interval of BreastScreen Australia of 2 years) was about 60% after a woman's first screening round. This was higher after their second screening round, at about 70%, and higher again after their third or subsequent screening round, at about 80%.

Factors associated with a woman not rescreening varied by screening round. Women who did not rescreen after their first screen were more likely to report symptoms, whereas women who did not rescreen after a third or subsequent screen were more likely to have been recalled to assessment for further investigation.

1 Introduction

1.1 Cancer screening programs in Australia

Disease screening is the use of a test in an asymptomatic population that is designed to identify individuals who are more likely to have a given disease and therefore require further diagnostic testing to determine if they have the disease. Because the screening test is used on individuals without overt signs or symptoms of the disease, screening is able to detect disease at an earlier stage, which can lead to better outcomes than if the disease was detected at a later stage.

Screening for a given disease should only progress if it meets the World Health Organization (WHO) principles of screening (Wilson & Jungner 1968). These screening principles are:

- the condition should be an important health problem
- there should be a recognisable latent or early symptomatic stage
- the natural history of the condition, including development from latent to declared disease, should be adequately understood
- there should be an accepted treatment for patients with recognised disease
- there should be a suitable test or examination that has a high level of accuracy
- the test should be acceptable to the population
- there should be an agreed policy on whom to treat as patients
- facilities for diagnosis and treatment should be available
- the cost of screening (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole
- screening should be a continuing process and not a 'once and for all' project.

Australia has built on these WHO criteria for population screening in developing the Australian Population Based Screening Framework that additionally takes into account:

- the need for a strong evidence base in making a decision about the introduction of a screening program including evidence of the safety, reproducibility and accuracy of the screening test and efficacy of treatment
- the requirement that a screening program offers more benefit than harm to the target population (CCPHPC 2016).

Australia currently has three population-based cancer screening programs that meet both the WHO principles and the additional considerations under the Australian criteria for the assessment of population screening (CCPHPC 2016). These are BreastScreen Australia for breast cancer, the National Cervical Screening Program (NCSP) for cervical cancer, and the National Bowel Cancer Screening Program (NBCSP) for bowel cancer. These programs all aim to reduce mortality from their respective cancer. The National Cervical Screening Program and the National Bowel Cancer Screening Program also aim to reduce the incidence of cervical and bowel cancer, respectively, through identifying and treating their precursors.

This report focuses on BreastScreen Australia. Results for the National Cervical Screening Program can be found in the AIHW report for all three screening programs (AIHW 2018a), and results for the National Bowel Cancer Screening Program can be found in this same AIHW report, as well as two AIHW reports specific to the program (AIHW 2014, 2018b).

1.2 Breast cancer screening reduces mortality

The principles of cancer screening include the requirement for evidence that a screening program is effective in reducing mortality from cancer (Cancer Council Australia 2017). This relates to the requirement that benefits of screening outweigh potential harms. Studies are required to assess mortality benefits due to screening, since assessing mortality trend data alone does not distinguish between reductions in mortality due to screening and reductions due to treatment advancements that have occurred over the same time period.

In considering the available evidence of the benefits of cancer screening, several studies have looked specifically at the Australian setting when considering whether participation in BreastScreen Australia reduces mortality from breast cancer.

Decreases in breast cancer mortality have occurred since BreastScreen Australia commenced. Advancements in treatment for breast cancer have contributed substantially to this decrease, along with the early detection of breast cancer through screening mammography. Several Australian studies, at both the jurisdictional and national level, have demonstrated a reduction in mortality in screening participants (DoHA 2009; Morrell et al. 2012; Nickson et al. 2012; Roder et al. 2008; Taylor et al. 2004).

Estimates from these Australian studies align with those based on international data; in 2015, the International Agency for Research on Cancer (IARC) conducted a full review of available high quality observational studies to ensure that evidence compiled in 2002, which showed a reduction in mortality as a result of screening mammography (IARC 2002), was still relevant today. The IARC determined that women aged 50–69 who attended breast cancer screening using screening mammography had about a 40% reduction in the risk of death from breast cancer (Lauby-Secretan et al. 2015), which is similar to Australian estimates.

More recently, the AIHW used linked data to demonstrate that screen-detected breast cancers in women aged 50–69 had a 42% lower risk of death from breast cancer than breast cancers diagnosed in women who had never screened (AIHW 2018a).

1.3 Participation in BreastScreen Australia

The AIHW reports on participation in Australia's three national cancer screening programs, including BreastScreen Australia. The latest participation data by population subgroup for BreastScreen Australia are shown in Table 1.3.1 (although the target age group for BreastScreen Australia has been widened to 50–74, women aged 50–69 are shown here so as to align with the rest of the data in this report, for which the target age group was 50–69).

Briefly, across remoteness areas, participation is highest in *Inner regional* and *Outer regional* areas; across **socioeconomic groups**, participation is lowest in the most disadvantaged socioeconomic group, but thereafter there is no clear trend; participation is far lower for **Indigenous Australians**, and participation is also lower for participants that report speaking a **language other than English** at home.

While these data provide insights into patterns of participation in BreastScreen Australia, there are many more aspects of screening behaviour that require data linkage to explore, knowledge of which would provide BreastScreen Australia with key data to optimise the recruitment, retention, and management of women in BreastScreen Australia.

Table 1.3.1: Participation in BreastScreen Australia by population groups, women aged 50–69, 2015–2016

Population group	Participation
State or territory	
NSW	52.8
Vic	53.9
Qld	55.9
WA	56.3
SA	58.9
Tas	57.3
ACT	57.7
NT	37.2
Remoteness area	
Major cities	53.7
Inner regional	56.6
Outer regional	57.1
Remote	52.8
Very remote	43.6
Socioeconomic group	
1 (most disadvantage)	51.9
2	54.9
3	54.5
4	55.3
5 (least disadvantage)	55.5
Indigenous status	
Indigenous	39.4
Non-Indigenous	54.6
Language spoken at home	
English only	55.0
Language other than English	51.6
Australia	**55.1**

Note: Participation data shown are for ages 50–69 in 2015–2016. Rates are age-standardised except for Australia, for which the crude rate is shown.

Source: AIHW analysis of state and territory BreastScreen register data (AIHW 2018c).

2 Objectives

This report is part of a broader cancer screening data linkage project, the objectives of which are detailed below. This report aims to fulfil these objectives for BreastScreen Australia.

2.1 Premise of the broader data linkage project

On examining the available research related to Australia's three cancer screening programs, while there have been a number of rich and high-quality studies, we identified the potential to make a significant additional contribution to these. By building on previous studies, identifying and filling data gaps, and performing novel studies, we aim to provide answers to key questions and a greater understanding of screening outcomes and behaviour across all three cancer screening programs in Australia. The opportunity was also taken to investigate the effects and effectiveness of the human papillomavirus (HPV) vaccine in Australia. This is possible due to the role of HPV in the development of cervical abnormalities (and ultimately cervical cancers), data for which were held on state and territory cervical screening registers.

To allow us to investigate the outcomes and screening behaviour of cancer screening programs in Australia, this major data linkage project was undertaken to link data from:

- the eight state and territory BreastScreen registers
- the eight state and territory cervical screening registers
- the National Bowel Cancer Screening Program Register
- the Australian Cancer Database
- the National Death Index
- the National HPV Vaccination Program Register.

These data sources are detailed in the 'Data and methods' chapter.

2.2 Objectives of the broader data linkage project

The data linkage project has three objectives.

Objective 1 Determine key cancer outcomes in screening and non-screening individuals to determine whether screen-detected cancers are less likely to result in death than cancers detected outside screening programs.

Objective 2 Gain an understanding of the screening behaviour of participants, such as who screens, in which programs, and whether this is influenced by any common factors such as socioeconomic status, history of positive test results, or other events.

Objective 3 Use the linked data to enhance currently available screening data, such as analysis of linked cervical screening and human papillomavirus (HPV) vaccination data to look at the effect of HPV vaccination on cervical abnormalities, cancers and participation in cervical screening.

2.3 Dissemination of findings from the broader data linkage project

Given the size and complexity of this data linkage project, dissemination of findings was carefully considered. It was concluded that the results of this project would be best disseminated over a series of reports, each with a particular focus, with other products used where appropriate to best communicate findings.

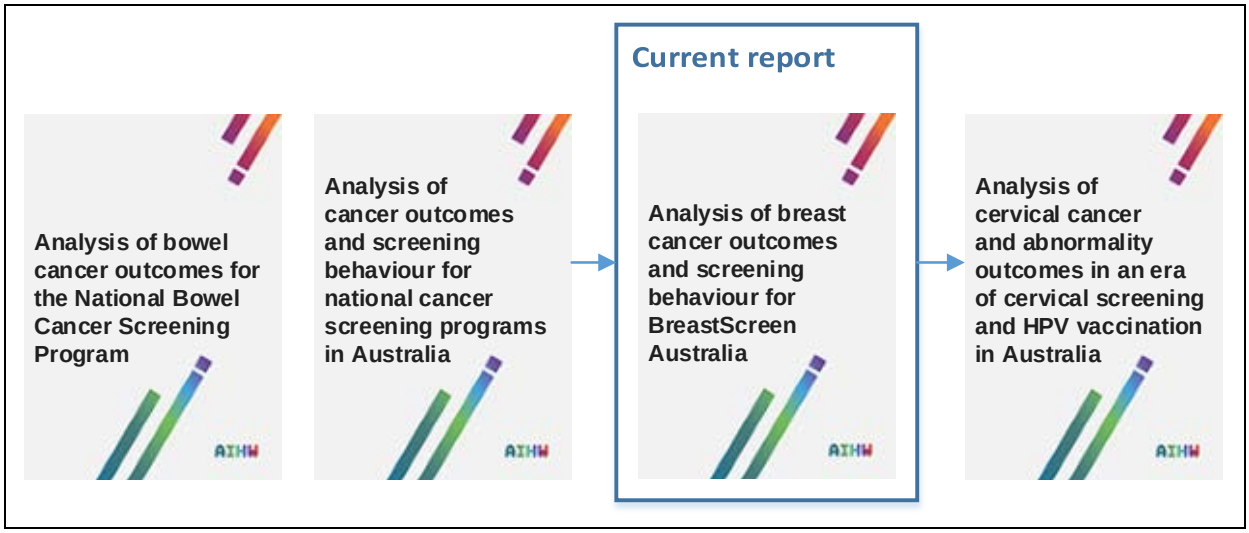
The first of these reports was *Analysis of cancer outcomes and screening behaviour for national cancer screening programs in Australia* (AIHW 2018a). It presented primary cancer outcomes for all three cancer screening programs, as well as examining screening behaviour across the three cancer screening programs. While contributing greatly to the pool of knowledge on the mortality benefits of participating in BreastScreen Australia, it noted that further investigations would be required to explore the study data in greater detail. These would include looking at age groups outside the target group (from ages 40 to 85+ instead of only ages 50–69), and investigating breast cancer outcomes in more detail by using different correction factors for lead-time bias and screening selection bias that may be more appropriate for these Australian data. They would also include screening behaviour analyses focused on key areas identified to be of particular interest to BreastScreen Australia.

Acknowledgement that progression of this work would broaden the knowledge base for key stakeholders within BreastScreen Australia and breast cancer researchers in Australia more broadly led to the development of this second report, *Analysis of breast cancer outcomes and screening behaviour for BreastScreen Australia* that includes additional breast cancer outcomes analyses, and screening behaviour analyses specific to BreastScreen Australia participants.

A third report, expected to be called *Analysis of cervical cancer and abnormality outcomes in an era of cervical screening and HPV vaccination in Australia*, will present more detailed analyses on cervical cancer outcomes and cervical screening behaviour as well as the effects and effectiveness of HPV vaccination in Australia.

All three will follow on from a report from a similar data linkage project specific to the National Bowel Cancer Screening Program initially released in 2014 and repeated in May 2018 (AIHW 2018b).

These four reports in combination will provide comprehensive reporting of cancer outcomes and screening behaviour for national cancer screening programs in Australia.



3 Data and methods

3.1 Data sources for the data linkage project

The broader data linkage project included data from six data sources (Table 3.1.1), with a total of 20 individual data sets combined to form the master linked data set (though this report only focuses on data sources specific to BreastScreen Australia, highlighted in the table below).

Table 3.1.1: Data sources

Data source	Data set	Data provider
BreastScreen Australia	BreastScreen NSW register data	Cancer Institute NSW
	BreastScreen Victoria register data	BreastScreen Victoria
	BreastScreen Queensland register data	Queensland Health
	BreastScreen WA register data	WA Department of Health
	BreastScreen SA register data	SA Department for Health and Ageing
	BreastScreen Tasmania data	Department of Health Tasmania
	BreastScreen ACT data	ACT Health
	BreastScreen NT	NT Department of Health
National Cervical Screening Program	NSW Pap test register data	Cancer Institute NSW
	Victorian cervical cytology register data	Victorian Cytology Service Foundation
	Queensland Health Pap smear register data	Queensland Health
	WA cervical cytology register data	WA Department of Health
	SA cervix screening register data	Victorian Cytology Service Foundation
	Tasmanian cervical screening register data	Department of Health Tasmania
	ACT cervical screening register	ACT Health
	NT Pap smear register data	NT Department of Health
National Bowel Cancer Screening Program	National Bowel Cancer Screening Program Register data	Department of Human Services
Australian Cancer Database	Australian Cancer Database	Australian Institute of Health and Welfare
National Death Index	National Death Index	Australian Institute of Health and Welfare
National HPV Vaccination Program	National HPV Vaccination Program Register data	Victorian Cytology Service Foundation

Further details about each of the six data sources follow.

BreastScreen Australia data

BreastScreen Australia is Australia's national breast cancer screening program, operational since 1991. BreastScreen services are delivered at the state and territory level. Eligibility is determined by age: women 40 and over can attend free 2-yearly mammograms, although only women in the target age group are actively targeted. From 1991, the target age group of BreastScreen Australia was women aged 50–69, widened to 50–74 from 1 July 2013.

To attend, a woman contacts BreastScreen in her state or territory to book a screening visit. At the time of her screening visit, a woman is able to self-report clinical details such as the presence and type of symptoms, as well as personal and family history of breast cancer.

Data for women who participate in BreastScreen Australia are collected and maintained on state and territory BreastScreen registers.

BreastScreen Australia data in this project are a subset of variables from each of the eight state and territory BreastScreen registers, for women screened between 1 January 2000 and 31 December 2014. The target group used for these data was women aged 50–69.

National Cervical Screening Program data

The National Cervical Screening Program is Australia's national cervical screening program, and began operating in 1991. There were substantial changes to the cervical screening program on 1 December 2017, including a change in screening test, screening interval and target age group. However, this project includes only data collected under the previous program, and so only the National Cervical Screening Program as it existed from 1991 to 30 November 2017 is described here and considered throughout this project.

Under the previous program, women were recommended to have 2-yearly Pap tests commencing between the ages of 18 and 20, or 1 or 2 years after first having sexual intercourse, whichever was later. Data for women who participated in the previous program were collected and maintained on state and territory cervical screening registers.

National Cervical Screening Program data in this project are a subset of variables from each of the 8 state and territory cervical screening registers that operated under the previous program, for women screened between 1 January 2000 and 31 December 2014. The target group used for these data was women aged 20–69.

National Bowel Cancer Screening Program data

The National Bowel Cancer Screening Program is Australia's national bowel screening program, and has operated since 1 August 2006. Eligibility to participate in this program is determined by age, with individuals who are registered as an Australian citizen or migrant in the Medicare enrolment file, or registered with a Department of Veterans' Affairs gold card, invited to screen when they reach one of the target ages. Invitees are sent an invitation pack containing an iFOBT kit (an immunochemical faecal occult blood test, the screening test of the National Bowel Cancer Screening Program) and can then choose to participate by completing the screening test at home and returning it to be processed in a pathology laboratory, or not to participate.

The target ages initially invited to screen in 2006 were people turning 55 and 65, with 50-year-olds added from July 2008. Since then, additional ages have been progressively invited to participate in the program, and from 2019, the National Bowel Cancer Screening Program will offer all Australians aged 50–74 bowel screening every 2 years.

Data on people who are eligible to be invited to participate in bowel screening appears on the National Bowel Cancer Screening Program Register. This national register is maintained by the Department of Human Services (formerly Medicare Australia) on behalf of the Department of Health. Bowel screening that occurs outside the National Bowel Cancer Screening Program is not included in the national register, and therefore this project.

National Bowel Cancer Screening Program data in this project are a subset of variables from the National Bowel Cancer Screening Program Register, for individuals invited between 1 August 2006 and 31 December 2014. As the target ages have changed over this period, invitations were used to determine screening eligibility. The target group used for these data was people aged 50–69.

Australian Cancer Database data

The Australian Cancer Database is a data collection of all primary, malignant cancers diagnosed in Australia since 1982. Data are collected by state and territory cancer registries from a number of sources and are supplied annually to the AIHW. The AIHW compiles and maintains the Australian Cancer Database, in partnership with the Australasian Association of Cancer Registries, which includes representatives from each state and territory cancer registry.

The Australian Cancer Database does not include: recurrences and metastases—only the first occurrence of a cancer is included; basal cell carcinomas (BCC) and squamous cell carcinomas (SCC) of the skin—these are not notifiable diseases; or benign, borderline malignancy or in situ tumours—this means that ductal carcinoma in situ (DCIS) and other breast in situ cases were unable to be included in this project.

The 2013 Australian Cancer Database was the latest version available at the time of data linkage for this project. This database includes cancer data to 2013 for all states and territories except New South Wales, for which cancer data was available only to 2012; therefore, only cancer incidence data from 1 January 1982 to 31 December 2012 were used.

Breast, cervical and bowel cancers were identified using International Statistical Classification of Disease and Related Health Problems, Tenth Revision (ICD-10) codes. Female breast cancers were defined as cancers coded in the ICD-10 as C50 where sex was female, cervical cancers were defined as cancers coded in the ICD-10 as C53 where sex was female, and bowel cancers were defined as cancers coded in the ICD-10 as C18–C20. The grouping of all cancers combined was defined as cancers coded in the ICD-10 as C00–C97, D45, D46, D47.1 and D47.3–D47.5.

National Death Index data

The National Death Index contains information on all deaths in Australia since 1980. It is maintained by the AIHW for the purpose of data linkage. The state and territory registrars of births, deaths and marriages supply these data monthly. While fact-of-death information is generally up to date in the National Death Index, underlying-cause-of-death information is usually some years behind. At the time of data linkage for this project, underlying-cause-of-death data contained in the National Death Index were available to 31 December 2015.

Deaths were considered to be from breast cancer if the ICD-10 code was C50; from cervical cancer if the ICD-10 code was C53, and from bowel cancer if the ICD-10 code was C18–C20 or C26.0 (Malignant neoplasm of the intestinal tract, part unspecified, which many bowel cancer deaths are coded as in Australia—ABS 2016). All-cause deaths were any deaths recorded, regardless of the underlying cause.

National HPV Vaccination Program data

The National HPV Vaccination Program was introduced on 1 April 2007 to immunise girls (and extended in 2013 to also immunise boys) against HPV types 16, 18, 6 and 11 (with an HPV vaccine against nine HPV types introduced from 2018). In addition to the ongoing school-based program introduced in 2007 for girls aged 12–13, and in 2013 for boys aged 12–13, there was a catch-up program for girls aged 14–26 in 2007–2009, and for boys aged 14–15 in 2013–2014.

HPV vaccination records are sent to the National HPV Vaccination Program Register by school or community providers, state or territory departments of health, and general practitioners, depending on whether the vaccine was administered through school or by

a general practitioner. The National HPV Vaccination Program Register is operated and maintained by the VCS on behalf of the Department of Health.

National HPV Vaccination Program data in this project are a subset of variables from the National HPV Vaccination Program Register, for females vaccinated between 1 April 2007 and 31 December 2014.

3.2 Data flow and data linkage methods for the data linkage project

Data flow

The AIHW Data Linkage Unit performed all data linkage for this project. To ensure privacy and confidentiality of participants, data suppliers sent two sets of data to the AIHW: the Data Linkage Unit was provided with identified data only, while the Cancer and Screening Unit (now the Screening Analysis and Monitoring Unit) was provided with deidentified analysis variables only. This ensured that no one person had access to both identified and analysis variables. Identification numbers common to both data supplies then allowed the Data Linkage Unit to inform the former Cancer and Screening Unit which individuals were common across the data sets. This data flow is illustrated in Figure 3.2.1.

Data linkage

The AIHW Data Linkage Unit performed probabilistic data linkage based on the method developed by Fellegi and Sunter (1969).

Briefly, data linkage across the data sets was carried out in a step-wise fashion using the identifying variables of name, sex, date of birth and postcode. In the first step, links in which the identifying variables matched exactly were accepted. In the second step, the identifying variables were allowed to vary, with all potential pairs given a weight based on the amount of variation between records and the discriminatory ability of the variable. A sample-based clerical review determined a cut-off weight to accept a link, and all potential pairs above this cut-off were accepted as true links. In the final step, all remaining potential pairs were checked manually to determine if they were likely to be a link.

This is a robust method of data linkage; however, it is important to note that, due to the nature of probabilistic data linkage, there may be some unavoidable inaccuracy in the data linkages.

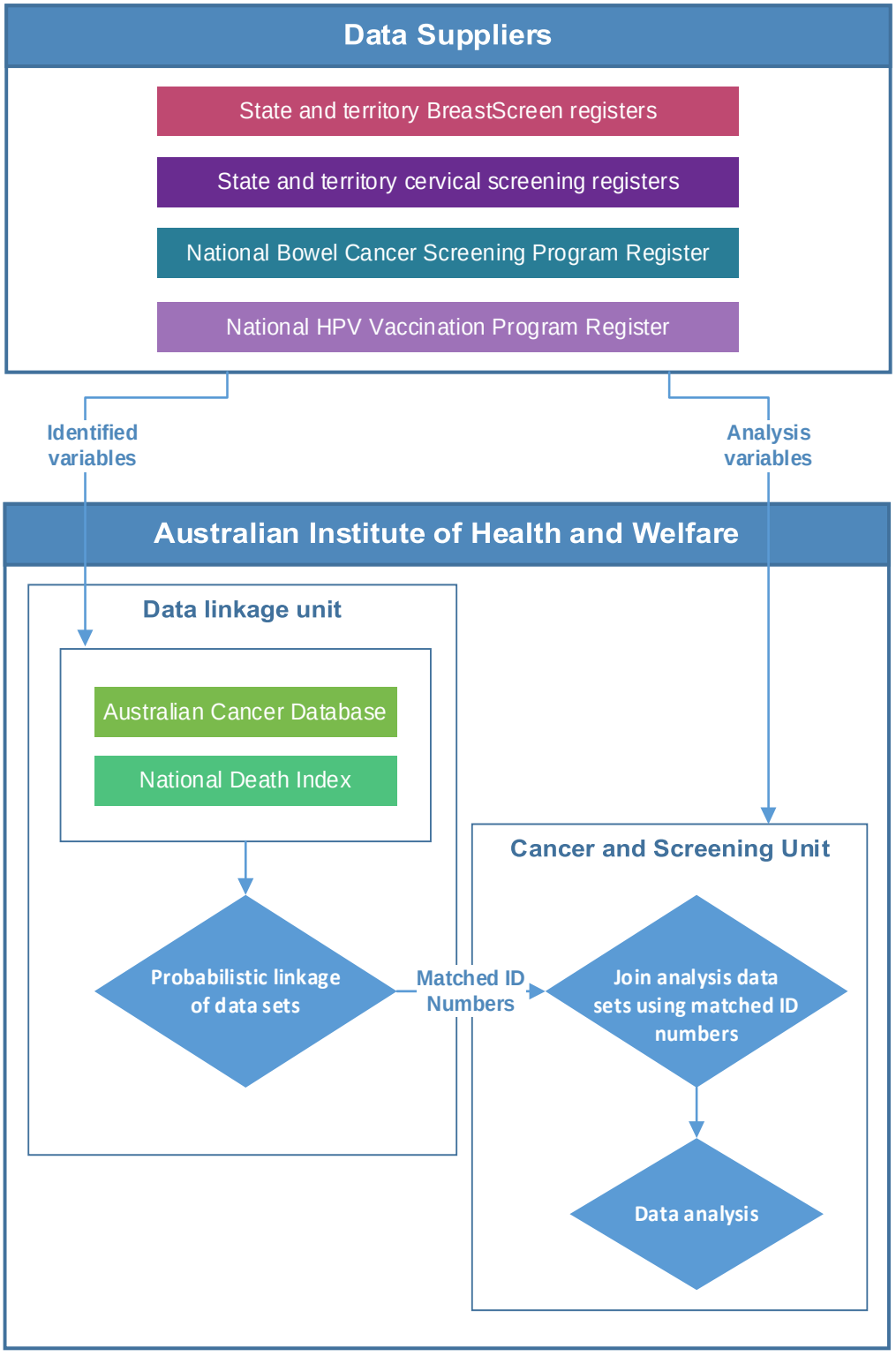


Figure 3.2.1: Data flow for the data linkage project

3.3 Methods used in this report

Statistical analyses

Retrospective cohort studies were undertaken to assess survival of screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Breast cancer survival by screening status

Breast cancers were identified on the Australian Cancer Database (coded in the ICD-10 as C50) in women aged 40 and over with a date of diagnosis between 1 January 2002 and 31 December 2012 inclusive. Because in situ tumours are not included on the Australian Cancer Database, the term breast cancers used throughout this report refers to invasive breast cancers only.

These breast cancers were linked with available data from BreastScreen registers (from 1 January 2000), and the screening history prior to each cancer used to assign a screening status to each breast cancer. These were:

- **Screen-detected cancers**—breast cancers diagnosed in 2002–2012 in women aged 40 and over who had a screening mammogram through BreastScreen Australia and the cancer was identified as screen-detected by BreastScreen Australia
- **Non-screen-detected cancers in screened women**—breast cancers diagnosed in 2002–2012 in women aged 40 and over who had a screening mammogram through BreastScreen Australia but the cancer was not identified by BreastScreen Australia as screen-detected or interval
- **Interval cancers**—breast cancers diagnosed in 2002–2012 in women aged 40 and over who had a screening mammogram through BreastScreen Australia and the cancer was identified as an interval cancer by BreastScreen Australia and/or the cancer met the BreastScreen Australia definition of an interval cancer using the available variables
- **Non-screen-detected cancers in never-screened women**—breast cancers diagnosed in 2002–2012 in women aged 40 and over who did not have a screening mammogram through BreastScreen Australia prior to the cancer diagnosis.

These individuals were then linked with data from the National Death Index to ascertain date of death and cause of death for those who had died by 31 December 2015.

Cohort design

For the cohort studies, women entered the cohort on the date of their breast cancer diagnosis and were followed to 31 December 2015. For analyses that used death from breast cancer as the event, individuals were censored if they died from a cause other than breast cancer, or at 31 December 2015 if they did not die during the study period. Person time at risk was calculated in days from the date of breast cancer diagnosis to either the date of event (for those who died from breast cancer) or to date of censor (for those who did not die, or died from another cause).

Statistical tests

The χ^2 test was used to analyse differences across categorical variables.

Kaplan–Meier survival curves were generated and log-rank tests used to assess differences in survival across groups.

Cox proportional hazards models were used to produce a hazard ratio with 95% confidence intervals, which were used to determine any reduction in risk of death associated with a breast cancer being screen-detected compared with it being diagnosed in an unscreened woman. Analyses were adjusted for confounding by age at diagnosis, year of diagnosis, remoteness area, and socioeconomic disadvantage, as well as the clinical characteristics of histological type and breast cancer size that were available on the Australian Cancer Database.

Adjusting for potential biases

There are three potential biases that require consideration in breast cancer survival analyses: lead-time bias, screening selection bias, and length bias. All three biases can appear to improve outcomes for screened women, therefore corrections that are made are applied to this cohort, as illustrated in Figure 3.2.2. Note that while outcomes can also change for interval and non-screen-detected cancers in screened women, the primary purpose of the bias corrections is to improve comparability between screen-detected and never-screened breast cancers, and so any changes to other cancers may not be appropriate to use.

Bias corrections either add additional time or decrease the relative risk to allow comparisons to be made with unscreened women without these factors potentially biasing the results towards better survival in screened women. In this way, if screened women still fare better than unscreened women—even with corrections to remove biases—we can be more confident that this effect is real.

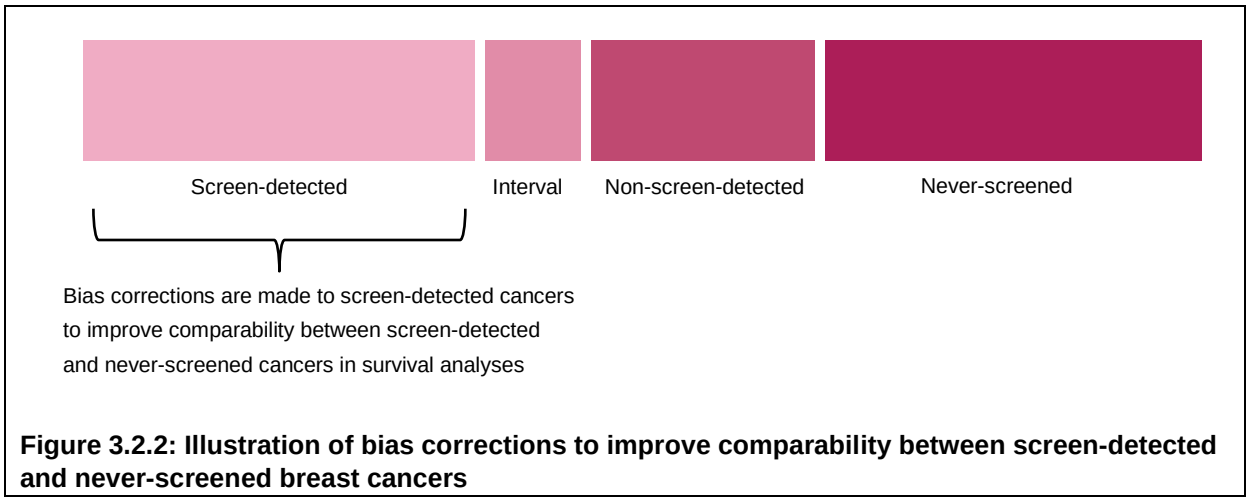


Figure 3.2.2: Illustration of bias corrections to improve comparability between screen-detected and never-screened breast cancers

The three potential biases that can affect estimates of breast cancer survival are described below, along with the methodology used to correct for these.

‘Lead time’ is the length of time between when a cancer is detected by screening, and when the cancer would have been detected due to the development of clinical signs or symptoms if screening had not occurred. Detecting a cancer early by screening can improve survival through effective treatment and management, delaying the time until death. However, a diagnosis of cancer can also be made earlier without affecting the date on which the individual would have died. In this case, the additional lead-time in the screened individual makes it look as though time until death is longer. This results in an increase in survival in screened individuals that may not be ‘real’, and is known as ‘**lead-time bias**’ (Duffy et al. 2008).

Cox proportional hazards models for breast cancer were corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years, using methods previously described (Duffy et al. 2008; Brenner et al. 2011). Further details are provided in Appendix D.

‘**Screening selection bias**’ in breast cancer screening exists in countries or regions in which the women who choose to participate in breast cancer screening are at a lower risk of death than those who do not participate, which would lead to an increase in survival in screened women that may not be real (Paap et al. 2011).

To correct for screening selection bias, hazard ratios were adjusted for the estimated decrease in risk of death that is due to women who choose to screen being less likely to die than women who choose to not screen. This report examines the effect of using correction factors of 1.36 and 1.17, which are pooled estimates from previously published randomised control trials, as well as a correction factor derived from the linked data in this project of 0.91. These correction factors were used to correct for screening selection bias using methods previously described (Duffy & Cuzick 2002). Further details are provided in Appendix D.

‘**Length bias**’ is the phenomenon whereby more slowly growing cancers are more likely to be detected by screening, as they have a longer pre-symptomatic-period, again leading to an apparent increase in survival in screened individuals (Duffy et al. 2008).

No corrections were made for length bias, which is difficult to quantify (Duffy et al. 2008). Instead, additional analyses were performed to provide further information that may allow inferences about the effects of length bias to be made.

Ethics approvals

To access the data required for this data linkage project, ethics approvals were obtained from the AIHW Ethics Committee (EO 2014-4-130)—also used by the Department of Health for ethics approval to access National Bowel Cancer Screening Program Register data and National HPV Vaccination Program Register data—and state and territory human research ethics committees to access state and territory cancer registry data (through the Australian Cancer Database), BreastScreen register data, and cervical screening register data.

4 Description of cohort

The following section examines breast cancer diagnoses in women aged 40 and over between 1 January 2002 and 31 December 2012, who were followed up until 31 December 2015. Breast cancers were restricted to those diagnosed in women aged 40 and over to align with the age at which women are eligible to attend BreastScreen Australia. Breast cancers were also restricted to invasive breast cancers, as in situ tumours (including DCIS) were not available on the Australian Cancer Database, the source of all cancer data.

Although BreastScreen Australia data were available from 2000, which would have allowed the inclusion of breast cancers from that year, it has been postulated (Nickson et al. 2012) that the inclusion of data too soon after the introduction of the screening program may reduce the effect of screening on mortality, since women screening for the first time when the program commenced had less opportunity to benefit from screening. By only selecting breast cancers diagnosed from 2002 onwards, it is considered that sufficient time would have passed since the introduction of the program for any mortality benefits to be evident (Nickson et al. 2012).

4.1 Breast cancer definitions

Box 4.1.1: Breast cancer definitions

Breast cancers were invasive breast cancers diagnosed in women aged 40 and over in the years 2002–2012. Breast cancers were categorised as:

- **screen-detected cancers:** Breast cancers diagnosed in women with a positive screening result through BreastScreen Australia, where the cancers were identified as screen-detected by BreastScreen Australia
- **interval cancers:** Breast cancers diagnosed in women with a negative screening test result through BreastScreen Australia and diagnosed outside BreastScreen Australia in the 2 years following their negative screening result (or in 1 year following if their previous screening recommendation was to rescreen in 12 months), or who were diagnosed within BreastScreen Australia in the 2 years following their negative screening result (or in the 1 year following if their previous screening recommendation was to rescreen in 12 months) either at early recall if the breast cancer was diagnosed more than 6 months after their previous negative screening result, or at early rescreen if they presented with a breast lump and/or clear or blood-stained nipple discharge
- **non-screen-detected cancers in screened women:** Breast cancers diagnosed in women who had previously screened through BreastScreen Australia, but not identified as screen-detected cancers or interval cancers
- **non-screen-detected cancers in never-screened women:** Breast cancers diagnosed in women who had not screened through BreastScreen Australia prior to diagnosis.

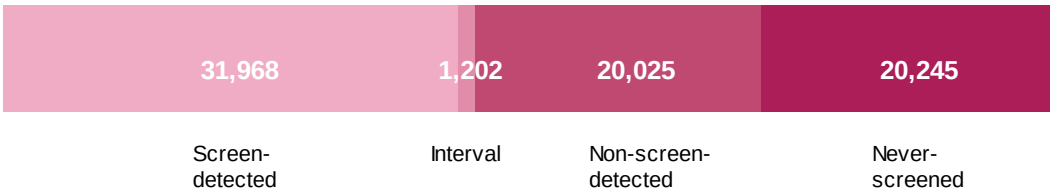
Breast cancers have been broadly grouped into those diagnosed in women aged:

- **50–69** (actively targeted by BreastScreen Australia)
- **40–49** (eligible to attend but not actively targeted by BreastScreen Australia)
- **70 and over** (eligible to attend but not actively targeted by BreastScreen Australia)
- **40 and over** (total of all women eligible to attend BreastScreen Australia).

4.2 Summary statistics

Between 1 January 2002 and 31 December 2012, 137,471 breast cancers were diagnosed in women aged 40 and over. Of these breast cancers, 73,440 (53.4%) were diagnosed in women aged 50–69 (the target age group), 26,463 (19.2%) were diagnosed in women aged 40–49, and 37,568 (27.3%) were diagnosed in women aged 70 and over.

In **2002–2012,** there were **73,440 breast cancers** diagnosed in women aged **50–69**



20,245 (27.6%) were never-screened breast cancers (breast cancers diagnosed in women who had never been screened through BreastScreen Australia).

The remaining **53,195** (72.4%) breast cancers occurred in women who had previously been screened:

- **20,025** breast cancers (27.3%) were non-screen-detected cancers in screened women (breast cancers diagnosed in women who had previously screened through BreastScreen Australia, but were not screen-detected)
- **1,202** breast cancers (1.6%) were interval cancers diagnosed after a negative screen through BreastScreen Australia in the interval between screens
- **31,968** breast cancers (43.5%) were screen-detected cancers diagnosed as a result of a screen.

In **2002–2012,** there were **26,463 breast cancers** diagnosed in women aged **40–49**

18,059 (68.2%) were never-screened breast cancers (breast cancers diagnosed in women who had never been screened through BreastScreen Australia).

The remaining **8,404** (31.8%) breast cancers occurred in women who had previously been screened:

- **4,577** breast cancers (17.3%) were non-screen-detected cancers in screened women (breast cancers diagnosed in women who had previously screened through BreastScreen Australia, but were not screen-detected)
- **366** breast cancers (1.4%) were interval cancers diagnosed after a negative screen through BreastScreen in the interval between screens
- **3,461** breast cancers (13.1%) were screen-detected cancers diagnosed as a result of a screen.

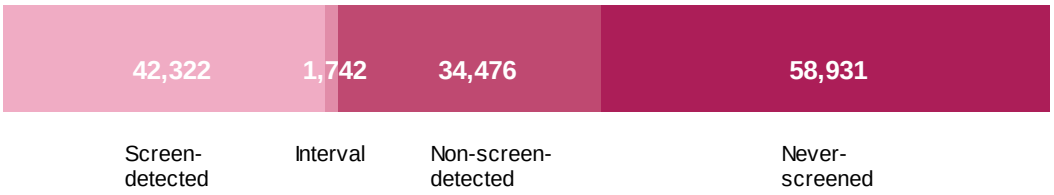
In **2002–2012,** there were **37,568 breast cancers** diagnosed in women aged **70 and over**

20,627 (54.9%) were never-screened breast cancers (breast cancers diagnosed in women who had never been screened through BreastScreen Australia).

The remaining **16,941** (45.1%) breast cancers occurred in women who had previously been screened:

- **9,874** breast cancers (26.3%) were non-screen-detected cancers in screened women (breast cancers diagnosed in women who had previously screened through BreastScreen Australia, but were not screen-detected)
- **174** breast cancers (0.5%) were interval cancers diagnosed after a negative screen through BreastScreen Australia in the interval between screens
- **6,893** breast cancers (18.3%) were screen-detected cancers diagnosed as a result of a screen.

In **2002–2012,** there were **137,471 breast cancers** diagnosed in women aged **40 and over**



58,931 (42.9%) were never-screened breast cancers (breast cancers diagnosed in women who had never been screened through BreastScreen Australia).

The remaining **78,540** (57.1%) breast cancers occurred in women who had previously been screened:

- **34,476** breast cancers (25.1%) were non-screen-detected cancers in screened women (breast cancers diagnosed in women who had previously screened through BreastScreen Australia, but were not screen-detected)
- **1,742** breast cancers (1.3%) were interval cancers diagnosed after a negative screen through BreastScreen Australia in the interval between screens
- **42,322** breast cancers (30.8%) were screen-detected cancers diagnosed as a result of a screen.

4.3 Descriptive statistics

Descriptive statistics tables allow assessment of similarities and differences between the individuals diagnosed within the different screen detection categories of breast cancer by key factors such as age group at diagnosis, remoteness area of residence, socioeconomic group of residence, as well as cancer features that were available on the Australian Cancer Database.

Characteristics of women diagnosed with breast cancers in each of the four categories of screen detection status are shown in tables 4.3.1–4.3.4.

Key features of women aged 50–69 (Table 4.3.1) include:

- compared with breast cancers diagnosed in never-screened women, a lower proportion of screen-detected breast cancers were diagnosed in women aged 50–54, and a higher proportion in women aged 60–69
- a higher proportion of screen-detected breast cancers were diagnosed in *Inner regional* and *Outer regional* areas compared with never-screened cancers
- there were some differences in the histological types of breast cancers across the screen detection status categories. The most notable difference was the proportionately higher number of *Other—specified* and *Unspecified* breast cancers diagnosed in women who had never screened through BreastScreen Australia
- screen-detected breast cancers were more likely to be small (≤15 mm) compared with interval breast cancers, non-screen-detected breast cancers in screened women, and breast cancers in never-screened women. Never-screened women also had higher proportion of cancers for which the size was unknown (or not applicable).

Key features of women aged 40–49 (Table 4.3.2) include:

- compared with breast cancers diagnosed in never-screened women, a lower proportion of screen-detected breast cancers were diagnosed in women aged 40–44, and a higher proportion in women aged 45–49.
- a higher proportion of screen-detected cancers were diagnosed in 2002–2007, and a lower proportion in 2008–2012, compared with breast cancers diagnosed in never-screened women.
- a higher proportion of screen-detected breast cancers were diagnosed in *Outer regional*, *Remote* and *Very remote* areas compared with never-screened cancers.
- there were some differences in the histological types of breast cancers across the screen detection status categories. The most notable difference was the proportionately higher number of *Other—specified* and *Unspecified* breast cancers diagnosed in women who had never screened through BreastScreen Australia.
- screen-detected breast cancers were more likely to be small (≤15 mm) compared with interval breast cancers, non-screen-detected breast cancers in screened women, and breast cancers in never-screened women. Never-screened women also had a higher proportion of cancers for which the size was unknown (or not applicable).

Key features of women aged 70 and over (Table 4.3.3) include:

- compared with breast cancers diagnosed in never-screened women, a higher proportion of screen-detected breast cancers were diagnosed in women aged 70–79, and a lower proportion in women aged 80 and over.
- a higher proportion of screen-detected breast cancers were diagnosed in *Inner regional* and *Outer regional* areas compared with never-screened cancers.
- screen-detected breast cancers were more likely to be small (≤15 mm) compared with interval breast cancers, non-screen-detected breast cancers in screened women, and breast cancers in never-screened women. Never-screened women also had a higher proportion of cancers for which the size was unknown (or not applicable).

All women diagnosed with breast cancer aged 40 and over are shown in Table 4.3.4.

- compared with cancers diagnosed in women who had never screened through BreastScreen Australia, the proportion of breast cancers that were screen-detected was higher between the ages of 50 and 74 and lower in women aged 40–49 and 75 and over (Figure 4.3.1). This aligns with the target age group of BreastScreen Australia of 50–69 used in this project, with the exception of women aged 70–74, who are now actively targeted by the program.
- overall, compared with cancers diagnosed in women who had never screened through BreastScreen Australia, the proportion of breast cancers that were screen-detected was higher in regional and remote areas, and higher in areas of greater socioeconomic disadvantage (Figure 4.3.1). BreastScreen Australia aims to provide services that are accessible to women including those living in remote areas and those who are at a socioeconomic disadvantage, which has likely played a role in the higher proportion of screen-detected breast cancers in these groups.
- breast cancers detected through BreastScreen Australia were also more likely to be small (≤15 mm). Overall, more than half (54.5%) of all screen-detected breast cancers were small compared with less than one quarter (23.6%) of breast cancers diagnosed in women who had never screened through BreastScreen Australia (Figure 4.3.1).
- for other breast cancer characteristics available, overall it was noted that breast cancers diagnosed in women who had never screened through BreastScreen Australia were more likely than screen-detected breast cancers to have:
  - a tumour size that was *Unknown* or *Not applicable*
  - a histological type that was *Unspecified*
  - a sub-site that was *Unspecified*.

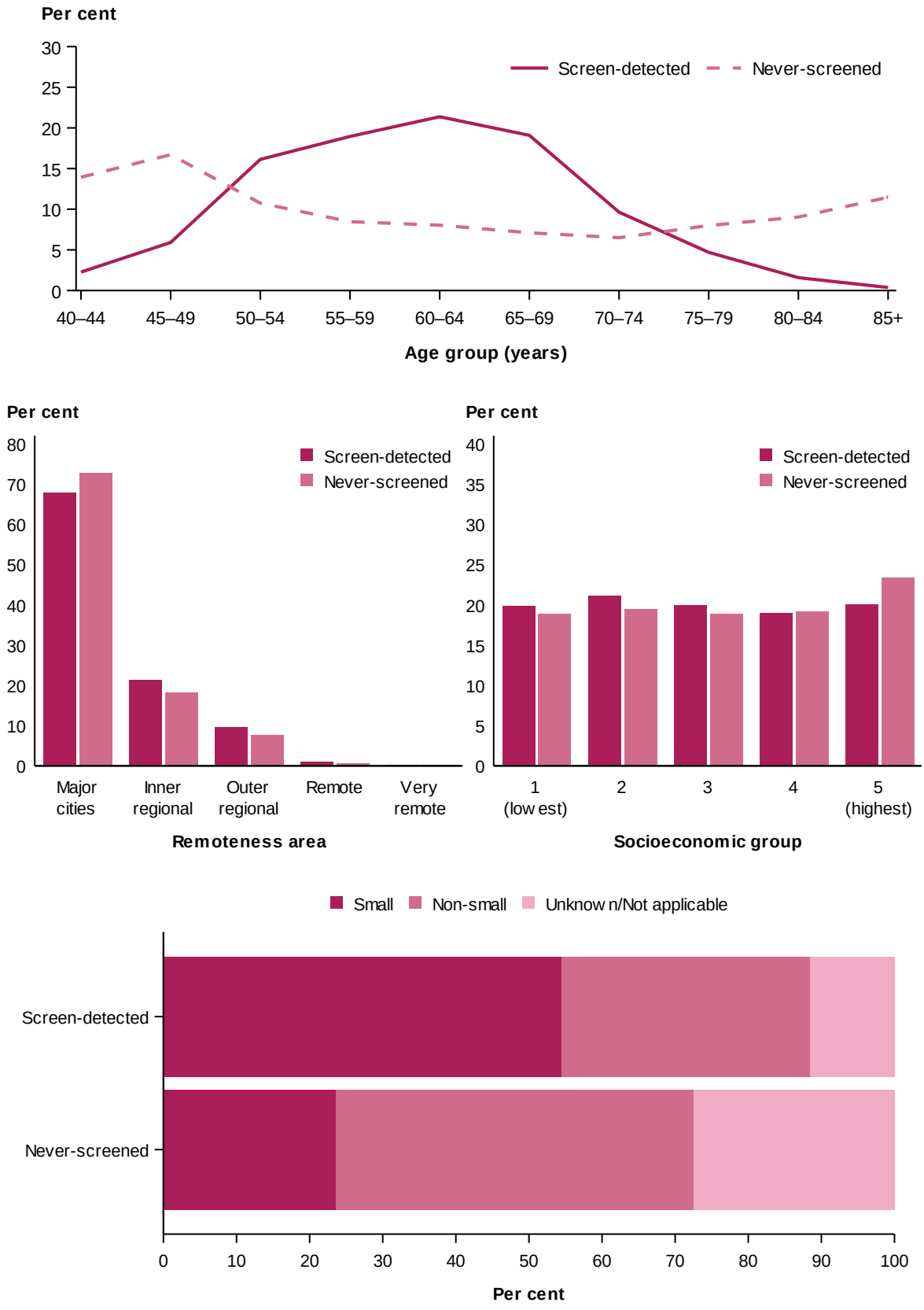


Figure 4.3.1: Proportion of breast cancers screen-detected and never-screened by age group, remoteness area, socioeconomic group, and tumour size, for women diagnosed with breast cancer in 2002–2012 aged 40 and over

Table 4.3.1: Characteristics of women diagnosed with breast cancer by screen detection status, women aged 50–69, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group	50–54	6,826	21.4	375	31.2	5,104	25.5	6,334	31.3	18,639	25.4
	55–59	8,020	25.1	343	28.5	5,479	27.4	4,988	24.6	18,830	25.6
	60–64	9,044	28.3	265	22.0	5,310	26.5	4,736	23.4	19,355	26.4
	65–69	8,078	25.3	219	18.2	4,132	20.6	4,187	20.7	16,616	22.6
Year of diagnosis	2002–2007	15,492	48.5	518	43.1	9,848	49.2	10,785	53.3	36,643	49.9
	2008–2012	16,476	51.5	684	56.9	10,177	50.8	9,460	46.7	36,797	50.1
Remoteness area	Major cities	21,739	68.0	784	65.2	12,922	64.5	14,748	72.8	50,193	68.3
	Inner regional	6,847	21.4	218	18.1	4,493	22.4	3,607	17.8	15,165	20.6
	Outer regional	2,985	9.3	174	14.5	2,195	11.0	1,590	7.9	6,944	9.5
	Remote	278	0.9	15	1.2	289	1.4	185	0.9	767	1.0
	Very remote	110	0.3	9	0.7	106	0.5	82	0.4	307	0.4
Socioeconomic group	1 (most disadvantage)	6,336	19.8	169	14.1	4,030	20.1	3,778	18.7	14,313	19.5
	2	6,730	21.1	234	19.5	3,951	19.7	3,897	19.2	14,812	20.2
	3	6,327	19.8	271	22.5	3,924	19.6	3,781	18.7	14,303	19.5
	4	6,069	19.0	228	19.0	3,888	19.4	3,840	19.0	14,025	19.1
	5 (least disadvantage)	6,486	20.3	297	24.7	4,204	21.0	4,906	24.2	15,893	21.6

Table 4.3.1 (continued): Characteristics of women diagnosed with breast cancer by screen detection status, women aged 50–69, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Histological type	Invasive ductal carcinoma	25,871	80.9	927	77.1	15,766	78.7	15,847	78.3	58,411	79.5
	Invasive lobular carcinoma	3,601	11.3	155	12.9	2,613	13.0	2,294	11.3	8,663	11.8
	Medullar carcinoma & atypical medullary carcinoma	102	0.3	5	0.4	97	0.5	71	0.4	275	0.4
	Tubular carcinoma & invasive cribriform carcinoma	1,015	3.2	16	1.3	293	1.5	286	1.4	1,610	2.2
	Mucinous carcinoma	497	1.6	16	1.3	256	1.3	256	1.3	1,025	1.4
	Invasive papillary carcinoma	312	1.0	14	1.2	174	0.9	208	1.0	708	1.0
	Inflammatory carcinoma	16	0.1	4	0.3	49	0.2	48	0.2	117	0.2
	Mesenchymal	11	0.0	1	0.1	11	0.1	30	0.1	53	0.1
	Other—specified	238	0.7	32	2.7	365	1.8	467	2.3	1,102	1.5
	Unspecified	305	1.0	32	2.7	401	2.0	738	3.6	1,476	2.0
Tumour size	Small	17,679	55.3	405	33.7	6,814	34.0	5,592	27.6	30,490	41.5
	Non-small	10,883	34.0	633	52.7	10,170	50.8	9,997	49.4	31,683	43.1
	Unknown/Not applicable	3,406	10.7	164	13.6	3,041	15.2	4,656	23.0	11,267	15.3
Sub-site	Unspecified	14,387	45.0	334	27.8	9,652	48.2	10,160	50.2	34,533	47.0
	Nipple and areola	116	0.4	32	2.7	230	1.1	165	0.8	543	0.7
	Central portion	935	2.9	67	5.6	765	3.8	727	3.6	2,494	3.4
	Upper-inner quadrant	2,593	8.1	98	8.2	1,494	7.5	1,491	7.4	5,676	7.7
	Lower-inner quadrant	1,249	3.9	61	5.1	657	3.3	668	3.3	2,635	3.6
	Upper-outer quadrant	7,639	23.9	305	25.4	4,083	20.4	3,936	19.4	15,963	21.7
	Lower-outer quadrant	1,758	5.5	83	6.9	1,166	5.8	1,143	5.6	4,150	5.7
	Axillary tail	74	0.2	13	1.1	77	0.4	67	0.3	231	0.3
	Overlapping lesion	3,217	10.1	209	17.4	1,901	9.5	1,888	9.3	7,215	9.8

Table 4.3.2: Characteristics of women diagnosed with breast cancer by screen detection status, women aged 40–49, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group	40–44	960	27.7	117	32.0	1,180	25.8	8,214	45.5	10,471	39.6
	45–49	2,501	72.3	249	68.0	3,397	74.2	9,845	54.5	15,992	60.4
Year of diagnosis	2002–2007	1,839	53.1	163	44.5	2,761	60.3	9,115	50.5	13,878	52.4
	2008–2012	1,622	46.9	203	55.5	1,816	39.7	8,944	49.5	12,585	47.6
Remoteness area	Major cities	2,348	67.8	252	68.9	3,038	66.4	13,275	73.5	18,913	71.5
	Inner regional	637	18.4	51	13.9	926	20.2	3,180	17.6	4,794	18.1
	Outer regional	398	11.5	50	13.7	493	10.8	1,361	7.5	2,302	8.7
	Remote	55	1.6	10	2.7	80	1.7	138	0.8	283	1.1
	Very remote	23	0.7	3	0.8	37	0.8	80	0.4	143	0.5
Socioeconomic group	1 (most disadvantage)	578	16.7	63	17.2	766	16.7	2,996	16.6	4,403	16.6
	2	680	19.6	51	13.9	877	19.2	3,322	18.4	4,930	18.6
	3	725	20.9	76	20.8	925	20.2	3,429	19.0	5,155	19.5
	4	723	20.9	90	24.6	943	20.6	3,737	20.7	5,493	20.8
	5 (least disadvantage)	751	21.7	86	23.5	1,061	23.2	4,539	25.1	6,437	24.3

(continued)

Table 4.3.2 (continued): Characteristics of women diagnosed with breast cancer by screen detection status, women aged 40–49, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Histological type	Invasive ductal carcinoma	2,920	84.4	300	82.0	3,747	81.9	15,065	83.4	22,032	83.3
	Invasive lobular carcinoma	326	9.4	39	10.7	468	10.2	1,581	8.8	2,414	9.1
	Medullar carcinoma & atypical medullary carcinoma	16	0.5	2	0.5	25	0.5	111	0.6	154	0.6
	Tubular carcinoma & invasive cribriform carcinoma	80	2.3	3	0.8	88	1.9	226	1.3	397	1.5
	Mucinous carcinoma	33	1.0	4	1.1	56	1.2	245	1.4	338	1.3
	Invasive papillary carcinoma	25	0.7	4	1.1	31	0.7	107	0.6	167	0.6
	Inflammatory carcinoma	3	0.1	1	0.3	8	0.2	48	0.3	60	0.2
	Mesenchymal	1	—	—	—	4	0.1	7	—	12	—
	Other—specified	28	0.8	10	2.7	65	1.4	292	1.6	395	1.5
	Unspecified	29	0.8	3	0.8	85	1.9	377	2.1	494	1.9
Tumour size	Small	1,629	47.1	124	33.9	1,546	33.8	5,224	28.9	8,523	32.2
	Non-small	1,430	41.3	198	54.1	2,330	50.9	9,784	54.2	13,742	51.9
	Unknown/Not applicable	402	11.6	44	12.0	701	15.3	3,051	16.9	4,198	15.9
Sub-site	Unspecified	1,275	36.8	99	27.0	1,971	43.1	9,141	50.6	12,486	47.2
	Nipple and areola	29	0.8	9	2.5	37	0.8	134	0.7	209	0.8
	Central portion	143	4.1	17	4.6	150	3.3	490	2.7	800	3.0
	Upper-inner quadrant	336	9.7	38	10.4	353	7.7	1,315	7.3	2,042	7.7
	Lower-inner quadrant	123	3.6	18	4.9	162	3.5	539	3.0	842	3.2
	Upper-outer quadrant	935	27.0	100	27.3	1,143	25.0	3,613	20.0	5,791	21.9
	Lower-outer quadrant	206	6.0	31	8.5	311	6.8	957	5.3	1,505	5.7
	Axillary tail	10	0.3	6	1.6	24	0.5	58	0.3	98	0.4
	Overlapping lesion	404	11.7	48	13.1	426	9.3	1,812	10.0	2,690	10.2

Table 4.3.3: Characteristics of women diagnosed with breast cancer by screen detection status, women aged 70 and over, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group	70–74	4,078	59.2	132	75.9	3,634	36.8	3,830	18.6	11,674	31.1
	75–79	1,987	28.8	34	19.5	3,264	33.1	4,711	22.8	9,996	26.6
	80–84	669	9.7	6	3.4	2,062	20.9	5,328	25.8	8,065	21.5
	85+	159	2.3	2	1.1	914	9.3	6,758	32.8	7,833	20.9
Year of diagnosis	2002–2007	3,770	54.7	75	43.1	3,412	34.6	11,805	57.2	19,062	50.7
	2008–2012	3,123	45.3	99	56.9	6,462	65.4	8,822	42.8	18,506	49.3
Remoteness area	Major cities	4,596	66.7	115	66.1	6,534	66.2	14,837	71.9	26,082	69.4
	Inner regional	1,539	22.3	38	21.8	2,330	23.6	3,984	19.3	7,891	21.0
	Outer regional	668	9.7	17	9.8	887	9.0	1,583	7.7	3,155	8.4
	Remote	72	1.0	2	1.1	82	0.8	110	0.5	266	0.7
	Very remote	16	0.2	1	0.6	28	0.3	42	0.2	87	0.2
Socioeconomic group	1 (most disadvantage)	1,474	21.4	34	19.5	2,196	22.2	4,351	21.1	8,055	21.4
	2	1,539	22.3	39	22.4	2,138	21.7	4,268	20.7	7,984	21.3
	3	1,404	20.4	34	19.5	1,953	19.8	3,888	18.8	7,279	19.4
	4	1,240	18.0	25	14.4	1,647	16.7	3,737	18.1	6,649	17.7
	5 (least disadvantage)	1,231	17.9	41	23.6	1,923	19.5	4,306	20.9	7,501	20.0

(continued)

Table 4.3.3 (continued): Characteristics of women diagnosed with breast cancer by screen detection status, women aged 70 and over, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Histological type	Invasive ductal carcinoma	5,265	76.4	119	68.4	7,139	72.3	13,540	65.6	26,063	69.4
	Invasive lobular carcinoma	906	13.1	35	20.1	1,404	14.2	2,306	11.2	4,651	12.4
	Medullar carcinoma & atypical medullary carcinoma	16	0.2	—	—	30	0.3	26	0.1	72	0.2
	Tubular carcinoma & invasive cribriform carcinoma	195	2.8	—	—	80	0.8	122	0.6	397	1.1
	Mucinous carcinoma	245	3.6	3	1.7	374	3.8	820	4.0	1,442	3.8
	Invasive papillary carcinoma	101	1.5	2	1.1	159	1.6	261	1.3	523	1.4
	Inflammatory carcinoma	—	—	—	—	21	0.2	22	0.1	43	0.1
	Mesenchymal	7	0.1	—	—	8	0.1	26	0.1	41	0.1
	Other—specified	76	1.1	11	6.3	268	2.7	640	3.1	995	2.6
	Unspecified	82	1.2	4	2.3	391	4.0	2,864	13.9	3,341	8.9
Tumour size	Small	3,755	54.5	50	28.7	2,711	27.5	3,095	15.0	9,611	25.6
	Non-small	2,038	29.6	85	48.9	5,229	53.0	9,043	43.8	16,395	43.6
	Unknown/Not applicable	1,100	16.0	39	22.4	1,934	19.6	8,489	41.2	11,562	30.8
Sub-site	Unspecified	3,238	47.0	48	27.6	4,602	46.6	12,144	58.9	20,032	53.3
	Nipple and areola	38	0.6	10	5.7	156	1.6	251	1.2	455	1.2
	Central portion	232	3.4	16	9.2	403	4.1	778	3.8	1,429	3.8
	Upper-inner quadrant	516	7.5	14	8.0	727	7.4	1,204	5.8	2,461	6.6
	Lower-inner quadrant	286	4.1	10	5.7	350	3.5	569	2.8	1,215	3.2
	Upper-outer quadrant	1,583	23.0	34	19.5	1,873	19.0	3,145	15.2	6,635	17.7
	Lower-outer quadrant	383	5.6	14	8.0	632	6.4	936	4.5	1,965	5.2
	Axillary tail	18	0.3	2	1.1	38	0.4	54	0.3	112	0.3
	Overlapping lesion	599	8.7	26	14.9	1,093	11.1	1,546	7.5	3,264	8.7

Table 4.3.4: Characteristics of women diagnosed with breast cancer by screen detection status, women aged 40 and over, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group	40–44	960	2.3	117	6.7	1,180	3.4	8,214	13.9	10,471	7.6
	45–49	2,501	5.9	249	14.3	3,397	9.9	9,845	16.7	15,992	11.6
	50–54	6,826	16.1	375	21.5	5,104	14.8	6,334	10.7	18,639	13.6
	55–59	8,020	18.9	343	19.7	5,479	15.9	4,988	8.5	18,830	13.7
	60–64	9,044	21.4	265	15.2	5,310	15.4	4,736	8.0	19,355	14.1
	65–69	8,078	19.1	219	12.6	4,132	12.0	4,187	7.1	16,616	12.1
	70–74	4,078	9.6	132	7.6	3,634	10.5	3,830	6.5	11,674	8.5
	75–79	1,987	4.7	34	2.0	3,264	9.5	4,711	8.0	9,996	7.3
	80–84	669	1.6	6	0.3	2,062	6.0	5,328	9.0	8,065	5.9
	85+	159	0.4	2	0.1	914	2.7	6,758	11.5	7,833	5.7
Year of diagnosis	2002–2007	21,101	49.9	756	43.4	16,021	46.5	31,705	53.8	69,583	50.6
	2008–2012	21,221	50.1	986	56.6	18,455	53.5	27,226	46.2	67,888	49.4
Remoteness area	Major cities	28,683	67.8	1,151	66.1	22,494	65.2	42,860	72.7	95,188	69.2
	Inner regional	9,023	21.3	307	17.6	7,749	22.5	10,771	18.3	27,850	20.3
	Outer regional	4,051	9.6	241	13.8	3,575	10.4	4,534	7.7	12,401	9.0
	Remote	405	1.0	27	1.5	451	1.3	433	0.7	1,316	1.0
	Very remote	149	0.4	13	0.7	171	0.5	204	0.3	537	0.4

(continued)

Table 4.3.4 (continued): Characteristics of women diagnosed with breast cancer by screen detection status, women aged 40 and over, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Socioeconomic group	1 (most disadvantage)	8,388	19.8	266	15.3	6,992	20.3	11,125	18.9	26,771	19.5
	2	8,949	21.1	324	18.6	6,966	20.2	11,487	19.5	27,726	20.2
	3	8,456	20.0	381	21.9	6,802	19.7	11,098	18.8	26,737	19.4
	4	8,032	19.0	343	19.7	6,478	18.8	11,314	19.2	26,167	19.0
	5 (least disadvantage)	8,468	20.0	424	24.3	7,188	20.8	13,751	23.3	29,831	21.7
Histological type	Invasive ductal carcinoma	34,056	80.5	1,346	77.3	26,652	77.3	44,452	75.4	106,506	77.5
	Invasive lobular carcinoma	4,833	11.4	229	13.1	4,485	13.0	6,181	10.5	15,728	11.4
	Medullar carcinoma & atypical medullary carcinoma	134	0.3	7	0.4	152	0.4	208	0.4	501	0.4
	Tubular carcinoma & invasive cribriform carcinoma	1,290	3.0	19	1.1	461	1.3	634	1.1	2,404	1.7
	Mucinous carcinoma	775	1.8	23	1.3	686	2.0	1,321	2.2	2,805	2.0
	Invasive papillary carcinoma	438	1.0	20	1.1	364	1.1	576	1.0	1,398	1.0
	Inflammatory carcinoma	19	—	5	0.3	78	0.2	118	0.2	220	0.2
	Mesenchymal	19	—	1	0.1	23	0.1	63	0.1	106	0.1
	Other—specified	342	0.8	53	3.0	698	2.0	1,399	2.4	2,492	1.8
	Unspecified	416	1.0	39	2.2	877	2.5	3,979	6.8	5,311	3.9
Tumour size	Small	23,063	54.5	579	33.2	11,071	32.1	13,911	23.6	48,624	35.4
	Non-small	14,351	33.9	916	52.6	17,729	51.4	28,824	48.9	61,820	45.0
	Unknown/Not applicable	4,908	11.6	247	14.2	5,676	16.5	16,196	27.5	27,027	19.7

(continued)

Table 4.3.4 (continued): Characteristics of women diagnosed with breast cancer by screen detection status, women aged 40 and over, 2002–2012

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Sub-site	Unspecified	18,900	44.7	481	27.6	16,225	47.1	31,445	53.4	67,051	48.8
	Nipple and areola	183	0.4	51	2.9	423	1.2	550	0.9	1,207	0.9
	Central portion	1,310	3.1	100	5.7	1,318	3.8	1,995	3.4	4,723	3.4
	Upper-inner quadrant	3,445	8.1	150	8.6	2,574	7.5	4,010	6.8	10,179	7.4
	Lower-inner quadrant	1,658	3.9	89	5.1	1,169	3.4	1,776	3.0	4,692	3.4
	Upper-outer quadrant	10,157	24.0	439	25.2	7,099	20.6	10,694	18.1	28,389	20.7
	Lower-outer quadrant	2,347	5.5	128	7.3	2,109	6.1	3,036	5.2	7,620	5.5
	Axillary tail	102	0.2	21	1.2	139	0.4	179	0.3	441	0.3
	Overlapping lesion	4,220	10.0	283	16.2	3,420	9.9	5,246	8.9	13,169	9.6

5 Breast cancer outcomes

5.1 Summary cancer and death statistics

There were 137,471 breast cancers diagnosed in the cohort selected for survival analyses (women aged 40 and over diagnosed between 1 January 2002 and 31 December 2012).

There were **73,440 breast cancers** diagnosed in women aged **50–69** (Table 5.1.1).

- The majority of breast cancers diagnosed in this age group were screen-detected, comprising 43.5% of all cancers, with 27.6% of breast cancers diagnosed in women who had never screened through BreastScreen Australia.
- Women diagnosed with screen-detected breast cancers were less likely to die from breast cancer than women whose breast cancer was not screen-detected, with 4.6% of screen-detected breast cancers in this age group causing death, followed by 10.9% of interval cancers, 11.4% of non-screen-detected breast cancers in screened women, and 18.4% of breast cancers diagnosed in women who had never screened through BreastScreen Australia causing death (Figure 5.1.1).
- In this age group, the proportion of deaths due to breast cancer was dependent on screen detection status, with 50.5% of the deaths in women with screen-detected breast cancer due to breast cancer, compared with 74.2% of deaths in diagnosed women who had never screened.

There were **26,463 breast cancers** diagnosed in women aged **40–49** (Table 5.1.2).

- The majority of breast cancers diagnosed in this age group were in women who had never screened, comprising 68.2% of all cancers, with only 13.1% screen-detected.
- Women diagnosed with screen-detected breast cancers were less likely to die from breast cancer than women whose breast cancer was not screen-detected, with 5.3% of screen-detected breast cancers in this age group causing death, followed by 7.4% of non-screen-detected breast cancers in screened women, 10.4% of interval cancers and 13.3% of breast cancers diagnosed in women who had never screened through BreastScreen Australia causing death (Figure 5.1.2).
- In this age group, most deaths were due to breast cancer—80.0% of deaths in women with screen-detected breast cancer and 88.2% of deaths in diagnosed women who had never screened.

There were **37,568 breast cancers** diagnosed in women aged **70 and over** (Table 5.1.3).

- The majority of breast cancers diagnosed in this age group were in women who had never screened, comprising 54.9% of all cancers, with only 18.3% screen-detected.
- Women diagnosed with screen-detected breast cancers were less likely to die from breast cancer than women whose breast cancer was not screen-detected, with 6.9% of screen-detected breast cancers in this age group causing death, followed by 14.9% of interval cancers, 15.8% of non-screen-detected breast cancers in screened women, and 27.7% of breast cancers diagnosed in women who had never screened through BreastScreen Australia causing death (Figure 5.1.3).
- In this age group, the proportion of deaths due to breast cancer was dependent on screen detection status, with 26.8% of deaths in women with screen-detected breast cancer due to breast cancer, compared with 42.7% of deaths in diagnosed women who had never screened.

Table 5.1.1: Deaths in women diagnosed with breast cancer by screen detection status, women aged 50–69, 2002–2012

	Screen-detected	Interval	Non-screen-detected	Never-screened	Total
Number diagnosed with breast cancer	31,968	1,202	20,025	20,245	73,440
Number died from breast cancer	1,455	131	2,292	3,734	7,612
Rate of death from breast cancer (%)	4.6	10.9	11.4	18.4	10.4
Number died from any cause	2,883	179	3,150	5,032	11,244
Rate of death from any cause (%)	9.0	14.9	15.7	24.9	15.3
Mean age at diagnosis (years)	60.4 (±5.6)	58.9 (±5.6)	59.6 (±5.5)	59.1 (±5.9)	59.8 (±5.7)
Minimum–Maximum (years)	*50.0–70.0*	*50.0–69.9*	*50.0–70.0*	*50.0–70.0*	*50.0–70.0*
Median age at diagnosis (years)	60.6	58.4	59.5	58.8	59.8
Mean age at death (years)	67.2 (±6.5)	63.5 (±6.1)	64.7 (±6.3)	63.8 (±6.6)	64.9 (±6.6)
Minimum–Maximum (years)	*50.3–82.7*	*51.2–79.5*	*50.4–81.9*	*50.3–82.5*	*50.3–82.7*
Median age at death (years)	67.5	63.4	64.6	63.8	65.0

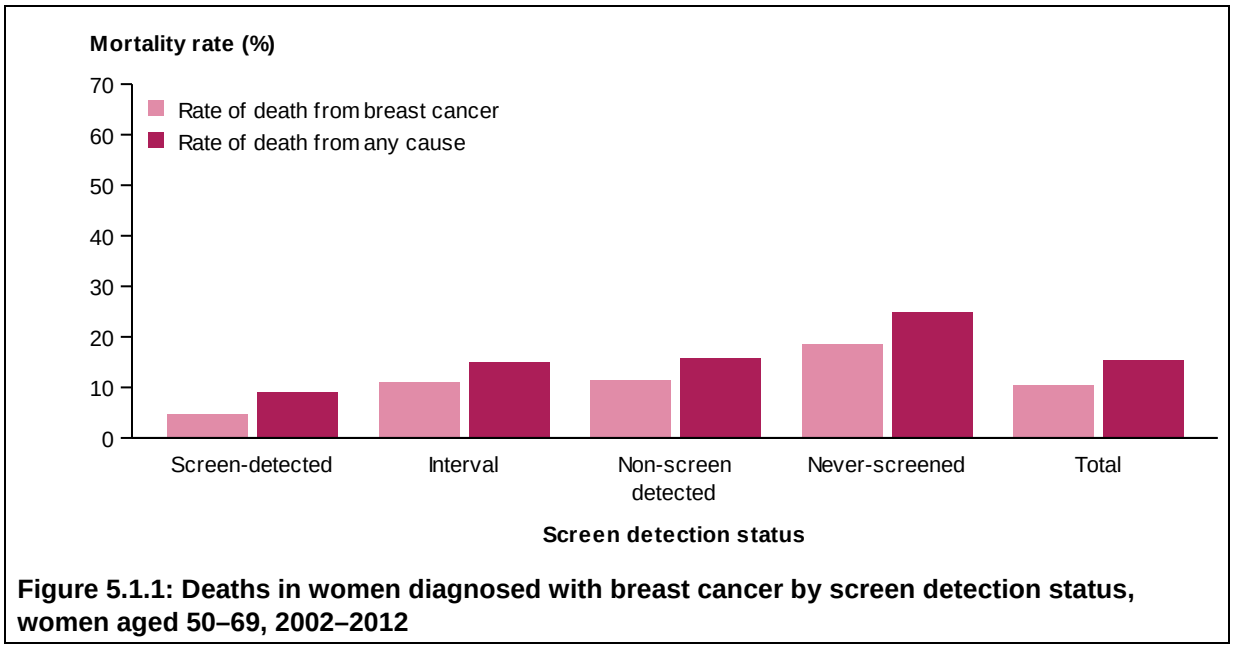


Figure 5.1.1: Deaths in women diagnosed with breast cancer by screen detection status, women aged 50–69, 2002–2012

Table 5.1.2: Deaths in women diagnosed with breast cancer by screen detection status, women aged 40–49, 2002–2012

	Screen-detected	Interval	Non-screen-detected	Never-screened	Total
Number diagnosed with breast cancer	3,461	366	4,577	18,059	26,463
Number died from breast cancer	184	38	337	2,406	2,965
Rate of death from breast cancer (%)	5.3	10.4	7.4	13.3	11.2
Number died from any cause	230	40	386	2,729	3,385
Rate of death from any cause (%)	6.6	10.9	8.4	15.1	12.8
Mean age at diagnosis (years)	46.5 (±2.6)	46.1 (±2.5)	46.6 (±2.4)	45.3 (±2.8)	45.7 (±2.8)
Minimum–Maximum (years)	*40.1–50.0*	*40.1–50.0*	*40.0–50.0*	*40.0–50.0*	*40.0–50.0*
Median age at diagnosis (years)	47.0	46.4	46.9	45.4	46.0
Mean age at death (years)	51.1 (±4.1)	50.9 (±3.7)	51.8 (±3.8)	49.6 (±4.0)	50.0 (±4.0)
Minimum–Maximum (years)	*42.6–60.9*	*44.1–59.0*	*42.4–62.5*	*40.4–62.5*	*40.4–62.5*
Median age at death (years)	50.9	50.8	51.5	49.5	49.9

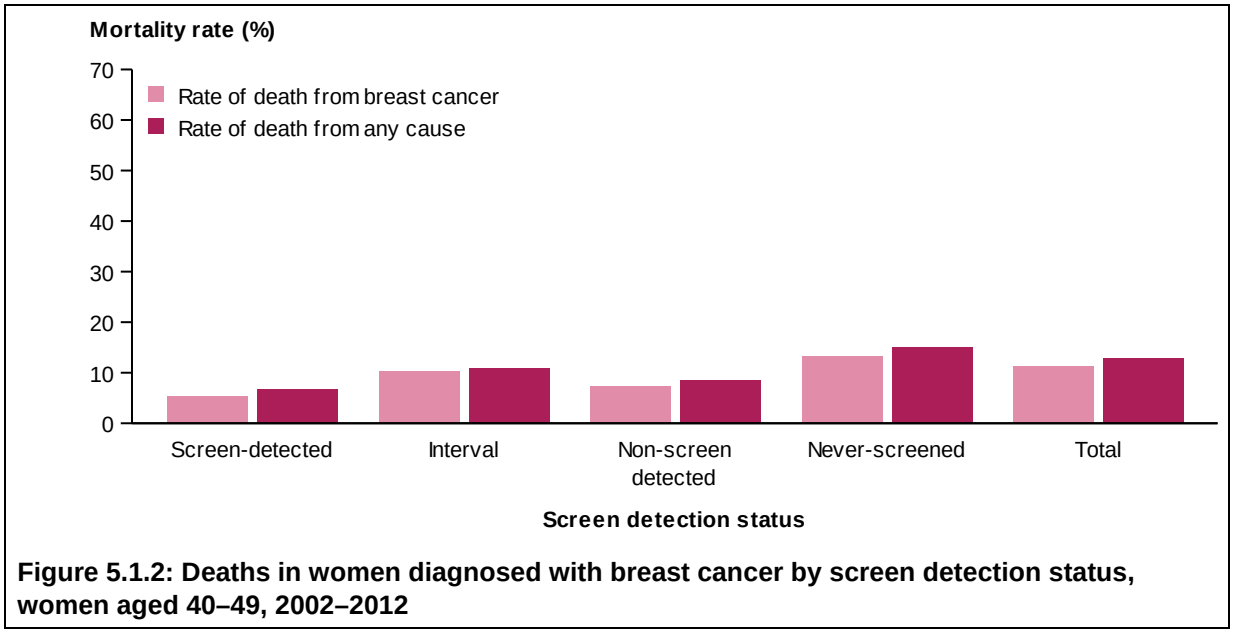


Figure 5.1.2: Deaths in women diagnosed with breast cancer by screen detection status, women aged 40–49, 2002–2012

Table 5.1.3: Deaths in women diagnosed with breast cancer by screen detection status, women aged 70 and over, 2002–2012

	Screen-detected	Interval	Non-screen-detected	Never-screened	Total
Number diagnosed with breast cancer	6,893	174	9,874	20,627	37,568
Number died from breast cancer	474	26	1,556	5,708	7,764
Rate of death from breast cancer (%)	6.9	14.9	15.8	27.7	20.7
Number died from any cause	1,766	52	3,546	13,368	18,732
Rate of death from any cause (%)	25.6	29.9	35.9	64.8	49.9
Mean age at diagnosis (years)	75 (±4.0)	73.6 (±2.9)	77.5 (±5.1)	81.9 (±6.8)	79.4 (±6.5)
Minimum–Maximum (years)	*70.0–92.6*	*70.1–85.5*	*70.0–98.9*	*70.0–108.4*	*70.0–108.4*
Median age at diagnosis (years)	74.1	72.9	76.8	81.7	78.4
Mean age at death (years)	82.3 (±5.5)	78.5 (±4.8)	82.9 (±5.8)	86.8 (±6.6)	85.6 (±6.7)
Minimum–Maximum (years)	*70.7–102.9*	*70.4–88.5*	*70.2–102.2*	*70.2–112.6*	*70.2–112.6*
Median age at death (years)	82.2	77.3	82.7	87.1	85.7

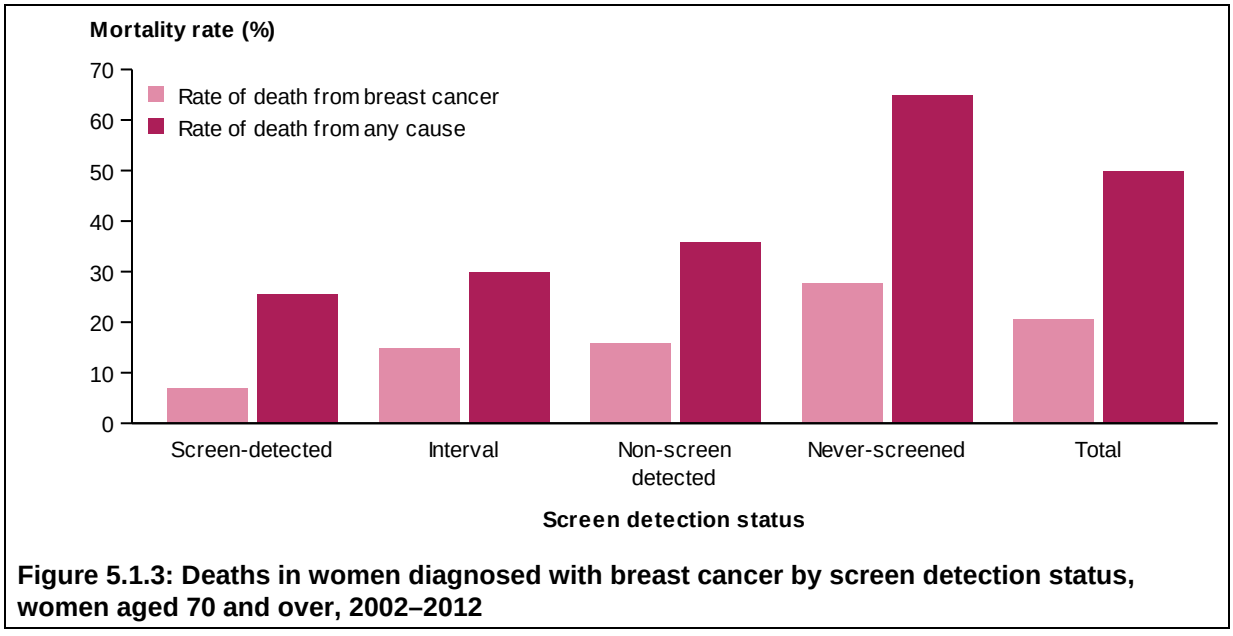


Figure 5.1.3: Deaths in women diagnosed with breast cancer by screen detection status, women aged 70 and over, 2002–2012

Table 5.1.4: Deaths in women diagnosed with breast cancer by screen detection status, women aged 40 and over, 2002–2012

	Screen-detected	Interval	Non-screen-detected	Never-screened	Total
Number diagnosed with breast cancer	42,322	1,742	34,476	58,931	137,471
Number died from breast cancer	2,113	195	4,185	11,848	18,341
Rate of death from breast cancer (%)	5.0	11.2	12.1	20.1	13.3
Number died from any cause	4,879	271	7,082	21,129	33,361
Rate of death from any cause (%)	11.5	15.6	20.5	35.9	24.3
Mean age at diagnosis (years)	61.6 (±8.7)	57.7 (±8.8)	63 (±11.4)	62.8 (±16)	62.4 (±12.9)
Minimum–Maximum (years)	*40.1–92.6*	*40.1–85.5*	*40.0–98.9*	*40.0–108.4*	*40.0–108.4*
Median age at diagnosis (years)	61.6	57.2	61.9	60.1	61.2
Mean age at death (years)	71.9 (±10.5)	64.5 (±9.8)	73.1 (±11.8)	76.5 (±15.5)	75 (±14.2)
Minimum–Maximum (years)	*42.6–102.9*	*44.1–88.5*	*42.4–102.2*	*40.4–112.6*	*40.4–112.6*
Median age at death (years)	72.2	63.5	74.2	81.2	77.4

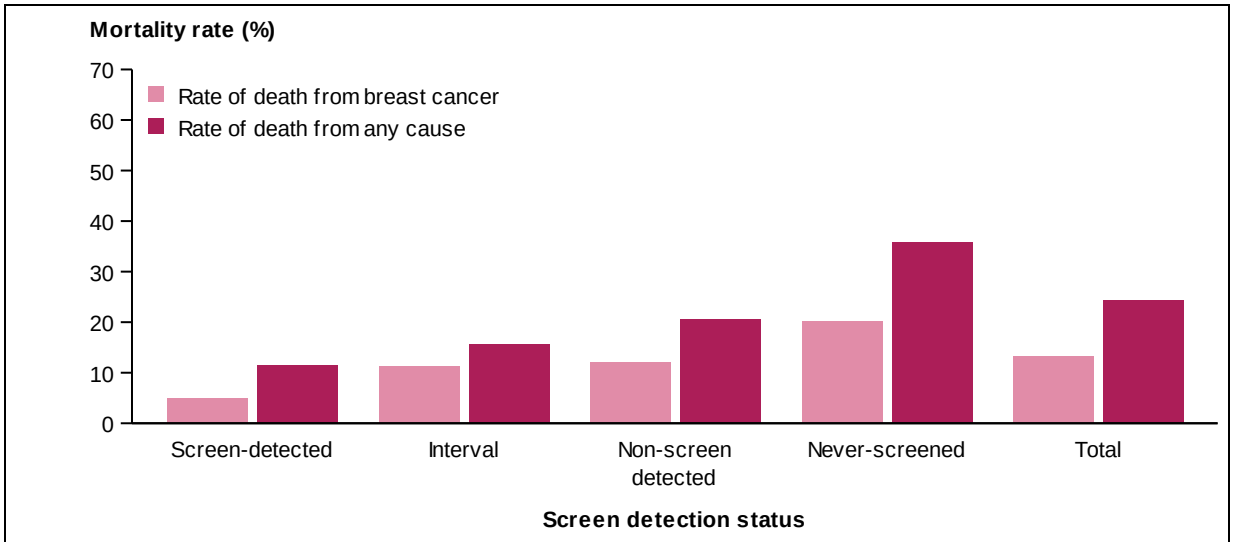


Figure 5.1.4: Deaths in women diagnosed with breast cancer by screen detection status, women aged 40 and over, 2002–2012

5.2 Survival

Survival analyses were undertaken to explore the differences in breast cancer deaths between screen-detected breast cancers and breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Tables 5.2.1–5.2.4 show the number and proportion of women diagnosed with breast cancer who died from breast cancer in each year of follow-up, as well as the total number who died by 31 December 2015 (the end of follow-up), by screen detection status.

The related survival curves are shown in figures 5.2.1–5.2.4.

These tables and figures show that, while screen-detected breast cancers always had a lower risk of breast cancer death than never-screened breast cancers, difference in risk differed across age groups. The difference was smallest for women aged 40–49 (0.9 percentage points after 1 year and 8.0 percentage points at the end of follow-up), followed by women aged 50–69 (3.1 after 1 year and 13.8 at the end of follow-up), and largest for women aged 70 and over (9.3 after 1 year and 20.8 at the end of follow-up).

This difference was reflected in the general log rank test statistics showing there was a strong effect of screen detection status on breast cancer mortality. For ages 50–69, 40–49, 70 and over, and 40 and over, these were, respectively: $\chi^2 = 2313.41$ with 3 degrees of freedom ($p < 0.0001$), $\chi^2 = 169.64$ with 3 degrees of freedom ($p < 0.0001$), $\chi^2 = 1275.17$ with 3 degrees of freedom ($p < 0.0001$) and $\chi^2 = 4311.84$ with 3 degrees of freedom ($p < 0.0001$).

Note that, while tables and figures show 10 years of follow up for all breast cancers diagnosed in the period 2002–2012, not all breast cancers would have been able to be followed for this length of time. In reality, only breast cancers diagnosed in the period 2002–2005 had adequate time between diagnosis and 31 December 2015 to allow 10 years of follow-up.

Table 5.2.1: Breast cancer deaths in women aged 50–69 diagnosed with breast cancer, by screen detection status

Screen detection status		Deaths											
			Years since diagnosis										
		2002–2012 diagnoses	1	2	3	4	5	6	7	8	9	10	At 31/12/2015
Screen-detected	Number	31,968	72	149	215	206	185	156	128	98	96	54	1,455
	Proportion (%)	. .	0.2	0.5	0.7	0.6	0.6	0.5	0.4	0.3	0.3	0.2	4.6
Interval	Number	1,202	18	17	30	19	14	13	11	5	1	2	131
	Proportion (%)	. .	1.5	1.4	2.5	1.6	1.2	1.1	0.9	0.4	0.1	0.2	10.9
Non-screen-detected	Number	20,025	244	403	373	337	292	193	142	116	82	46	2,292
	Proportion (%)	. .	1.2	2.0	1.9	1.7	1.5	1.0	0.7	0.6	0.4	0.2	11.4
Never-screened	Number	20,245	678	683	620	496	391	252	193	146	104	73	3,734
	Proportion (%)	. .	3.3	3.4	3.1	2.4	1.9	1.2	1.0	0.7	0.5	0.4	18.4

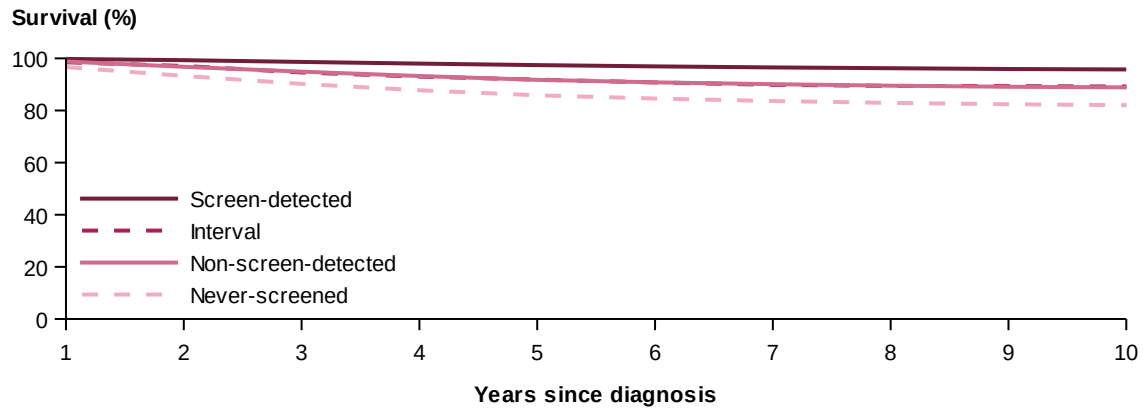


Figure 5.2.1: Crude survival for breast cancer mortality following a diagnosis of breast cancer in women aged 50–69, by screen detection status

Table 5.2.2: Breast cancer deaths in women aged 40–49 diagnosed with breast cancer, by screen detection status

Screen detection status		Deaths											
			Years since diagnosis										
		2002–2012 diagnoses	1	2	3	4	5	6	7	8	9	10	At 31/12/2015
Screen-detected	Number	3,461	6	18	27	26	26	16	19	16	10	7	184
	Proportion (%)	. .	0.2	0.5	0.8	0.8	0.8	0.5	0.5	0.5	0.3	0.2	5.3
Interval	Number	366	3	7	5	4	6	3	2	2	2	2	38
	Proportion (%)	. .	0.8	1.9	1.4	1.1	1.6	0.8	0.5	0.5	0.5	0.5	10.4
Non-screen-detected	Number	4,577	17	35	55	54	32	39	30	23	17	15	337
	Proportion (%)	. .	0.4	0.8	1.2	1.2	0.7	0.9	0.7	0.5	0.4	0.3	7.4
Never-screened	Number	18,059	200	353	404	353	294	243	177	108	94	81	2,406
	Proportion (%)	. .	1.1	2.0	2.2	2.0	1.6	1.3	1.0	0.6	0.5	0.4	13.3

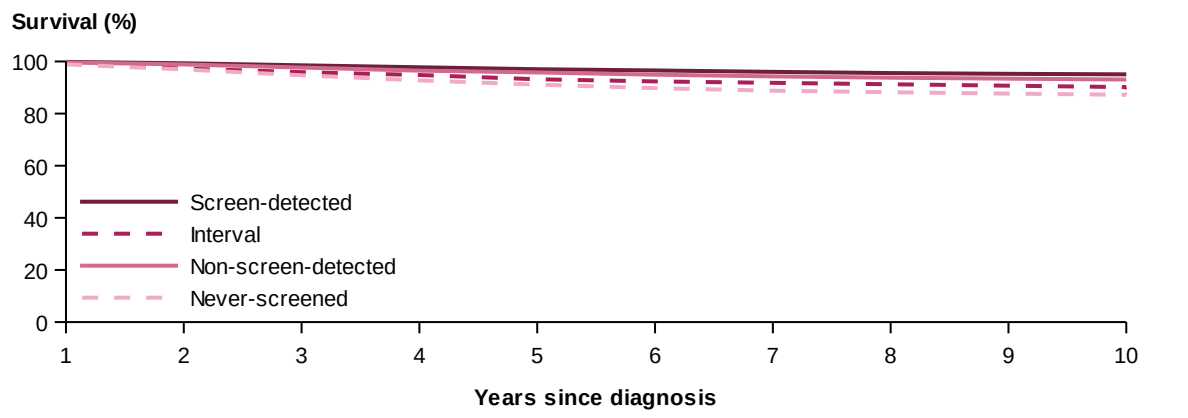


Figure 5.2.2: Crude survival for breast cancer mortality following a diagnosis of breast cancer in women aged 40–49, by screen detection status

Table 5.2.3: Breast cancer deaths in women aged 70 and over diagnosed with breast cancer, by screen detection status

		Deaths											
			Years since diagnosis										
Screen detection status		2002–2012 diagnoses	1	2	3	4	5	6	7	8	9	10	At 31/12/2015
Screen-detected	Number	6,893	52	64	87	53	48	46	29	28	21	15	474
	Proportion (%)	. .	0.8	0.9	1.3	0.8	0.7	0.7	0.4	0.4	0.3	0.2	6.9
Interval	Number	174	5	5	6	3	4	2	1	—	—	—	26
	Proportion (%)	. .	2.9	2.9	3.4	1.7	2.3	1.1	0.6	—	—	—	14.9
Non-screen-detected	Number	9,874	358	315	286	223	139	91	46	38	24	23	1,556
	Proportion (%)	. .	3.6	3.2	2.9	2.3	1.4	0.9	0.5	0.4	0.2	0.2	15.8
Never-screened	Number	20,627	2,080	1,003	817	588	408	276	193	122	96	59	5,708
	Proportion (%)	. .	10.1	4.9	4.0	2.9	2.0	1.3	0.9	0.6	0.5	0.3	27.7

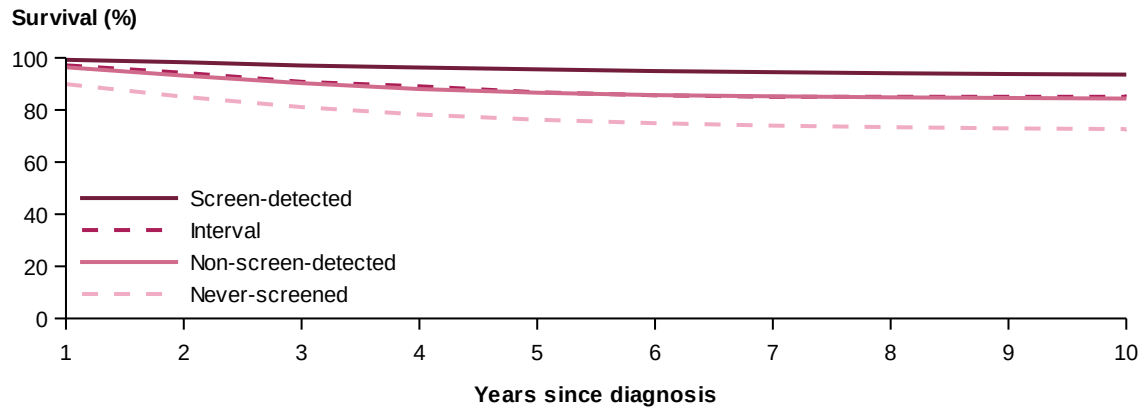


Figure 5.2.3: Crude survival for breast cancer mortality following a diagnosis of breast cancer in women aged 70 and over, by screen detection status

Table 5.2.4: Breast cancer deaths in women aged 40 and over diagnosed with breast cancer, by screen detection status

Screen detection status		Deaths											
			Years since diagnosis										
		2002–2012 diagnoses	1	2	3	4	5	6	7	8	9	10	At 31/12/2015
Screen-detected	Number	42,322	130	231	329	285	259	218	176	142	127	76	2,113
	Proportion (%)	. .	0.3	0.5	0.8	0.7	0.6	0.5	0.4	0.3	0.3	0.2	5.0
Interval	Number	1,742	26	29	41	26	24	18	14	7	3	4	195
	Proportion (%)	. .	1.5	1.7	2.4	1.5	1.4	1.0	0.8	0.4	0.2	0.2	11.2
Non-screen-detected	Number	34,476	619	753	714	614	463	323	218	177	123	84	4,185
	Proportion (%)	. .	1.8	2.2	2.1	1.8	1.3	0.9	0.6	0.5	0.4	0.2	12.1
Never-screened	Number	58,931	2,958	2,039	1,841	1,437	1,093	771	563	376	294	213	11,848
	Proportion (%)	. .	5.0	3.5	3.1	2.4	1.9	1.3	1.0	0.6	0.5	0.4	20.1

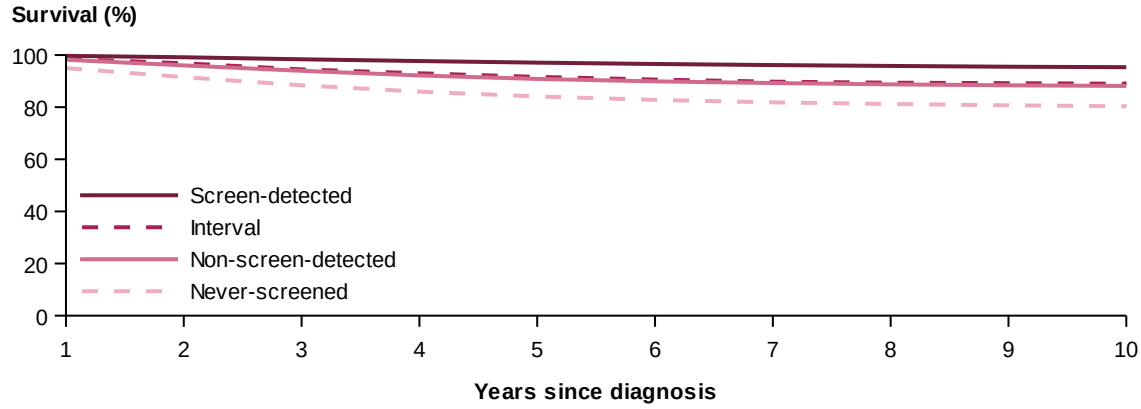


Figure 5.2.4: Crude survival for breast cancer mortality following a diagnosis of breast cancer in women aged 40 and over, by screen detection status

Univariate survival analyses

Cox proportional hazards regression models were used to quantify the relationship between survival and a set of explanatory variables for women diagnosed with breast cancer for each broad age group—40–49, 50–69 and 70 and over—and for all women aged 40 and over.

Univariate Cox proportional hazards models were fitted to each of the variables: screen detection status, age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site.

The crude hazard ratios for each are shown in tables 5.2.5–5.2.14. These showed that, compared with never-screened women, the risk of death from breast cancer for women with screen-detected breast cancers was significantly lower. Compared with never-screened breast cancers, the risk of breast cancer death was highest for women aged 40–49 with a hazard ratio of 0.37 (0.32–0.43), followed by women aged 50–69 with a hazard ratio of 0.23 (0.21–0.24). This was lowest in women aged 70 years and over with a hazard ratio of 0.18 (0.16–0.20).

Across all broad age groups, risk of death from breast cancer was lower in 2008–2012 than in 2002–2007, and increased with increasing remoteness and increasing disadvantage.

Risk of death from breast cancer differed by age in older women. While it was similar across the younger ages, risk of death from breast cancer increased with age for older women.

Breast cancer mortality outcomes also differed by histological type. Compared with women diagnosed with *Invasive ductal carcinoma:* women diagnosed with *Medullar carcinoma & atypical medullary carcinoma*, *Tubular carcinoma & invasive cribriform carcinoma*, *Mucinous carcinoma*, or *Invasive papillary carcinoma* had a lower risk of breast cancer death, while women diagnosed with *Inflammatory carcinoma*, *Mesenchymal* breast cancers, and *Other specified* and *Unspecified* breast cancers had a statistically significantly higher risk of breast cancer mortality. This was true for all broad age groups except for women aged 40–49, for whom *Mesenchymal* breast cancers did not have a greater risk of causing death, but for whom *Inflammatory carcinoma* had a very high risk of causing death.

Tumour size was also a statistically significant predictor of breast cancer mortality, with breast cancers greater than 15 mm or those with an unknown size (or for which tumour size was not applicable) shown to have a statistically significant higher risk of breast cancer mortality compared with small breast cancers (tumour size ≤15 mm).

This report also included sub-site, which is the area within the breast affected (Figure 5.2.5).

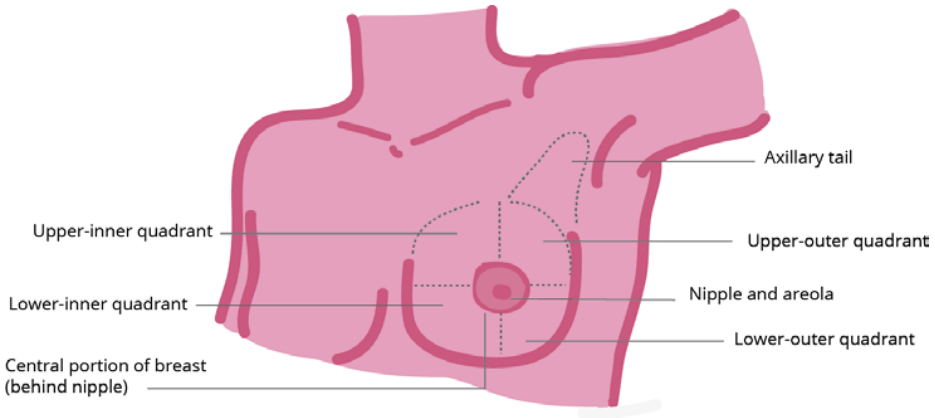


Figure 5.2.5: Sub-sites of the breast

The sub-site of the diagnosed breast cancer is not always known, and the proportion of breast cancers for which this was unspecified affects the results. Nonetheless, some trends in risk were apparent, which changed with age. For example, in breast cancers diagnosed in women aged 40–49, risk of death from breast cancer was higher for *Central portion* and lower for *Axillary tail*. This trend was not apparent in women aged 50–69. In women aged 70 and over, the risk of death from breast cancer was higher for *Axillary tail*.

Table 5.2.5: Crude breast cancer mortality hazard ratios for women aged 50–69 diagnosed with breast cancer

Category		HR	95% CI	*p* value
Screen detection status	Never-screened	1.0	. .	. .
	Interval	0.59	0.50–0.70	<0.0001
	Non-screen-detected	0.59	0.56–0.63	<0.0001
	Screen-detected	0.23	0.21–0.24	<0.0001
Age group	50–54	1.0	. .	. .
	55–59	1.14	1.07–1.21	<0.0001
	60–64	1.12	1.05–1.19	0.0006
	65–69	1.18	1.11–1.26	<0.0001
Year of diagnosis	2002–2007	1.0	. .	. .
	2008–2012	0.89	0.84–0.93	<0.0001
Remoteness area	Major cities	1.0	. .	. .
	Inner regional	1.11	1.04–1.17	0.0006
	Outer regional	1.20	1.11–1.29	<0.0001
	Remote	1.33	1.08–1.62	0.0061
	Very remote	1.67	1.26–2.22	0.0004
Socioeconomic group	1 (most disadvantage)	1.0	. .	. .
	2	0.91	0.85–0.98	0.0091
	3	0.89	0.83–0.96	0.0012
	4	0.80	0.74–0.85	<0.0001
	5 (least disadvantage)	0.67	0.62–0.72	<0.0001
Histological type	Invasive ductal carcinoma	1.0	. .	. .
	Invasive lobular carcinoma	0.98	0.91–1.05	0.5038
	Medullar carcinoma & atypical medullary carcinoma	0.78	0.52–1.16	0.2243
	Tubular carcinoma & invasive cribriform carcinoma	0.11	0.07–0.18	<0.0001
	Mucinous carcinoma	0.35	0.25–0.49	<0.0001
	Invasive papillary carcinoma	0.52	0.37–0.71	<0.0001
	Inflammatory carcinoma	5.26	4.02–6.90	<0.0001
	Mesenchymal	3.37	2.09–5.42	<0.0001
	Other—specified	2.40	2.13–2.72	<0.0001
	Unspecified	2.96	2.68–3.26	<0.0001
Tumour size	Small	1.0	. .	. .
	Non-small	3.50	3.25–3.76	<0.0001
	Unknown/Not applicable	7.43	6.89–8.01	<0.0001

(continued)

Table 5.2.5 (continued): Crude breast cancer mortality hazard ratios for women aged 50–69 diagnosed with breast cancer

Category		HR	95% CI	*p* value
Sub-site	Nipple and areola	1.0	. .	. .
	Central portion	1.56	1.17–2.09	0.0024
	Upper-inner quadrant	0.97	0.73–1.28	0.8100
	Lower-inner quadrant	1.34	1.00–1.80	0.0495
	Upper-outer quadrant	1.08	0.83–1.42	0.5633
	Lower-outer quadrant	1.24	0.94–1.65	0.1336
	Axillary tail	1.51	0.96–2.35	0.0719
	Overlapping lesion	1.30	0.98–1.71	0.0676
	Unspecified	1.39	1.06–1.82	0.0163

Multivariate survival analyses

Women aged 50–69

A crude hazard ratio of 0.23 (0.21–0.24) for women aged 50–69 showed that, compared with never-screened women, the risk of death from breast cancer was lower for women with a screen-detected breast cancer; a multivariate Cox proportional hazards model was generated to calculate this risk after taking into account possible confounders.

After adjusting for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site, the risk of death from breast cancer was significantly lower in screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia, with a hazard ratio of 0.31 (0.29–0.33) (Table 5.2.6). Risk was also lower for interval breast cancers and non-screen-detected breast cancers in screened women, both with a hazard ratio of 0.65 (Table 5.2.6).

There was a relatively large difference of 34 percentage points between the risk of breast cancer death in screen-detected breast cancers compared with the risk of death in non-screen-detected breast cancers in screened women.

As a sensitivity analysis, the multivariate Cox proportional hazards regression was repeated for breast cancers diagnosed in 2000–2012. The adjusted hazard ratio was 0.33 (0.32–0.35), which was not significantly different from the hazard ratio for 2002–2012 of 0.31 (0.29–0.33). This demonstrates that we have not biased the results towards screening by omitting breast cancers diagnosed in 2000 and 2001. Results of this sensitivity analysis for the 5-year age groups between 50 and 69 are shown in Table A5.

Analyses were repeated for all-cause mortality: crude hazard ratios showed that, compared with never-screened women, the risk of death from all causes for women aged 50–69 with a screen-detected breast cancer was significantly lower, as indicated by a hazard ratio of 0.33 (0.32–0.35) (Table 5.2.7).

A multivariate Cox proportional hazards model adjusted for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site found that the risk of death from all causes was significantly lower in women with a screen-detected breast cancer compared with women diagnosed with breast cancer who had never screened through BreastScreen Australia, with a hazard ratio of 0.41 (0.39–0.43) (Table 5.2.7).

Table 5.2.6: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 50–69 diagnosed with breast cancer

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.59	0.50–0.70	<0.0001
Non-screen-detected	0.59	0.56–0.63	<0.0001
Screen-detected	0.23	0.21–0.24	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.65	0.54–0.77	<0.0001
Non-screen-detected	0.65	0.61–0.68	<0.0001
Screen-detected	0.31	0.29–0.33	<0.0001

Table 5.2.7: Unadjusted (crude) and adjusted hazard ratios for all-cause mortality for women aged 50–69 diagnosed with breast cancer

	HR	95% CI	*p* value
All-cause mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.61	0.53–0.71	<0.0001
Non-screen-detected	0.61	0.58–0.64	<0.0001
Screen-detected	0.33	0.32–0.35	<0.0001
All-cause mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.66	0.57–0.77	<0.0001
Non-screen-detected	0.64	0.61–0.67	<0.0001
Screen-detected	0.41	0.39–0.43	<0.0001

Table 5.2.8: Crude breast cancer mortality hazard ratios for women aged 40–49 diagnosed with breast cancer

Category		HR	95% CI	*p* value
Screen detection status	Never-screened	1.0	. .	. .
	Interval	0.78	0.57–1.08	0.1306
	Non-screen-detected	0.49	0.44–0.55	<0.0001
	Screen-detected	0.37	0.32–0.43	<0.0001
Age group	40–44	1.0	. .	. .
	45–49	0.95	0.88–1.02	0.1281
Year of diagnosis	2002–2007	1.0	. .	. .
	2008–2012	0.75	0.69–0.82	<0.0001
Remoteness area	Major cities	1.0	. .	. .
	Inner regional	1.12	1.02–1.23	0.0163
	Outer regional	1.17	1.03–1.32	0.0174
	Remote	1.35	0.97–1.87	0.0777
	Very remote	1.50	0.97–2.33	0.0703
Socioeconomic group	1 (most disadvantage)	1.0	. .	. .
	2	0.90	0.81–1.01	0.0838
	3	0.87	0.77–0.97	0.0128
	4	0.80	0.71–0.89	<0.0001
	5 (least disadvantage)	0.66	0.59–0.74	<0.0001
Histological type	Invasive ductal carcinoma	1.0	. .	. .
	Invasive lobular carcinoma	0.91	0.79–1.03	0.1351
	Medullar carcinoma & atypical medullary carcinoma	0.20	0.08–0.54	0.0015
	Tubular carcinoma & invasive cribriform carcinoma	0.02	0.00–0.15	0.0001
	Mucinous carcinoma	0.20	0.10–0.41	<0.0001
	Invasive papillary carcinoma	0.66	0.36–1.19	0.1680
	Inflammatory carcinoma	4.60	3.10–6.82	<0.0001
	Mesenchymal	0.99	0.14–6.99	0.9878
	Other—specified	2.02	1.62–2.51	<0.0001
	Unspecified	1.84	1.51–2.24	<0.0001
Tumour size	Small	1.0	. .	. .
	Non-small	3.69	3.26–4.18	<0.0001
	Unknown/Not applicable	6.65	5.83–7.58	<0.0001

(continued)

Table 5.2.8 (continued): Crude breast cancer mortality hazard ratios for women aged 40–49 diagnosed with breast cancer

Category		HR	95% CI	*p* value
Sub-site	Nipple and areola	1.0	. .	. .
	Central portion	1.40	0.91–2.16	0.1264
	Upper-inner quadrant	0.90	0.59–1.36	0.6172
	Lower-inner quadrant	1.06	0.68–1.65	0.7819
	Upper-outer quadrant	0.93	0.62–1.39	0.7218
	Lower-outer quadrant	1.03	0.68–1.57	0.8854
	Axillary tail	0.64	0.27–1.47	0.2896
	Overlapping lesion	1.06	0.70–1.59	0.7929
	Unspecified	1.02	0.69–1.52	0.9127

Women aged 40–49

A crude hazard ratio of 0.37 (0.32–0.43) for women aged 40–49 showed that, compared with never-screened women, the risk of death from breast cancer was lower for women with a screen-detected breast cancer; a multivariate Cox proportional hazards model was generated to calculate this risk after taking into account possible confounders.

After adjusting for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site, the risk of death from breast cancer was significantly lower in screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia, with a hazard ratio of 0.45 (0.38–0.52) (Table 5.2.9). Risk was also lower for non-screen-detected breast cancers diagnosed in screened women, with a hazard ratio of 0.51 (0.45–0.57) (Table 5.2.9). Of note, the risk of breast cancer death was only slightly higher for non-screen-detected breast cancers in screened women than for screen-detected breast cancers, with an overall difference of just 6 percentage points in women aged 40–49.

Analyses were repeated for all-cause mortality: crude hazard ratios showed that, compared with never-screened women, the risk of death from all causes for women aged 40–49 with screen-detected breast cancers was significantly lower, as indicated by a hazard ratio of 0.41 (0.35–0.46) (Table 5.2.10).

A multivariate Cox proportional hazards model adjusted for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site found that the risk of death from all causes was significantly lower in women with a screen-detected breast cancer compared with women diagnosed with breast cancer who had never screened through BreastScreen Australia, with a hazard ratio of 0.48 (0.42–0.55) (Table 5.2.10). Again, there was almost no difference in the risk of death for screen-detected breast cancers compared with non-screen-detected breast cancers in screened women, the latter with a hazard ratio of 0.50 (0.45–0.56) (Table 5.2.10).

Table 5.2.9: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 40–49 diagnosed with breast cancer

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.78	0.57–1.08	0.1306
Non-screen-detected	0.49	0.44–0.55	<0.0001
Screen-detected	0.37	0.32–0.43	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.82	0.60–1.14	0.2370
Non-screen-detected	0.51	0.45–0.57	<0.0001
Screen-detected	0.45	0.38–0.52	<0.0001

Table 5.2.10: Unadjusted (crude) and adjusted hazard ratios for all-cause mortality for women aged 40–49 diagnosed with breast cancer

	HR	95% CI	*p* value
All-cause mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.73	0.53–0.99	0.0450
Non-screen-detected	0.49	0.44–0.55	<0.0001
Screen-detected	0.41	0.35–0.46	<0.0001
All-cause mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.76	0.56–1.04	0.0882
Non-screen-detected	0.50	0.45–0.56	<0.0001
Screen-detected	0.48	0.42–0.55	<0.0001

Table 5.2.11: Crude breast cancer mortality hazard ratios for women aged 70 and over diagnosed with breast cancer

Category		HR	95% CI	*p* value
Screen detection status	Never-screened	1.0	. .	. .
	Interval	0.44	0.30–0.64	<0.0001
	Non-screen-detected	0.50	0.47–0.53	<0.0001
	Screen-detected	0.18	0.16–0.20	<0.0001
Age group	70–74	1.0	. .	. .
	75–79	1.15	1.08-1.23	<0.0001
	80–84	1.48	1.38–1.58	<0.0001
	85+	2.26	2.11–2.42	<0.0001
Year of diagnosis	2002–2007	1.0	. .	. .
	2008–2012	1.04	0.99–1.09	0.0812
Remoteness area	Major cities	1.0	. .	. .
	Inner regional	1.15	1.08–1.21	<0.0001
	Outer regional	1.25	1.15–1.35	<0.0001
	Remote	0.98	0.73–1.31	0.8800
	Very remote	0.98	0.60–1.59	0.9222
Socioeconomic group	1 (most disadvantage)	1.0	. .	. .
	2	0.96	0.90–1.03	0.2354
	3	0.89	0.83–0.95	0.0009
	4	0.87	0.81–0.93	<0.0001
	5 (least disadvantage)	0.79	0.73–0.84	<0.0001
Histological type	Invasive ductal carcinoma	1.0	. .	. .
	Invasive lobular carcinoma	1.05	0.98–1.13	0.2024
	Medullar carcinoma & atypical medullary carcinoma	0.60	0.30–1.19	0.1428
	Tubular carcinoma & invasive cribriform carcinoma	0.19	0.11–0.34	<0.0001
	Mucinous carcinoma	0.34	0.28–0.42	<0.0001
	Invasive papillary carcinoma	0.44	0.33–0.59	<0.0001
	Inflammatory carcinoma	4.77	3.29–6.92	<0.0001
	Mesenchymal	4.33	2.82–6.65	<0.0001
	Other—specified	2.42	2.17–2.69	<0.0001
	Unspecified	4.68	4.42–4.96	<0.0001
Tumour size	Small	1.0	. .	. .
	Non-small	3.15	2.86–3.47	<0.0001
	Unknown/Not applicable	8.87	8.06–9.76	<0.0001

(continued)

Table 5.2.11 (continued): Crude breast cancer mortality hazard ratios for women aged 70 and over diagnosed with breast cancer

Category		HR	95% CI	*p* value
Sub-site	Nipple and areola	1.0	. .	. .
	Central portion	1.32	1.02–1.71	0.0318
	Upper–inner quadrant	0.92	0.71–1.18	0.5035
	Lower–inner quadrant	1.00	0.77–1.31	0.9893
	Upper–outer quadrant	1.08	0.86–1.37	0.5021
	Lower–outer quadrant	1.14	0.89–1.47	0.2997
	Axillary tail	2.09	1.36–3.21	0.0008
	Overlapping lesion	1.21	0.95–1.54	0.1264
	Unspecified	1.66	1.32–2.09	<0.0001

Women aged 70 and over

A crude hazard ratio of 0.18 (0.16–0.20) for women aged 70 and over showed that, compared with never-screened women, the risk of death from breast cancer was lower for women with a screen-detected breast cancer; a multivariate Cox proportional hazards model was generated to calculate this risk after taking into account possible confounders.

After adjusting for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site, the risk of death from breast cancer was significantly lower in screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia, with a hazard ratio of 0.36 (0.32–0.39) (Table 5.2.12). Risk was also lower for interval breast cancers and non-screen-detected breast cancers in screened women, with hazard ratios of 0.63 and 0.73, respectively (Table 5.2.12).

Similar to women aged 50–69, there was a relatively large difference of 37 percentage points between the risk of breast cancer death for screen-detected breast cancers and that for non-screen-detected breast cancers in screened women.

Analyses were repeated for all-cause mortality: crude hazard ratios showed that, compared with never-screened women, the risk of death from all causes for women aged 70 and over with screen-detected breast cancers was significantly lower, as indicated by a hazard ratio of 0.26 (0.25–0.28) (Table 5.2.13).

A multivariate Cox proportional hazards model adjusted for age group at diagnosis, period of diagnosis, remoteness area, socioeconomic group, histological type, tumour size and sub-site found that the risk of death from all causes was significantly lower in women with a screen-detected breast cancer compared with women diagnosed with breast cancer who had never screened through BreastScreen Australia, with a hazard ratio of 0.50 (0.47–0.53) (Table 5.2.13).

Table 5.2.12: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 70 and over diagnosed with breast cancer

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.44	0.30–0.64	<0.0001
Non-screen-detected	0.50	0.47–0.53	<0.0001
Screen-detected	0.18	0.16–0.20	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.43–0.93	0.0191
Non-screen-detected	0.73	0.69–0.78	<0.0001
Screen-detected	0.36	0.32–0.39	<0.0001

Table 5.2.13: Unadjusted (crude) and adjusted hazard ratios for all-cause mortality for women aged 70 and over diagnosed with breast cancer

	HR	95% CI	*p* value
All-cause mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.36	0.28–0.48	<0.0001
Non-screen-detected	0.49	0.47–0.51	<0.0001
Screen-detected	0.26	0.25–0.28	<0.0001
All-cause mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.64	0.49–0.84	0.0016
Non-screen-detected	0.74	0.71–0.77	<0.0001
Screen-detected	0.50	0.47–0.53	<0.0001

Table 5.2.14: Crude breast cancer mortality hazard ratios for women aged 40 and over diagnosed with breast cancer

Category		HR	95% CI	*p* value
Screen detection status	Never-screened	1.0	. .	. .
	Interval	0.51	0.44–0.59	<0.0001
	Non-screen-detected	0.56	0.54–0.58	<0.0001
	Screen-detected	0.21	0.20–0.22	<0.0001
Age group	40–44	1.0	. .	. .
	45–49	0.95	0.88–1.02	0.1316
	50–54	1.27	1.18–1.36	<0.0001
	55–59	1.44	1.34–1.54	<0.0001
	60–64	1.41	1.31–1.51	<0.0001
	65–69	1.49	1.38–1.60	<0.0001
	70–74	1.91	1.78–2.06	<0.0001
	75–79	2.22	2.06–2.38	<0.0001
	80–84	2.89	2.70–3.10	<0.0001
	85+	4.61	4.31–4.94	<0.0001
Year of diagnosis	2002–2007	1.0	. .	. .
	2008–2012	0.92	0.89–0.95	<0.0001
Remoteness area	Major cities	1.0	. .	. .
	Inner regional	1.14	1.10–1.18	<0.0001
	Outer regional	1.20	1.14–1.26	<0.0001
	Remote	1.15	0.99–1.33	0.0719
	Very remote	1.29	1.04–1.60	0.0208
Socioeconomic group	1 (most disadvantage)	1.0	. .	. .
	2	0.92	0.88–0.96	0.0002
	3	0.86	0.82–0.90	<0.0001
	4	0.79	0.75–0.82	<0.0001
	5 (least disadvantage)	0.68	0.65–0.71	<0.0001
Histological type	Invasive ductal carcinoma	1.0	. .	. .
	Invasive lobular carcinoma	1.05	1.00–1.10	0.0539
	Medullar carcinoma & atypical medullary carcinoma	0.51	0.37–0.71	<0.0001
	Tubular carcinoma & invasive cribriform carcinoma	0.11	0.08–0.16	<0.0001
	Mucinous carcinoma	0.40	0.34–0.47	<0.0001
	Invasive papillary carcinoma	0.55	0.45–0.67	<0.0001
	Inflammatory carcinoma	4.50	3.71–5.44	<0.0001
	Mesenchymal	3.82	2.79–5.23	<0.0001
	Other—specified	2.56	2.38–2.76	<0.0001
	Unspecified	4.75	4.54–4.97	<0.0001

(continued)

Table 5.2.14 (continued): Crude breast cancer mortality hazard ratios for women aged 40 and over diagnosed with breast cancer

Category		HR	95% CI	*p* value
Tumour size	Small	1.0	. .	. .
	Non-small	3.47	3.29–3.66	<0.0001
	Unknown/Not applicable	8.78	8.33–9.26	<0.0001
Sub-site	Nipple and areola	1.0	. .	. .
	Central portion	1.39	1.17–1.65	0.0002
	Upper-inner quadrant	0.86	0.73–1.02	0.0907
	Lower-inner quadrant	1.08	0.91–1.30	0.3792
	Upper-outer quadrant	0.96	0.82–1.13	0.6387
	Lower-outer quadrant	1.08	0.91–1.28	0.3927
	Axillary tail	1.33	1.00–1.78	0.0518
	Overlapping lesion	1.11	0.94–1.32	0.2058
	Unspecified	1.35	1.15–1.58	0.0003

Women aged 40 and over

For women aged 40 and over, compared with never-screened women, the crude risk of death from breast cancer for women with a screen-detected breast cancer was 0.21 (0.20–0.22); compared with never-screened women, the adjusted risk of death from breast cancer for women with a screen-detected breast cancer was 0.34 (0.32–0.35) (Table 5.2.15).

Repeating these analyses for all-cause mortality showed that, compared with never-screened women, the crude risk of death from all causes for women with a screen-detected breast cancer was 0.27 (0.26–0.28); compared to never-screened women, the adjusted risk of death from all causes for women with a screen-detected breast cancer was 0.45 (0.43–0.46) (Table 5.2.16).

Table 5.2.15: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 40 and over diagnosed with breast cancer

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.51	0.44–0.59	<0.0001
Non-screen-detected	0.56	0.54–0.58	<0.0001
Screen-detected	0.21	0.20–0.22	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.68	0.59–0.79	<0.0001
Non-screen-detected	0.67	0.64–0.69	<0.0001
Screen-detected	0.34	0.32–0.35	<0.0001

Table 5.2.16: Unadjusted (crude) and adjusted hazard ratios for all-cause mortality for women aged 40 and over diagnosed with breast cancer

	HR	95% CI	*p* value
All-cause mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.40	0.36–0.45	<0.0001
Non-screen-detected	0.53	0.51–0.54	<0.0001
Screen-detected	0.27	0.26–0.28	<0.0001
All-cause mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.69	0.61–0.78	<0.0001
Non-screen-detected	0.68	0.66–0.70	<0.0001
Screen-detected	0.45	0.43–0.46	<0.0001

5.3 Age differences

To better understand survival trends noted in Section 5.2, breast cancer survival analyses were repeated for 5-year age groups, with the results shown in Table 5.3.1.

The risk of death from screen-detected breast cancers compared with never-screened breast cancers was lowest in women aged 50–54, 55–59, 60–64, 65–69 and 70–74, with a hazard ratio between 0.30 and 0.32 for all these age groups. Risk of death from screen-detected breast cancers compared with never-screened breast cancers was higher outside these age groups. It was highest in those aged 40–44, with a hazard ratio of 0.58; this was followed by women aged 80–84 and 85+, with hazard ratios of 0.40 and 0.41, respectively; then by women aged 45–49, with a hazard ratio of 0.39; and then by women aged 75–79, with a hazard ratio of 0.36 (Figure 5.3.1).

The reason for the higher risk of breast cancer death in women aged 40–49 shown in section 5.2, as well as the similar hazard ratios for screen-detected and non-screen-detected breast cancers in screened women in this age group, are elucidated when data are reported for 5-year age groups in tables 5.3.2.a–5.3.2.j. These data show that—in opposition to all other 5-year age groups—in women aged 40–44, risk of breast cancer death was lower in non-screen-detected breast cancers in screened women than in screen-detected breast cancers (Table 5.3.1). This means that the similar hazard ratios for screen-detected and non-screen-detected in screened women breast cancers seen in women aged 40–49 is due to opposing results between women aged 40–44 and those aged 45–49; effectively, they 'cancel each other out', giving the appearance of no difference.

The reason that risk of breast cancer death for women aged 40–44 diagnosed with breast cancer was lowest for non-screen-detected breast cancers in screened women was not immediately clear. Clinical characteristics of breast cancers diagnosed by 5-year age group were examined to see if this would provide clues as to the reason for this anomalous result.

It was noted that this was the only age group for which the majority of screen-detected breast cancers were not small, with 42.9% of these cancers found to be less than or equal to 15 mm, and 45.7% greater than 15 mm (Table 5.3.2.a). This is likely to be a contributor to the relatively high risk of breast cancer death compared with other age groups, but does not explain why non-screen-detected breast cancers in screened women had a lower risk of death than screen-detected breast cancers. It may be that the definition used affects the outcomes in this youngest age group. Women aged 40–44 are new screeners, and while the definition of non-screen-detected breast cancers in screened women requires that women have been screened previously, the screen-detected breast cancer definition does not. It is therefore possible that a large proportion of screen-detected breast cancers are diagnosed after a woman's first screen, which are likely to be prevalent cancers that may be larger and/or at a later stage than incident cancers that grow between screens.

It may also be the case that the relatively higher risk of breast cancer death in women aged 40–49 is due to these women being at higher risk of breast cancer death at the time of their screen. It is possible that uptake of screening by women aged 40–49 is more likely in women from high-risk families (that is, with a strong family history of breast cancer).

The screening behaviour section 6.3 looks more closely at the 40–49 age group to better understand their BreastScreen Australia experience and possible reasons for screening.

Table 5.3.1: Adjusted hazard ratios for breast cancer mortality in women diagnosed with breast cancer by screen detection status and by 5-year age group

Age group		HR	95% CI	*p* value
40–44	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.55	0.29–1.06	0.0752
	Non-screen-detected	0.39	0.31–0.49	<0.0001
	Screen-detected	0.58	0.46–0.74	<0.0001
45–49	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.97	0.67–1.41	0.8898
	Non-screen-detected	0.56	0.49–0.64	<0.0001
	Screen-detected	0.39	0.32–0.47	<0.0001
50–54	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.56	0.39–0.79	0.0010
	Non-screen-detected	0.64	0.57–0.71	<0.0001
	Screen-detected	0.32	0.28–0.37	<0.0001
55–59	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.84	0.64–1.12	0.2330
	Non-screen-detected	0.61	0.55–0.68	<0.0001
	Screen-detected	0.31	0.28–0.35	<0.0001
60–64	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.57	0.38–0.84	0.0051
	Non-screen-detected	0.64	0.57–0.71	<0.0001
	Screen-detected	0.30	0.27–0.34	<0.0001
65–69	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.56	0.36–0.87	0.0107
	Non-screen-detected	0.72	0.65–0.81	<0.0001
	Screen-detected	0.32	0.28–0.36	<0.0001
70–74	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.81	0.54–1.22	0.3184
	Non-screen-detected	0.64	0.57–0.71	<0.0001
	Screen-detected	0.31	0.27–0.36	<0.0001

(continued)

Table 5.3.1 (continued): Adjusted hazard ratios for breast cancer mortality in women diagnosed with breast cancer by screen detection status and by 5-year age group

Age group		HR	95% CI	*p* value
75–79	Never-screened	1.0	. .	. .
	Screening women			
	Interval	0.18	0.04–0.70	0.0141
	Non-screen-detected	0.75	0.67–0.83	<0.0001
	Screen-detected	0.36	0.30–0.43	<0.0001
80–84	Never-screened	1.0	. .	. .
	Screening women			
	Interval	—	—	0.9215
	Non-screen-detected	0.78	0.70–0.88	<0.0001
	Screen-detected	0.40	0.31–0.50	<0.0001
85+	Never-screened	1.0	. .	. .
	Screening women			
	Interval	—	—	0.9311
	Non-screen-detected	0.79	0.69–0.92	0.0018
	Screen-detected	0.41	0.26–0.65	0.0002

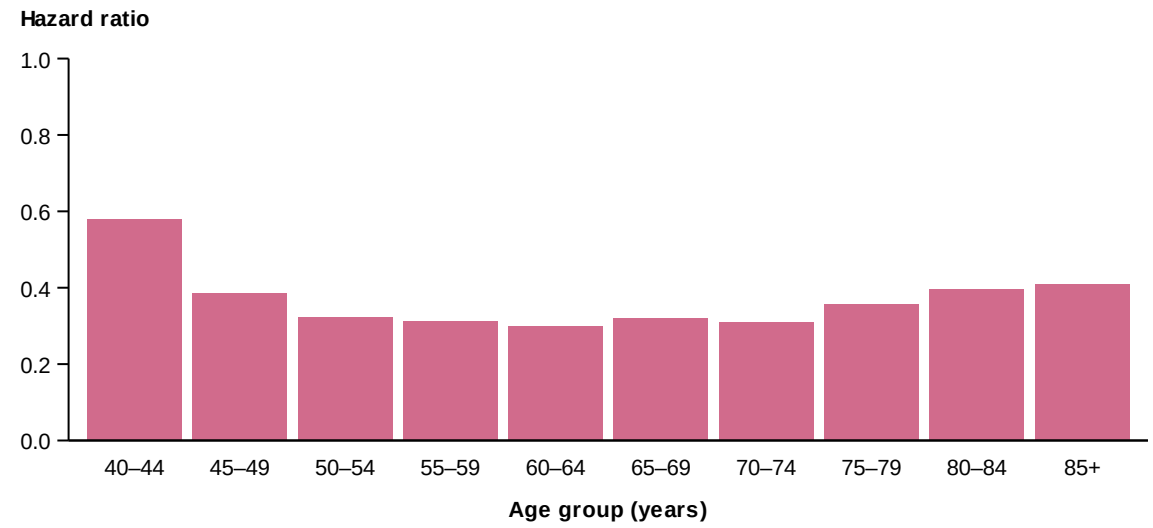


Figure 5.3.1: Adjusted hazard ratios for breast cancer mortality in women diagnosed with screen-detected breast cancer compared with never-screened women, by 5-year age group

Table 5.3.2.a: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 40–44

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 40–44											
Histological type	Invasive ductal carcinoma	825	85.9	100	85.5	978	82.9	6,944	84.5	8,847	84.5
	Invasive lobular carcinoma	77	8.0	10	8.5	111	9.4	611	7.4	809	7.7
	Medullar carcinoma & atypical medullary carcinoma	3	0.3	1	0.9	8	0.7	66	0.8	78	0.7
	Tubular carcinoma & invasive cribriform carcinoma	21	2.2	1	0.9	21	1.8	85	1.0	128	1.2
	Mucinous carcinoma	10	1.0	1	0.9	14	1.2	124	1.5	149	1.4
	Invasive papillary carcinoma	6	0.6	2	1.7	9	0.8	54	0.7	71	0.7
	Inflammatory carcinoma	3	0.3	—	—	1	0.1	19	0.2	23	0.2
	Mesenchymal	—	—	—	—	1	0.1	2	—	3	—
	Other—specified	8	0.8	2	1.7	18	1.5	143	1.7	171	1.6
	Unspecified	7	0.7	—	—	19	1.6	166	2.0	192	1.8
Tumour size	Small	412	42.9	45	38.5	370	31.4	2,336	28.4	3,163	30.2
	Non-small	439	45.7	58	49.6	605	51.3	4,460	54.3	5,562	53.1
	Unknown/Not applicable	109	11.4	14	12.0	205	17.4	1,418	17.3	1,746	16.7
Sub-site	Unspecified	357	37.2	28	23.9	519	44.0	4,091	49.8	4,995	47.7
	Nipple and areola	7	0.7	1	0.9	11	0.9	55	0.7	74	0.7
	Central portion	43	4.5	10	8.5	40	3.4	235	2.9	328	3.1
	Upper-inner quadrant	81	8.4	13	11.1	75	6.4	604	7.4	773	7.4
	Lower-inner quadrant	41	4.3	5	4.3	39	3.3	243	3.0	328	3.1
	Upper-outer quadrant	264	27.5	31	26.5	312	26.4	1,681	20.5	2,288	21.9
	Lower-outer quadrant	47	4.9	12	10.3	82	6.9	423	5.1	564	5.4
	Axillary tail	3	0.3	4	3.4	4	0.3	23	0.3	34	0.3
	Overlapping lesion	117	12.2	13	11.1	98	8.3	859	10.5	1,087	10.4

Table 5.3.2.b: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 45–49

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 45–49											
Histological type	Invasive ductal carcinoma	2,095	83.8	200	80.3	2,769	81.5	8,121	82.5	13,185	82.4
	Invasive lobular carcinoma	249	10.0	29	11.6	357	10.5	970	9.9	1,605	10.0
	Medullar carcinoma & atypical medullary carcinoma	13	0.5	1	0.4	17	0.5	45	0.5	76	0.5
	Tubular carcinoma & invasive cribriform carcinoma	59	2.4	2	0.8	67	2.0	141	1.4	269	1.7
	Mucinous carcinoma	23	0.9	3	1.2	42	1.2	121	1.2	189	1.2
	Invasive papillary carcinoma	19	0.8	2	0.8	22	0.6	53	0.5	96	0.6
	Inflammatory carcinoma	—	—	1	0.4	7	0.2	29	0.3	37	0.2
	Mesenchymal	1	—	—	—	3	0.1	5	0.1	9	0.1
	Other—specified	20	0.8	8	3.2	47	1.4	149	1.5	224	1.4
	Unspecified	22	0.9	3	1.2	66	1.9	211	2.1	302	1.9
Tumour size	Small	1,217	48.7	79	31.7	1,176	34.6	2,888	29.3	5,360	33.5
	Non-small	991	39.6	140	56.2	1,725	50.8	5,324	54.1	8,180	51.2
	Unknown/Not applicable	293	11.7	30	12.0	496	14.6	1,633	16.6	2,452	15.3
Sub-site	Unspecified	918	36.7	71	28.5	1,452	42.7	5,050	51.3	7,491	46.8
	Nipple and areola	22	0.9	8	3.2	26	0.8	79	0.8	135	0.8
	Central portion	100	4.0	7	2.8	110	3.2	255	2.6	472	3.0
	Upper-inner quadrant	255	10.2	25	10.0	278	8.2	711	7.2	1,269	7.9
	Lower-inner quadrant	82	3.3	13	5.2	123	3.6	296	3.0	514	3.2
	Upper-outer quadrant	671	26.8	69	27.7	831	24.5	1,932	19.6	3,503	21.9
	Lower-outer quadrant	159	6.4	19	7.6	229	6.7	534	5.4	941	5.9
	Axillary tail	7	0.3	2	0.8	20	0.6	35	0.4	64	0.4
	Overlapping lesion	287	11.5	35	14.1	328	9.7	953	9.7	1,603	10.0

Table 5.3.2.c: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 50–54

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 50–54											
Histological type	Invasive ductal carcinoma	5,627	82.4	306	81.6	4,123	80.8	5,144	81.2	15,200	81.5
	Invasive lobular carcinoma	696	10.2	41	10.9	578	11.3	615	9.7	1,930	10.4
	Medullar carcinoma & atypical medullary carcinoma	24	0.4	1	0.3	29	0.6	27	0.4	81	0.4
	Tubular carcinoma & invasive cribriform carcinoma	239	3.5	8	2.1	107	2.1	90	1.4	444	2.4
	Mucinous carcinoma	65	1.0	5	1.3	55	1.1	67	1.1	192	1.0
	Invasive papillary carcinoma	49	0.7	—	—	38	0.7	44	0.7	131	0.7
	Inflammatory carcinoma	3	—	2	0.5	6	0.1	21	0.3	32	0.2
	Mesenchymal	1	—	—	—	1	—	10	0.2	12	0.1
	Other—specified	51	0.7	3	0.8	68	1.3	129	2.0	251	1.3
	Unspecified	71	1.0	9	2.4	99	1.9	187	3.0	366	2.0
Tumour size	Small	3,546	51.9	125	33.3	1,768	34.6	1,737	27.4	7,176	38.5
	Non-small	2,553	37.4	204	54.4	2,608	51.1	3,276	51.7	8,641	46.4
	Unknown/Not applicable	727	10.7	46	12.3	728	14.3	1,321	20.9	2,822	15.1
Sub-site	Unspecified	3,128	45.8	103	27.5	2,373	46.5	3,262	51.5	8,866	47.6
	Nipple and areola	25	0.4	11	2.9	49	1.0	43	0.7	128	0.7
	Central portion	196	2.9	24	6.4	169	3.3	215	3.4	604	3.2
	Upper-inner quadrant	594	8.7	32	8.5	386	7.6	457	7.2	1,469	7.9
	Lower-inner quadrant	244	3.6	12	3.2	184	3.6	195	3.1	635	3.4
	Upper-outer quadrant	1,605	23.5	97	25.9	1,107	21.7	1,179	18.6	3,988	21.4
	Lower-outer quadrant	344	5.0	34	9.1	318	6.2	366	5.8	1,062	5.7
	Axillary tail	21	0.3	3	0.8	17	0.3	21	0.3	62	0.3
	Overlapping lesion	669	9.8	59	15.7	501	9.8	596	9.4	1,825	9.8

Table 5.3.2.d: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 55–59

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 55–59											
Histological type	Invasive ductal carcinoma	6,647	82.9	273	79.6	4,380	79.9	3,973	79.7	15,273	81.1
	Invasive lobular carcinoma	815	10.2	30	8.7	663	12.1	506	10.1	2,014	10.7
	Medullar carcinoma & atypical medullary carcinoma	34	0.4	3	0.9	29	0.5	24	0.5	90	0.5
	Tubular carcinoma & invasive cribriform carcinoma	234	2.9	2	0.6	73	1.3	77	1.5	386	2.0
	Mucinous carcinoma	83	1.0	5	1.5	52	0.9	61	1.2	201	1.1
	Invasive papillary carcinoma	69	0.9	6	1.7	43	0.8	44	0.9	162	0.9
	Inflammatory carcinoma	6	0.1	1	0.3	11	0.2	11	0.2	29	0.2
	Mesenchymal	2	—	—	—	7	0.1	6	0.1	15	0.1
	Other—specified	56	0.7	12	3.5	108	2.0	114	2.3	290	1.5
	Unspecified	74	0.9	11	3.2	113	2.1	172	3.4	370	2.0
Tumour size	Small	4,386	54.7	108	31.5	1,814	33.1	1,366	27.4	7,674	40.8
	Non-small	2,748	34.3	177	51.6	2,798	51.1	2,464	49.4	8,187	43.5
	Unknown/Not applicable	886	11.0	58	16.9	867	15.8	1,158	23.2	2,969	15.8
Sub-site	Unspecified	3,695	46.1	93	27.1	2,677	48.9	2,513	50.4	8,978	47.7
	Nipple and areola	26	0.3	10	2.9	62	1.1	43	0.9	141	0.7
	Central portion	249	3.1	15	4.4	210	3.8	174	3.5	648	3.4
	Upper-inner quadrant	641	8.0	24	7.0	404	7.4	366	7.3	1,435	7.6
	Lower-inner quadrant	281	3.5	28	8.2	162	3.0	155	3.1	626	3.3
	Upper-outer quadrant	1,913	23.9	91	26.5	1,138	20.8	981	19.7	4,123	21.9
	Lower-outer quadrant	458	5.7	21	6.1	313	5.7	276	5.5	1,068	5.7
	Axillary tail	19	0.2	5	1.5	24	0.4	15	0.3	63	0.3
	Overlapping lesion	738	9.2	56	16.3	489	8.9	465	9.3	1,748	9.3

Table 5.3.2.e: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 60–64

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 60–64											
Histological type	Invasive ductal carcinoma	7,283	80.5	196	74.0	4,128	77.7	3,611	76.2	15,218	78.6
	Invasive lobular carcinoma	1,059	11.7	45	17.0	747	14.1	604	12.8	2,455	12.7
	Medullar carcinoma & atypical medullary carcinoma	27	0.3	—	—	20	0.4	9	0.2	56	0.3
	Tubular carcinoma & invasive cribriform carcinoma	269	3.0	5	1.9	75	1.4	79	1.7	428	2.2
	Mucinous carcinoma	134	1.5	4	1.5	70	1.3	55	1.2	263	1.4
	Invasive papillary carcinoma	106	1.2	2	0.8	49	0.9	56	1.2	213	1.1
	Inflammatory carcinoma	6	0.1	—	—	15	0.3	8	0.2	29	0.1
	Mesenchymal	5	0.1	1	0.4	1	—	8	0.2	15	0.1
	Other—specified	60	0.7	6	2.3	106	2.0	123	2.6	295	1.5
	Unspecified	95	1.1	6	2.3	99	1.9	183	3.9	383	2.0
Tumour size	Small	5,050	55.8	90	34.0	1,849	34.8	1,378	29.1	8,367	43.2
	Non-small	3,049	33.7	144	54.3	2,662	50.1	2,248	47.5	8,103	41.9
	Unknown/Not applicable	945	10.4	31	11.7	799	15.0	1,110	23.4	2,885	14.9
Sub-site	Unspecified	3,925	43.4	71	26.8	2,582	48.6	2,325	49.1	8,903	46.0
	Nipple and areola	28	0.3	4	1.5	65	1.2	41	0.9	138	0.7
	Central portion	248	2.7	18	6.8	190	3.6	173	3.7	629	3.2
	Upper-inner quadrant	739	8.2	24	9.1	389	7.3	367	7.7	1,519	7.8
	Lower-inner quadrant	358	4.0	11	4.2	168	3.2	156	3.3	693	3.6
	Upper-outer quadrant	2,251	24.9	63	23.8	1,058	19.9	967	20.4	4,339	22.4
	Lower-outer quadrant	525	5.8	16	6.0	296	5.6	264	5.6	1,101	5.7
	Axillary tail	17	0.2	3	1.1	24	0.5	18	0.4	62	0.3
	Overlapping lesion	953	10.5	55	20.8	538	10.1	425	9.0	1,971	10.2

Table 5.3.2.f: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 65–69

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 65–69											
Histological type	Invasive ductal carcinoma	6,314	78.2	152	69.4	3,135	75.9	3,119	74.5	12,720	76.6
	Invasive lobular carcinoma	1,031	12.8	39	17.8	625	15.1	569	13.6	2,264	13.6
	Medullar carcinoma & atypical medullary carcinoma	17	0.2	1	0.5	19	0.5	11	0.3	48	0.3
	Tubular carcinoma & invasive cribriform carcinoma	273	3.4	1	0.5	38	0.9	40	1.0	352	2.1
	Mucinous carcinoma	215	2.7	2	0.9	79	1.9	73	1.7	369	2.2
	Invasive papillary carcinoma	88	1.1	6	2.7	44	1.1	64	1.5	202	1.2
	Inflammatory carcinoma	1	—	1	0.5	17	0.4	8	0.2	27	0.2
	Mesenchymal	3	—	—	—	2	—	6	0.1	11	0.1
	Other—specified	71	0.9	11	5.0	83	2.0	101	2.4	266	1.6
	Unspecified	65	0.8	6	2.7	90	2.2	196	4.7	357	2.1
Tumour size	Small	4,697	58.1	82	37.4	1,383	33.5	1,111	26.5	7,273	43.8
	Non-small	2,533	31.4	108	49.3	2,102	50.9	2,009	48.0	6,752	40.6
	Unknown/Not applicable	848	10.5	29	13.2	647	15.7	1,067	25.5	2,591	15.6
Sub-site	Unspecified	3,639	45.0	67	30.6	2,020	48.9	2,060	49.2	7,786	46.9
	Nipple and areola	37	0.5	7	3.2	54	1.3	38	0.9	136	0.8
	Central portion	242	3.0	10	4.6	196	4.7	165	3.9	613	3.7
	Upper-inner quadrant	619	7.7	18	8.2	315	7.6	301	7.2	1,253	7.5
	Lower-inner quadrant	366	4.5	10	4.6	143	3.5	162	3.9	681	4.1
	Upper-outer quadrant	1,870	23.1	54	24.7	780	18.9	809	19.3	3,513	21.1
	Lower-outer quadrant	431	5.3	12	5.5	239	5.8	237	5.7	919	5.5
	Axillary tail	17	0.2	2	0.9	12	0.3	13	0.3	44	0.3
	Overlapping lesion	857	10.6	39	17.8	373	9.0	402	9.6	1,671	10.1

Table 5.3.2.g: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 70–74

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 70–74											
Histological type	Invasive ductal carcinoma	3,160	77.5	90	68.2	2,710	74.6	2,791	72.9	8,751	75.0
	Invasive lobular carcinoma	524	12.8	27	20.5	512	14.1	485	12.7	1,548	13.3
	Medullar carcinoma & atypical medullary carcinoma	9	0.2	—	—	15	0.4	8	0.2	32	0.3
	Tubular carcinoma & invasive cribriform carcinoma	111	2.7	—	—	34	0.9	31	0.8	176	1.5
	Mucinous carcinoma	132	3.2	3	2.3	107	2.9	125	3.3	367	3.1
	Invasive papillary carcinoma	59	1.4	2	1.5	50	1.4	41	1.1	152	1.3
	Inflammatory carcinoma	—	—	—	—	8	0.2	6	0.2	14	0.1
	Mesenchymal	2	—	—	—	2	0.1	7	0.2	11	0.1
	Other—specified	39	1.0	9	6.8	102	2.8	119	3.1	269	2.3
	Unspecified	42	1.0	1	0.8	94	2.6	217	5.7	354	3.0
Tumour size	Small	2,382	58.4	37	28.0	1,149	31.6	845	22.1	4,413	37.8
	Non-small	1,182	29.0	69	52.3	1,896	52.2	1,893	49.4	5,040	43.2
	Unknown/Not applicable	514	12.6	26	19.7	589	16.2	1,092	28.5	2,221	19.0
Sub-site	Unspecified	1,947	47.7	36	27.3	1,681	46.3	1,964	51.3	5,628	48.2
	Nipple and areola	20	0.5	7	5.3	52	1.4	41	1.1	120	1.0
	Central portion	123	3.0	13	9.8	149	4.1	144	3.8	429	3.7
	Upper-inner quadrant	309	7.6	11	8.3	296	8.1	289	7.5	905	7.8
	Lower-inner quadrant	164	4.0	8	6.1	135	3.7	129	3.4	436	3.7
	Upper-outer quadrant	947	23.2	27	20.5	678	18.7	689	18.0	2,341	20.1
	Lower-outer quadrant	208	5.1	9	6.8	248	6.8	220	5.7	685	5.9
	Axillary tail	12	0.3	2	1.5	13	0.4	8	0.2	35	0.3
	Overlapping lesion	348	8.5	19	14.4	382	10.5	346	9.0	1,095	9.4

Table 5.3.2.h: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 75–79

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 75–79											
Histological type	Invasive ductal carcinoma	1,492	75.1	24	70.6	2,374	72.7	3,343	71.0	7,233	72.4
	Invasive lobular carcinoma	278	14.0	7	20.6	480	14.7	579	12.3	1,344	13.4
	Medullar carcinoma & atypical medullary carcinoma	7	0.4	—	—	9	0.3	8	0.2	24	0.2
	Tubular carcinoma & invasive cribriform carcinoma	66	3.3	—	—	32	1.0	24	0.5	122	1.2
	Mucinous carcinoma	63	3.2	—	—	110	3.4	188	4.0	361	3.6
	Invasive papillary carcinoma	32	1.6	—	—	53	1.6	62	1.3	147	1.5
	Inflammatory carcinoma	—	—	—	—	6	0.2	12	0.3	18	0.2
	Mesenchymal	3	0.2	—	—	5	0.2	8	0.2	16	0.2
	Other—specified	29	1.5	1	2.9	82	2.5	129	2.7	241	2.4
	Unspecified	17	0.9	2	5.9	113	3.5	358	7.6	490	4.9
Tumour size	Small	1,025	51.6	11	32.4	928	28.4	903	19.2	2,867	28.7
	Non-small	596	30.0	14	41.2	1,778	54.5	2,280	48.4	4,668	46.7
	Unknown/Not applicable	366	18.4	9	26.5	558	17.1	1,528	32.4	2,461	24.6
Sub-site	Unspecified	916	46.1	10	29.4	1,512	46.3	2,567	54.5	5,005	50.1
	Nipple and areola	11	0.6	3	8.8	49	1.5	64	1.4	127	1.3
	Central portion	67	3.4	3	8.8	142	4.4	215	4.6	427	4.3
	Upper-inner quadrant	142	7.1	3	8.8	227	7.0	318	6.8	690	6.9
	Lower-inner quadrant	89	4.5	2	5.9	116	3.6	163	3.5	370	3.7
	Upper-outer quadrant	451	22.7	5	14.7	650	19.9	772	16.4	1,878	18.8
	Lower-outer quadrant	126	6.3	5	14.7	206	6.3	233	4.9	570	5.7
	Axillary tail	5	0.3	—	—	12	0.4	11	0.2	28	0.3
	Overlapping lesion	180	9.1	3	8.8	350	10.7	368	7.8	901	9.0

Table 5.3.2.i: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 80–84

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 80–84											
Histological type	Invasive ductal carcinoma	502	75.0	4	66.7	1,430	69.4	3,571	67.0	5,507	68.3
	Invasive lobular carcinoma	84	12.6	1	16.7	312	15.1	629	11.8	1,026	12.7
	Medullar carcinoma & atypical medullary carcinoma	—	—	—	—	5	0.2	5	0.1	10	0.1
	Tubular carcinoma & invasive cribriform carcinoma	17	2.5	—	—	10	0.5	35	0.7	62	0.8
	Mucinous carcinoma	38	5.7	—	—	111	5.4	223	4.2	372	4.6
	Invasive papillary carcinoma	8	1.2	—	—	43	2.1	89	1.7	140	1.7
	Inflammatory carcinoma	—	—	—	—	5	0.2	1	—	6	0.1
	Mesenchymal	1	0.1	—	—	—	—	5	0.1	6	0.1
	Other—specified	5	0.7	1	16.7	53	2.6	153	2.9	212	2.6
	Unspecified	14	2.1	—	—	93	4.5	617	11.6	724	9.0
Tumour size	Small	290	43.3	1	16.7	473	22.9	794	14.9	1,558	19.3
	Non-small	211	31.5	2	33.3	1,132	54.9	2,497	46.9	3,842	47.6
	Unknown/Not applicable	168	25.1	3	50.0	457	22.2	2,037	38.2	2,665	33.0
Sub-site	Unspecified	304	45.4	1	16.7	984	47.7	3,127	58.7	4,416	54.8
	Nipple and areola	5	0.7	—	—	37	1.8	60	1.1	102	1.3
	Central portion	33	4.9	—	—	79	3.8	206	3.9	318	3.9
	Upper-inner quadrant	52	7.8	—	—	140	6.8	296	5.6	488	6.1
	Lower-inner quadrant	27	4.0	—	—	79	3.8	157	2.9	263	3.3
	Upper-outer quadrant	150	22.4	1	16.7	365	17.7	833	15.6	1,349	16.7
	Lower-outer quadrant	40	6.0	—	—	122	5.9	248	4.7	410	5.1
	Axillary tail	1	0.1	—	—	7	0.3	15	0.3	23	0.3
	Overlapping lesion	57	8.5	4	66.7	249	12.1	386	7.2	696	8.6

Table 5.3.2.j: Clinical characteristics of breast cancers by screen detection status and 5-year age group, ages 85 and over

		Screen detection status									
		Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
		Count	%	Count	%	Count	%	Count	%	Count	%
Age group 85+											
Histological type	Invasive ductal carcinoma	111	69.8	1	50.0	625	68.4	3,835	56.7	4,572	58.4
	Invasive lobular carcinoma	20	12.6	—	—	100	10.9	613	9.1	733	9.4
	Medullar carcinoma & atypical medullary carcinoma	—	—	—	—	1	0.1	5	0.1	6	0.1
	Tubular carcinoma & invasive cribriform carcinoma	1	0.6	—	—	4	0.4	32	0.5	37	0.5
	Mucinous carcinoma	12	7.5	—	—	46	5.0	284	4.2	342	4.4
	Invasive papillary carcinoma	2	1.3	—	—	13	1.4	69	1.0	84	1.1
	Inflammatory carcinoma	—	—	—	—	2	0.2	3	—	5	0.1
	Mesenchymal	1	0.6	—	—	1	0.1	6	0.1	8	0.1
	Other—specified	3	1.9	—	—	31	3.4	239	3.5	273	3.5
	Unspecified	9	5.7	1	50.0	91	10.0	1,672	24.7	1,773	22.6
Tumour size	Small	58	36.5	1	50.0	161	17.6	553	8.2	773	9.9
	Non-small	49	30.8	—	—	423	46.3	2,373	35.1	2,845	36.3
	Unknown/Not applicable	52	32.7	1	50.0	330	36.1	3,832	56.7	4,215	53.8
Sub-site	Unspecified	71	44.7	1	50.0	425	46.5	4,486	66.4	4,983	63.6
	Nipple and areola	2	1.3	—	—	18	2.0	86	1.3	106	1.4
	Central portion	9	5.7	—	—	33	3.6	213	3.2	255	3.3
	Upper-inner quadrant	13	8.2	—	—	64	7.0	301	4.5	378	4.8
	Lower-inner quadrant	6	3.8	—	—	20	2.2	120	1.8	146	1.9
	Upper-outer quadrant	35	22.0	1	50.0	180	19.7	851	12.6	1,067	13.6
	Lower-outer quadrant	9	5.7	—	—	56	6.1	235	3.5	300	3.8
	Axillary tail	—	—	—	—	6	0.7	20	0.3	26	0.3
	Overlapping lesion	14	8.8	—	—	112	12.3	446	6.6	572	7.3

5.4 Exploration of potential biases in survival

There are three potential biases that require consideration in these types of analyses: lead-time bias, screening selection bias, and length bias.

'Lead time' is the length of time between when a cancer is detected by screening, and when the cancer would have been diagnosed due to the development of clinical signs or symptoms if screening had not occurred. Detecting a cancer early by screening can improve survival through effective treatment and management, delaying the time until death. However, a diagnosis of cancer can also be made earlier without affecting the date on which the individual would have died, but the additional lead time in the screened individual makes it look as though time until death is longer. This results in an increase in survival in screened individuals that may not be 'real', and is known as '**lead-time bias**' (Duffy et al. 2008).

'**Screening selection bias**' in breast cancer screening exists in countries or regions where women who choose to participate in breast cancer screening are at a lower risk of death than those who do not participate, which would lead to an increase in survival in screened women that may not be real (Paap et al. 2011).

'**Length bias**' is the phenomenon whereby more slowly growing cancers are more likely to be detected by screening, as they have a longer pre-symptomatic period—again leading to an apparent increase in survival in screened individuals (Duffy et al. 2008).

Lead-time bias

There are many estimated lead times for breast cancer, most of which are between 2 and 4 years. In this report, hazard ratios from the survival analyses performed by screen detection status have been corrected for lead-time bias—using lead times of 2 years, 40 months, and 4 years—to investigate the outcome of using different estimates of lead time on the estimated risk of death from breast cancer for screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia.

These three lead times were carefully chosen—2 years aligns with the estimated mean sojourn time of 2.44 years for women aged 40–49 (Duffy et al. 1997), and so is likely to provide a better correction for this age group; 40 months is the mean lead time that has received a level of consensus (Duffy & Parmar 2013), and 4 years aligns with the estimated mean sojourn time for women aged 50–69 (Duffy et al. 1997).

Correcting for lead-time bias in women aged 50–69 increased the risk of breast cancer death for screen-detected breast cancers compared with never-screened breast cancers from 0.31 (0.29–0.33) to 0.43 (0.40–0.46) using a lead time of 40 months, or to 0.46 (0.43–0.48) using a lead time of 4 years (Table 5.4.1).

Correcting for lead-time bias in women aged 40–49 increased the risk of breast cancer death for screen-detected breast cancers compared with never-screened breast cancers from 0.45 (0.38–0.52) to 0.66 (0.57–0.77) using a lead time of 40 months, or to 0.58 (0.49–0.67) using a lead time of 2 years (Table 5.4.2).

Correcting for lead-time bias in women aged 70 and over increased the risk of breast cancer death for screen-detected breast cancers compared with never-screened breast cancers from 0.36 (0.32–0.39) to 0.45 (0.41–0.49) using a lead time of 40 months (Table 5.4.3).

Table 5.4.1: Adjusted hazard ratios for breast cancer mortality for women aged 50–69 diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years

	HR	95% CI	*p* value
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.65	0.54–0.77	<0.0001
Non-screen-detected	0.65	0.61–0.68	<0.0001
Screen-detected	0.31	0.29–0.33	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 2 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.65	0.54–0.77	<0.0001
Non-screen-detected	0.65	0.62–0.69	<0.0001
Screen-detected	0.38	0.36–0.41	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 40 months			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.64	0.54–0.77	<0.0001
Non-screen-detected	0.65	0.62–0.68	<0.0001
Screen-detected	0.43	0.40–0.46	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 4 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.64	0.54–0.77	<0.0001
Non-screen-detected	0.65	0.62–0.68	<0.0001
Screen-detected	0.46	0.43–0.48	<0.0001

Table 5.4.2: Adjusted hazard ratios for breast cancer mortality for women aged 40–49 diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years

	HR	95% CI	*p* value
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.82	0.60–1.14	0.2370
Non-screen-detected	0.51	0.45–0.57	<0.0001
Screen-detected	0.45	0.38–0.52	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 2 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.83	0.60–1.14	0.2392
Non-screen-detected	0.51	0.45–0.57	<0.0001
Screen-detected	0.58	0.49–0.67	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 40 months			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.82	0.60–1.14	0.2377
Non-screen-detected	0.51	0.45–0.57	<0.0001
Screen-detected	0.66	0.57–0.77	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 4 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.82	0.60–1.14	0.2370
Non-screen-detected	0.51	0.45–0.57	<0.0001
Screen-detected	0.71	0.61–0.83	<0.0001

Table 5.4.3: Adjusted hazard ratios for breast cancer mortality for women aged 70 and over diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years

	HR	95% CI	*p* value
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.43–0.93	0.0191
Non-screen-detected	0.73	0.69–0.78	<0.0001
Screen-detected	0.36	0.32–0.39	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 2 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.43–0.93	0.0197
Non-screen-detected	0.73	0.69–0.77	<0.0001
Screen-detected	0.42	0.38–0.46	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 40 months			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.43–0.93	0.0191
Non-screen-detected	0.73	0.69–0.77	<0.0001
Screen-detected	0.45	0.41–0.49	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 4 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.43–0.93	0.0188
Non-screen-detected	0.73	0.69–0.77	<0.0001
Screen-detected	0.46	0.42–0.51	<0.0001

Table 5.4.4: Adjusted hazard ratios for breast cancer mortality for women aged 40 and over diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years

	HR	95% CI	*p* value
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.68	0.59–0.79	<0.0001
Non-screen-detected	0.67	0.64–0.69	<0.0001
Screen-detected	0.34	0.32–0.35	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 2 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.68	0.59–0.79	<0.0001
Non-screen-detected	0.67	0.64–0.69	<0.0001
Screen-detected	0.41	0.39–0.43	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 40 months			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.68	0.59–0.78	<0.0001
Non-screen-detected	0.66	0.64–0.69	<0.0001
Screen-detected	0.45	0.43–0.48	<0.0001
Breast cancer mortality, adjusted, corrected for lead-time bias, lead time 4 years			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.68	0.59–0.78	<0.0001
Non-screen-detected	0.66	0.64–0.69	<0.0001
Screen-detected	0.48	0.45–0.50	<0.0001

Screening selection bias

Screening selection bias exists in countries or regions where women who choose to participate in breast cancer screening are at a lower risk of dying than those who do not participate (Paap et al. 2011). Duffy and Cuzick (2002) have put forth two equations to correct for screening selection bias when assessing screening programs.

The first equation corrects the calculated relative risk of the intention-to-treat effect of an invitation to screening. This is the relative risk of breast cancer death in a population where screening is available compared with a population where screening is not available. This does not reflect the risk that we calculate using BreastScreen Australia data, since screening is available to all women who reside in Australia, and is not dependent on receiving an invitation to screen.

The relative risk calculated using BreastScreen Australia data is described by Duffy and Cuzick (2002) as the 'effect of offering screening to those who would participate if invited'—the hazard ratio produced when estimating the risk of breast cancer death in screen-detected breast cancers compared with breast cancers diagnosed in never-screened women.

This second equation to correct for screening selection bias in these estimates of risk is:

$$RR_{corrected} = \frac{p\,\psi\,D_r}{1-(1-p)D_r}$$

ψ *estimated relative risk of breast cancer death for participants compared with non-participants*

D_r *relative risk of breast cancer death for non-participants compared with an uninvited comparison group*

p *proportion of participants*

The values for ψ and p are derived from the study group participants themselves, and the value for D_r is usually sourced from previously published randomised control trials. D_r is determined by comparing breast cancer mortality in women who choose not to participate in breast cancer screening, despite its availability, with breast cancer mortality in women for whom screening is not available, some of whom would screen if it were available (Duffy & Cuzick 2002).

However, the value for D_r can also be derived from the study itself. This may be preferable to using D_r from randomised control trials due to the observed differences in this measure, even across sub-groups of a screening program (Paap et al. 2011; Spix et al. 2016).

In the first report from this data linkage project, *Analysis of cancer outcomes and screening behaviour for national cancer screening programs in Australia* (AIHW 2018a), the risk of breast cancer deaths of screen-detected breast cancers compared with those diagnosed in never-screened women was corrected for screening selection bias using the most conservative correction factor of 1.36, and a less-conservative correction factor of 1.17 that may be more appropriate for Australian data. The range of corrected hazard ratios produced by this method demonstrated that a correction factor appropriate to the data is crucial to produce useful estimates of the effect of screening selection bias. In this report, we have the opportunity to examine screening selection bias in more detail and determine the appropriate correction factor to use in the Australian setting.

To achieve this, a range of D_r values have been used as correction factors, including a value of D_r derived from these study data themselves. The correction factors used in this report are listed in Table 5.4.5. They include the pooled estimate from five randomised control trials

(D_r = 1.36) (Duffy & Cuzick 2002), the pooled estimate from Swedish screening service studies (D_r = 1.17) (Swedish Organised Service Screening Evaluation Group 2006), and the estimate derived from data in this project (D_r = 0.91).

Table 5.4.5: Estimates of D_r, the relative risk of breast cancer death for non-participants compared with an uninvited comparison group

Data source	Non-participant data		Uninvited control data		Relative risk D_r	95% CI
	Deaths	*Non-participants*	*Deaths*	*Controls*		
Two-county trial[a]	62	11,111	234	55,985	1.34	1.01–1.62
Malmö[a]	31	5,905	66	21,195	1.69	1.09–2.58
Gothenburg[a]	6	2,191	40	14,217	0.97	0.41–2.29
Stockholm[a]	23	8,064	45	19,343	1.23	0.74–2.04
National breast screening study[a]	5	3,152	28	25,216	1.43	0.55–3.72
Combined[a]	**127**	**30,423**	**413**	**135,956**	**1.36**	**1.11–1.67**
Dalarna[b]	. .	. .	. .	. .	1.28	1.07–1.53
Gävleborg[b]	. .	. .	. .	. .	1.34	1.03–1.75
Örebro[b]	. .	. .	. .	. .	0.97	0.77–1.23
Norrbotten[b]	. .	. .	. .	. .	1.20	0.88–1.63
Västemorrland[b]	. .	. .	. .	. .	0.96	0.70–1.32
Södersjukhuset[b]	. .	. .	. .	. .	1.05	0.82–1.35
Uppsala[b]	. .	. .	. .	. .	1.32	0.92–1.89
Västmanland[b]	. .	. .	. .	. .	1.66	1.12–2.47
Södermanland[b]	. .	. .	. .	. .	1.44	1.04–2.00
Skärholmen[b]	. .	. .	. .	. .	0.82	0.61–1.10
Danderyd Hospital[b]	. .	. .	. .	. .	1.17	0.87–1.57
Karolinska Hospital[b]	. .	. .	. .	. .	1.26	0.91–1.73
Sankt Göran Hospital[b]	. .	. .	. .	. .	1.16	0.85–1.56
Combined[b]	. .	. .	. .	. .	**1.17**	**1.08–1.26**
Current project	**1,715**	**7,130**	**2,218**	**8,413**	**0.91**	**0.86–0.97**

(a) Duffy & Cuzick 2002.

(b) Swedish Organised Service Screening Evaluation Group 2006 (no counts were provided for these D_r values).

The method used to derive D_r from data in this study had to account for breast cancer screening being available to all Australian women, not only those invited to screen. Therefore, the uninvited controls were women with breast cancer diagnosed in the pre-screening epoch (that is, prior to the introduction of breast cancer screening pilots in the late 1980s and of BreastScreen Australia itself in 1991), and the non-participants were unscreened women with breast cancer diagnosed in the screening epoch (that is, after the introduction of BreastScreen Australia in 1991).

Although this introduces a historical component to the calculation of D_r that is not present when data are sourced from randomised control trials, effects of improvements in breast cancer treatment between the late 1980s and mid-1990s are captured by selecting uninvited controls around the time of these improvements (but still prior to the introduction of BreastScreen

Australia and its pilots) so that improved treatments would be experienced by both uninvited controls and non-participants. Benefits of using Australian-specific data may be considered large enough to outweigh any limitations in this methodology.

Uninvited controls were 8,413 women aged 50–69 diagnosed with breast cancer within the 3 years 1986–1988, followed to 31 December 2000 to determine the cumulative number of breast cancer deaths (2,218). Non-participants were 7,130 women aged 50–69 diagnosed with breast cancer within the 3 years 2000–2002, followed to 31 December 2014 to determine the cumulative number of breast cancer deaths (1,715) (Table 5.4.5).

The D_r calculated using these data was 0.91 (0.86–0.97), meaning that women diagnosed with breast cancer who had never screened through BreastScreen Australia (non-participants) had a mortality rate that was 9% lower than that of women diagnosed with breast cancer prior to the introduction of BreastScreen Australia (uninvited controls).

The following section examines the risk of death from breast cancer for screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia, corrected for any effect of screening selection bias using the equation developed by Duffy and Cuzick (2002), and using three different correction factors (D_r in the equation)—1.36, 1.17 and 0.91.

Using correction factor 1.36

A correction factor (D_r) of 1.36 means that, in the five randomised control trials combined, women who were invited to screen, but did not, had a mortality rate that was 36% higher than that of women who were not invited to screen.

Correcting for screening selection bias using the correction factor of 1.36 increased hazard ratios and widened confidence intervals to such a degree as to remove the apparently lower risk of death in screen-detected breast cancers compared with never-screened breast cancers for all age groups except ages 50–69 (tables 5.4.6–5.4.9). In this age group, the risk of death increased from 0.31 (0.29–0.33) to 0.59 (0.36–0.97) (Table 5.4.6).

Evidence suggests that the conservative correction factor of 1.36 does not reflect the Australian breast cancer screening program, and results in over-correction for screening selection bias. Paap et al. (2010) considered correction for screening selection bias and determined that the correction factor of 1.36 is probably not valid for other countries. They used the example that high attendance in the two-county trial (83%) means that the small proportion of women who did not participate in this trial are likely to be inherently different from the larger proportions of women who do not participate in breast cancer screening in other countries (such as Australia, where around 45% of women choose not to participate).

Using correction factor 1.17

A correction factor (D_r) of 1.17 means that, in the Swedish screening service studies combined, women who were invited to screen, but did not, had a mortality rate that was 17% higher than that of women who were not invited to screen.

Morrell et al. (2017) used the lower correction factor of 1.17 from the Swedish screening service studies (Swedish Organised Service Screening Evaluation Group 2006) as they considered that this correction factor better reflected the New Zealand breast cancer screening program they were evaluating.

Correcting for screening selection bias using the correction factor of 1.17 also increased hazard ratios and widened confidence intervals, but not to the same degree as the correction factor of 1.36. After correcting for screening selection bias using this correction factor, the risk of death was significantly lower in screen-detected breast cancers compared with breast

cancers diagnosed in women who had never screened through BreastScreen Australia, for all age groups.

For women aged 50–69, the corrected hazard ratio was 0.42 (0.36–0.50) (Table 5.4.6), for women aged 40–49 this was 0.60 (0.49–0.74) (Table 5.4.7), and for women aged 70 and over the corrected hazard ratio was 0.49 (0.41–0.58) (Table 5.4.8).

Using correction factor 0.91

There is considerable support for country-specific correction factors for screening selection bias (Paap et al. 2011; Spix et al. 2016), and so a correction factor for Australia was estimated from the linked data from this project. This derived correction factor (D_r) of 0.91 means that women diagnosed with breast cancer who had never screened through BreastScreen Australia despite its availability had a mortality rate that was 9% lower than that of women diagnosed with breast cancer prior to the introduction of BreastScreen Australia.

This differs from what was found in the randomised control trials; however, women who choose not to screen in an established breast cancer screening program (which constitute close to half of eligible women) are likely to be a very different group of women from the very small proportion who choose not to screen when invited under trial conditions.

Correcting for screening selection bias using the derived correction factor of 0.91 saw the risk of death from screen-detected breast cancers decrease below the level it was prior to correction. After correcting for screening selection bias using this correction factor, the risk of death remained significantly lower in screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia, for all age groups.

For women aged 50–69, the corrected hazard ratio was 0.27 (0.24–0.30) (Table 5.4.6), for women aged 40–49 this was 0.38 (0.32–0.45) (Table 5.4.7), and for women aged 70 and over the corrected hazard ratio was 0.31 (0.27–0.35) (Table 5.4.8).

Appropriate correction factor for Australia

Research by Roder et al. (2008), who conducted a survey of South Australian women, supports that there may not be a large impact of screening selection bias in the Australian setting. They determined that women who participated in BreastScreen Australia were more likely to have a family history of breast cancer, a history of breast surgery, and to have previously used hormone replacement therapy. This indicates that women who participate in BreastScreen Australia may have a higher background risk for breast cancer than women who do not participate.

While it is difficult to know exactly the requirement for correction of screening selection bias in Australia, it is likely that the previously published Australian data from this data linkage project (which used the conservative correction factor of 1.36) were over-corrected for selection bias, and that even the correction factor of 1.17 may be too high for Australia. We estimated a correction factor for Australia of 0.91; this may be a slight underestimate, due to treatment improvements over time, but suggests that screening selection bias has only a minor or no effect in Australia.

Therefore, while a range of possible corrections have been presented here, those that use the Australian correction factor of 0.91, and those that are uncorrected, are likely to be the most appropriate to use when estimating the risk of breast cancer deaths in screen-detected breast cancers compared with breast cancers diagnosed in women who have never screened in the Australian setting.

Correcting for screening selection bias and lead-time bias

Tables 5.4.10–5.4.13 show a range of hazard ratios corrected for both lead-time bias and screening selection bias. Only hazard ratios for screen-detected breast cancers compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia are shown in these tables, for all combinations of the three lead time estimates and the three screening selection correction factors.

For women aged 50–69, correcting for lead-time bias using a lead time of 4 years and for screening selection bias using the correction factor of 0.91 resulted in a hazard ratio of 0.39 (0.35–0.43). This was similar to the hazard ratio of 0.37 (0.33–0.41) derived using a lead time of 40 months and this same screening selection correction factor (Table 5.4.10).

For women aged 40–49, correcting for lead-time bias using a lead time of 2 years and for screening selection bias using the correction factor of 0.91 resulted in a hazard ratio of 0.49 (0.41–0.58). This was slightly higher at 0.56 (0.47–0.67) using a lead time of 40 months and this same screening selection correction factor (Table 5.4.11).

For women aged 70 and over, correcting for lead-time bias using a lead time of 40 months and for screening selection bias using the correction factor of 0.91 resulted in a hazard ratio of 0.38 (0.33–0.43) (Table 5.4.12).

For women aged 40 and over, hazard ratios ranged from 0.35 (0.31–0.38) to 0.90 (0.55–1.48) (Table 5.4.13), illustrating the impact of correcting for potential biases, and reinforcing the importance of using appropriate correction values for the analysis data.

Table 5.4.6: Adjusted hazard ratios for breast cancer mortality for women aged 50–69 diagnosed with breast cancer, corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Breast cancer mortality, adjusted		
Never-screened	1.0	. .
Screening women		
Interval	0.65	0.54–0.77
Non-screen-detected	0.65	0.61–0.68
Screen-detected	0.31	0.29–0.33
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.36		
Never-screened	1.0	. .
Screening women		
Interval	1.22	0.73–2.05
Non-screen-detected	1.22	0.75–2.01
Screen-detected	0.59	0.36–0.97
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.17		
Never-screened	1.0	. .
Screening women		
Interval	0.87	0.70–1.09
Non-screen-detected	0.87	0.74–1.03
Screen-detected	0.42	0.36–0.50
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 0.91		
Never-screened	1.0	. .
Screening women		
Interval	0.55	0.46–0.66
Non-screen-detected	0.55	0.50–0.61
Screen-detected	0.27	0.24–0.30

Table 5.4.7: Adjusted hazard ratios for breast cancer mortality for women aged 40–49 diagnosed with breast cancer, corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Breast cancer mortality, adjusted		
Never-screened	1.0	. .
Screening women		
Interval	0.82	0.60–1.14
Non-screen-detected	0.51	0.45–0.57
Screen-detected	0.45	0.38–0.52
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.36		
Never-screened	1.0	. .
Screening women		
Interval	1.56	0.87–2.77
Non-screen-detected	0.96	0.58–1.58
Screen-detected	0.84	0.50–1.40
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.17		
Never-screened	1.0	. .
Screening women		
Interval	1.11	0.79–1.56
Non-screen-detected	0.68	0.56–0.83
Screen-detected	0.60	0.49–0.74
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 0.91		
Never-screened	1.0	. .
Screening women		
Interval	0.70	0.51–0.96
Non-screen-detected	0.43	0.37–0.50
Screen-detected	0.38	0.32–0.45

Table 5.4.8: Adjusted hazard ratios for breast cancer mortality for women aged 70 and over diagnosed with breast cancer, corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Breast cancer mortality, adjusted		
Never-screened	1.0	. .
Screening women		
Interval	0.63	0.43–0.93
Non-screen-detected	0.73	0.69–0.78
Screen-detected	0.36	0.32–0.39
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.36		
Never-screened	1.0	. .
Screening women		
Interval	1.19	0.65–2.18
Non-screen-detected	1.39	0.85–2.27
Screen-detected	0.68	0.41–1.12
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.17		
Never-screened	1.0	. .
Screening women		
Interval	0.85	0.58–1.25
Non-screen-detected	0.99	0.84–1.16
Screen-detected	0.49	0.41–0.58
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 0.91		
Never-screened	1.0	. .
Screening women		
Interval	0.54	0.37–0.77
Non-screen-detected	0.62	0.56–0.69
Screen-detected	0.31	0.27–0.35

Table 5.4.9: Adjusted hazard ratios for breast cancer mortality for women aged 40 and over diagnosed with breast cancer, corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Breast cancer mortality, adjusted		
Never-screened	1.0	. .
Screening women		
Interval	0.68	0.59–0.79
Non-screen-detected	0.67	0.64–0.69
Screen-detected	0.34	0.32–0.35
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.36		
Never-screened	1.0	. .
Screening women		
Interval	1.29	0.78–2.15
Non-screen-detected	1.26	0.77–1.38
Screen-detected	0.63	0.39–1.04
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 1.17		
Never-screened	1.0	. .
Screening women		
Interval	0.92	0.75–1.13
Non-screen-detected	0.90	0.76–1.06
Screen-detected	0.45	0.38–0.53
Breast cancer mortality, adjusted, corrected for screening selection bias, correction factor 0.91		
Never-screened	1.0	. .
Screening women		
Interval	0.58	0.49–0.68
Non-screen-detected	0.57	0.51–0.62
Screen-detected	0.28	0.26–0.32

Table 5.4.10: Adjusted hazard ratios for breast cancer mortality for women aged 50–69 diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years and corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Never-screened	1.0	. .
Screen-detected		
Lead time 2 years, correction factor 1.36	0.73	0.44–1.19
Lead time 2 years, correction factor 1.17	0.52	0.44–0.61
Lead time 2 years, correction factor 0.91	0.33	0.29–0.36
Lead time 40 months, correction factor 1.36	0.81	0.50–1.33
Lead time 40 months, correction factor 1.17	0.58	0.49–0.68
Lead time 40 months, correction factor 0.91	0.37	0.33–0.41
Lead time 4 years, correction factor 1.36	0.86	0.52–1.41
Lead time 4 years, correction factor 1.17	0.61	0.52–0.72
Lead time 4 years, correction factor 0.91	0.39	0.35–0.43

Table 5.4.11: Adjusted hazard ratios for breast cancer mortality for women aged 40–49 diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years and corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Never-screened	1.0	. .
Screen-detected		
Lead time 2 years, correction factor 1.36	1.09	0.65–1.81
Lead time 2 years, correction factor 1.17	0.78	0.63–0.96
Lead time 2 years, correction factor 0.91	0.49	0.41–0.58
Lead time 40 months, correction factor 1.36	1.25	0.75–2.09
Lead time 40 months, correction factor 1.17	0.89	0.72–1.11
Lead time 40 months, correction factor 0.91	0.56	0.47–0.67
Lead time 4 years, correction factor 1.36	1.34	0.80–2.24
Lead time 4 years, correction factor 1.17	0.96	0.77–1.18
Lead time 4 years, correction factor 0.91	0.60	0.51–0.72

Table 5.4.12: Adjusted hazard ratios for breast cancer mortality for women aged 70 and over diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years and corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Never-screened	1.0	. .
Screen-detected		
Lead time 2 years, correction factor 1.36	0.79	0.48–1.30
Lead time 2 years, correction factor 1.17	0.56	0.47–0.67
Lead time 2 years, correction factor 0.91	0.35	0.31–0.40
Lead time 40 months, correction factor 1.36	0.85	0.51–1.39
Lead time 40 months, correction factor 1.17	0.60	0.50–0.72
Lead time 40 months, correction factor 0.91	0.38	0.33–0.43
Lead time 4 years, correction factor 1.36	0.88	0.53–1.44
Lead time 4 years, correction factor 1.17	0.62	0.52–0.75
Lead time 4 years, correction factor 0.91	0.39	0.35–0.45

Table 5.4.13: Adjusted hazard ratios for breast cancer mortality for women aged 40 and over diagnosed with breast cancer, corrected for lead-time bias using lead times of 2 years, 40 months, and 4 years and corrected for screening selection bias using correction factors of 1.36, 1.17, and 0.91

Screen detection status	HR	95% CI
Never-screened	1.0	. .
Screen-detected		
Lead time 2 years, correction factor 1.36	0.77	0.47–1.27
Lead time 2 years, correction factor 1.17	0.55	0.47–0.65
Lead time 2 years, correction factor 0.91	0.35	0.31–0.38
Lead time 40 months, correction factor 1.36	0.86	0.52–1.41
Lead time 40 months, correction factor 1.17	0.61	0.52–0.72
Lead time 40 months, correction factor 0.91	0.39	0.35–0.43
Lead time 4 years, correction factor 1.36	0.90	0.55–1.48
Lead time 4 years, correction factor 1.17	0.64	0.55–0.76
Lead time 4 years, correction factor 0.91	0.41	0.37–0.45

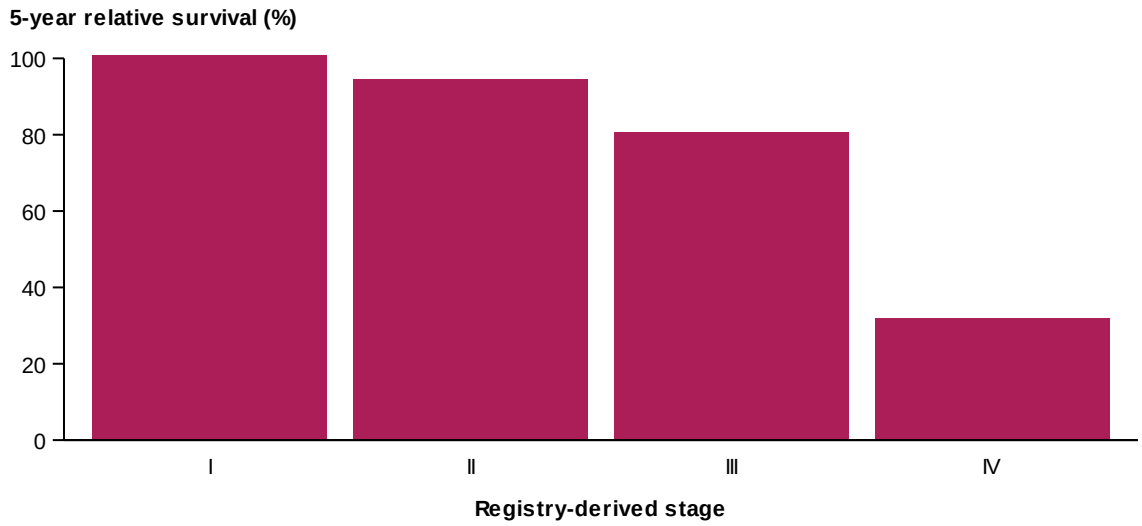
Length bias

Breast cancer screening will detect some non-progressive breast cancers. Including such cancers in survival estimates of screen-detected breast cancers is known as length bias. Length bias is a well-known phenomenon, but difficult to quantify (Duffy et al. 2008). In this study, we used additional analyses to provide further information that may allow the effects of length bias to be inferred.

These analyses were performed and interpreted on the premise that breast cancers at a later stage may be considered more likely to be progressive breast cancers.

Stage of breast cancer is a good predictor of survival. Data on stage of cancer at diagnosis are not currently collected nationally. Cancer Australia has been working in collaboration with all states and territory population-based cancer registries, the Australian Association of Cancer Registries and the AIHW to coordinate the collection of registry-derived stage at diagnosis for the five highest incidence cancers. In 2017, all state and territory cancer registries provided registry-derived staging data for diagnoses in 2011 to AIHW for the top five incidence cancers (breast cancer in females, prostate cancer, colorectal cancer, lung cancer and melanoma of the skin) for inclusion in the Australian Cancer Database.

Five-year relative survival was calculated according to registry-derived stage of female breast cancers, broadly grouped into stages I, II, III and IV. Figure 5.4.1 shows that survival decreases with increasing stage of breast cancer—from about 100% survival for Stage I breast cancers, to about 95% for Stage II, and 81% for Stage II breast cancers, dropping to about 32% survival for Stage IV breast cancers.



Source: AIHW Australian Cancer Database 2014.

Figure 5.4.1: Five-year relative survival from breast cancers in women diagnosed 2011, by registry-derived stage

Breast cancer stage data were not available for inclusion in the data linkage study, so it was not possible to report on stage for breast cancers by screen detection status. However, tumour size was available, which is one of the three factors used to determine the stage of a breast cancer (see Box 5.4.1 for the Cancer Australia definitions of breast cancer stage). As outlined in Box 5.4.1, Stage I breast cancers are those that are <20 mm, with more advanced stages more likely to be ≥20 mm (although there are instances where a small breast cancer can be at a more advanced stage if there is also lymph node involvement and/or distant metastases).

In this section, the tumour size groupings 0–10 mm, 11–15 mm, 16–19 mm, 20–29 mm, and 30+ mm were used as per a previous AIHW report (AIHW & NBCC 2007). The proportion of breast cancers within each screen detection category in each tumour size grouping are shown in tables 5.4.14–5.4.17. Of note, while screen-detected breast cancers were more likely to be small, they were also represented across all tumour size groupings.

Box 5.4.1: Breast cancer stage as per Cancer Australia definitions

The following information has been sourced from Cancer Australia <https://breast-cancer.canceraustralia.gov.au/diagnosis/stages-breast-cancer>.

The **stage** of breast cancer is a way of describing how big the breast cancer is and which parts of the body are affected.

- Stages I, IIA and IIB (early) refer to **early** breast cancer.
- Stages IIB (advanced), IIIA, IIIB, IIIC and IV refer to **advanced** breast cancer (locally advanced breast cancer or metastatic breast cancer).

Breast cancer stage	Size of cancer	Lymph node involvement	Metastasis
I	<20 mm	None	None
IIA	<20 mm 20 mm to 50 mm	Category 1 None	None None
IIB	20 mm to 50 mm >50 mm	Category 1 None	None None
IIIA	<20 mm or 20 mm to 50 mm >50 mm	Category 2 Category 1 or Category 2	None None
IIIB	Any, but cancer spread to nearby muscles and skin	Any	None
IIIC	Any	Category 3	None
IV	Any	Any	Yes

Category 1 = breast cancer cells have been found in one to three lymph nodes in the armpit.

Category 2 = breast cancer cells have been found in 4–9 lymph nodes in the armpit, and the lymph nodes are also enlarged, and/or attached to each other or to nearby tissue; or one or more lymph nodes under the breastbone, but not in any lymph nodes in the armpit.

Category 3 = breast cancer cells have been found in 10 or more lymph nodes in the armpit; or 1 or more lymph nodes above or below the collarbone; or one or more lymph nodes under the breastbone and one or more lymph nodes in the armpit.

Note: Some scenarios are not shown. See Cancer Australia at <https://breast-cancer.canceraustralia.gov.au/diagnosis/stages-breast-cancer> for a more comprehensive description of breast cancer stage.

Table 5.4.14: Size of breast cancers diagnosed in women aged 50–69

	Screen detection status									
	Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
Tumour size (mm)	Count	%	Count	%	Count	%	Count	%	Count	%
0–10	10,075	31.5	168	14.0	3,241	16.2	2,830	14.0	16,314	22.2
11–15	7,544	23.6	236	19.6	3,557	17.8	2,742	13.5	14,079	19.2
16–19	3,060	9.6	138	11.5	2,038	10.2	1,731	8.6	6,967	9.5
20–29	4,698	14.7	226	18.8	4,240	21.2	3,970	19.6	13,134	17.9
30+	3,099	9.7	269	22.4	3,871	19.3	4,282	21.2	11,521	15.7
Unknown/Not applicable	3,492	10.9	165	13.7	3,078	15.4	4,690	23.2	11,425	15.6

Table 5.4.15: Size of breast cancers diagnosed in women aged 40–49

	Screen detection status									
	Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
Tumour size (mm)	Count	%	Count	%	Count	%	Count	%	Count	%
0–10	922	26.6	54	14.8	728	15.9	2,415	13.4	4,119	15.6
11–15	705	20.4	70	19.1	814	17.8	2,793	15.5	4,382	16.6
16–19	304	8.8	33	9.0	476	10.4	1,700	9.4	2,513	9.5
20–29	639	18.5	84	23.0	1,008	22.0	3,845	21.3	5,576	21.1
30+	486	14.0	80	21.9	842	18.4	4,220	23.4	5,628	21.3
Unknown/Not applicable	405	11.7	45	12.3	709	15.5	3,086	17.1	4,245	16.0

Table 5.4.16: Size of breast cancers diagnosed in women aged 70 and over

	Screen detection status									
	Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
Tumour size (mm)	Count	%	Count	%	Count	%	Count	%	Count	%
0–10	2,157	31.3	23	13.2	1,148	11.6	1,254	6.1	4,582	12.2
11–15	1,595	23.1	27	15.5	1,557	15.8	1,834	8.9	5,013	13.3
16–19	557	8.1	20	11.5	923	9.3	1,375	6.7	2,875	7.7
20–29	898	13.0	31	17.8	2,247	22.8	3,607	17.5	6,783	18.1
30+	579	8.4	34	19.5	2,051	20.8	4,050	19.6	6,714	17.9
Unknown/Not applicable	1,107	16.1	39	22.4	1,948	19.7	8,507	41.2	11,601	30.9

Table 5.4.17: Size of breast cancers diagnosed in women aged 40 and over

	Screen detection status									
	Screen-detected		Interval		Non-screen-detected		Never-screened		Total	
Tumour size (mm)	Count	%	Count	%	Count	%	Count	%	Count	%
0–10	13,154	31.1	245	14.1	5,117	14.8	6,499	11.0	25,015	18.2
11–15	9,844	23.3	333	19.1	5,928	17.2	7,369	12.5	23,474	17.1
16–19	3,921	9.3	191	11.0	3,437	10.0	4,806	8.2	12,355	9.0
20–29	6,235	14.7	341	19.6	7,495	21.7	11,422	19.4	25,493	18.5
30+	4,164	9.8	383	22.0	6,764	19.6	12,552	21.3	23,863	17.4
Unknown/Not applicable	5,004	11.8	249	14.3	5,735	16.6	16,283	27.6	27,271	19.8

Survival analyses that include non-progressive breast cancers may make screen-detected breast cancers appear to have better survival than they do. Thus it is useful to demonstrate that progressive breast cancers that would have been diagnosed with or without screening also have better survival when they are screen-detected compared with those diagnosed in the absence of screening to show that a screening program is effective (Figure 5.4.2).

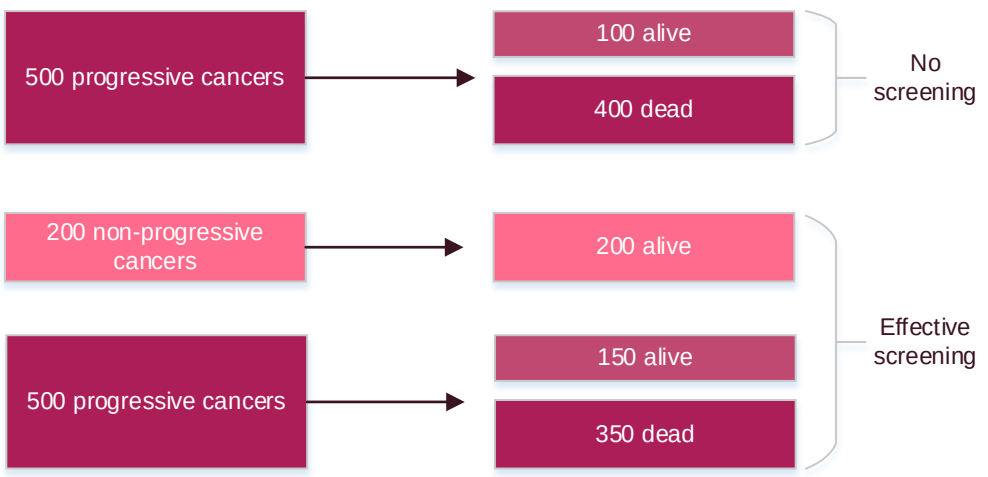


Figure 5.4.2: Survival of non-progressive and progressive breast cancers

Survival analyses were therefore repeated only on breast cancers with a tumour size ≥20 mm as a proxy for breast cancers at a stage that may be considered progressive, in the absence of other available data on the progressive nature of breast cancers.

It was found that screen-detected breast cancers ≥20 mm were less likely to cause death than the same sized breast cancers diagnosed in women who had never screened. This was true for women in the target age group of 50–69 with a hazard ratio of 0.29 (0.27–0.31) (Table 5.4.19), as well as for women outside the target age group. For women aged 40–49, the hazard ratio was 0.46 (0.38–0.54) (Table 5.4.21), and for women aged 70 and over, the hazard ratio was 0.35 (0.31–0.40) (Table 5.4.23). This indicates that for all age groups, screen-detected breast cancers that were ≥20 mm were less likely to cause death than breast cancers ≥20 mm that were diagnosed in women who had never screened.

These results suggest that, when breast cancers that are more likely to be non-progressive (defined here as breast cancers with a tumour size of <20 mm) are excluded from the survival analyses, there are still clear benefits from having a breast cancer detected through screening rather than due to symptoms. This better survival of screen-detected progressive breast cancers compared with progressive breast cancers diagnosed in the absence of screening indicates that breast cancer screening through BreastScreen Australia is effective.

Using the data and the premise described, it appears as though length bias does not account for the better survival of screen-detected breast cancers.

While length bias does not appear to play a large role in the better survival of screen-detected breast cancers, breast cancer screening will detect non-progressive breast cancers that may not have been apparent to women in their lifetime. The most extreme form of this is called ‘overdiagnosis’. However, it is currently not possible to know if a breast cancer will be progressive or non-progressive at the time of diagnosis. In future, molecular and genomic research may develop the means to identify cancers that are unlikely to progress, which would see a change in best practice to allow these breast cancers to be managed more conservatively (Cancer Australia 2017).

Table 5.4.18: Breast cancer survival for women aged 50–69 diagnosed with breast cancer, by screen detection status and tumour size

Tumour size (mm)		HR	95% CI	*p* value
0–10	Never-screened	1.0	. .	. .
	Interval	1.73	0.87–3.42	0.1166
	Non-screen-detected	0.86	0.65–1.15	0.3126
	Screen-detected	0.49	0.38–0.62	<0.0001
11–15	Never-screened	1.0	. .	. .
	Interval	1.08	0.60–1.95	0.7920
	Non-screen-detected	0.90	0.72–1.13	0.3588
	Screen-detected	0.58	0.47–0.72	<0.0001
16–19	Never-screened	1.0	. .	. .
	Interval	1.05	0.55–1.99	0.8877
	Non-screen-detected	0.96	0.76–1.22	0.7477
	Screen-detected	0.54	0.42–0.70	<0.0001
20–29	Never-screened	1.0	. .	. .
	Interval	0.55	0.33–0.92	0.0234
	Non-screen-detected	0.82	0.72–0.93	0.0019
	Screen-detected	0.60	0.52–0.69	<0.0001
30+	Never-screened	1.0	. .	. .
	Interval	0.63	0.46–0.87	0.0043
	Non-screen-detected	0.79	0.72–0.87	<0.0001
	Screen-detected	0.45	0.40–0.51	<0.0001
Unknown/Not applicable	Never-screened	1.0	. .	. .
	Interval	0.62	0.46–0.83	0.0016
	Non-screen-detected	0.51	0.47–0.56	<0.0001
	Screen-detected	0.14	0.12–0.15	<0.0001

Table 5.4.19: Breast cancer survival for women aged 50–69 diagnosed with breast cancers 20 mm in size or over, by screen detection status

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.56	0.46–0.69	<0.0001
Non-screen-detected	0.61	0.57–0.64	<0.0001
Screen-detected	0.28	0.26–0.30	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.58	0.48–0.71	<0.0001
Non-screen-detected	0.63	0.59–0.67	<0.0001
Screen-detected	0.29	0.27–0.31	<0.0001

Table 5.4.20: Breast cancer survival for women aged 40–49 diagnosed with breast cancer, by screen detection status and tumour size

Tumour size (mm)		HR	95% CI	*p* value
0–10	Never-screened	1.0	. .	. .
	Interval	1.67	0.53–5.26	0.3852
	Non-screen-detected	0.61	0.36–1.03	0.0633
	Screen-detected	0.48	0.28–0.81	0.0064
11–15	Never-screened	1.0	. .	. .
	Interval	0.65	0.16–2.62	0.5427
	Non-screen-detected	0.58	0.37–0.90	0.0148
	Screen-detected	0.59	0.37–0.96	0.0339
16–19	Never-screened	1.0	. .	. .
	Interval	0.77	0.19–3.13	0.7189
	Non-screen-detected	0.58	0.38–0.90	0.0153
	Screen-detected	0.28	0.13–0.61	0.0012
20–29	Never-screened	1.0	. .	. .
	Interval	1.34	0.76–2.38	0.3144
	Non-screen-detected	0.59	0.46–0.76	<0.0001
	Screen-detected	0.48	0.34–0.67	<0.0001
30+	Never-screened	1.0	. .	. .
	Interval	0.46	0.22–0.96	0.0392
	Non-screen-detected	0.54	0.44–0.66	<0.0001
	Screen-detected	0.60	0.46–0.77	<0.0001
Unknown/Not applicable	Never-screened	1.0	. .	. .
	Interval	0.94	0.53–1.66	0.8343
	Non-screen-detected	0.44	0.36–0.54	<0.0001
	Screen-detected	0.35	0.26–0.47	<0.0001

Table 5.4.21: Breast cancer survival for women aged 40–49 diagnosed with breast cancers 20 mm in size or over, by screen detection status

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Non-screen-detected	0.50	0.44–0.57	<0.0001
Interval	0.80	0.56–1.14	0.2153
Screen-detected	0.45	0.38–0.53	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Non-screen-detected	0.50	0.44–0.57	<0.0001
Interval	0.82	0.57–1.17	0.2641
Screen-detected	0.46	0.38–0.54	<0.0001

Table 5.4.22: Breast cancer survival for women aged 70 or over diagnosed with breast cancer, by screen detection status and tumour size

Tumour size (mm)		HR	95% CI	*p* value
0–10	Never-screened	1.0	. .	. .
	Interval	—	—	0.9673
	Non-screen-detected	0.77	0.54–1.09	0.1371
	Screen-detected	0.34	0.24–0.48	<0.0001
11–15	Never-screened	1.0	. .	. .
	Interval	1.05	0.26–4.26	0.9412
	Non-screen-detected	0.85	0.66–1.10	0.2210
	Screen-detected	0.45	0.34–0.61	<0.0001
16–19	Never-screened	1.0	. .	. .
	Interval	0.95	0.23–3.82	0.9395
	Non-screen-detected	0.69	0.52–0.90	0.0063
	Screen-detected	0.58	0.42–0.80	0.0009
20–29	Never-screened	1.0	. .	. .
	Interval	1.33	0.59–2.97	0.4907
	Non-screen-detected	0.79	0.69–0.91	0.0012
	Screen-detected	0.52	0.42–0.66	<0.0001
30+	Never-screened	1.0	. .	. .
	Interval	0.51	0.23–1.14	0.1007
	Non-screen-detected	0.76	0.68–0.85	<0.0001
	Screen-detected	0.50	0.41–0.62	<0.0001
Unknown/Not applicable	Never-screened	1.0	. .	. .
	Interval	0.38	0.20–0.71	0.0023
	Non-screen-detected	0.59	0.54–0.64	<0.0001
	Screen-detected	0.16	0.14–0.19	<0.0001

Table 5.4.23: Breast cancer survival for women aged 70 or over diagnosed with breast cancers 20 mm in size or over, by screen detection status

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Non-screen-detected	0.56	0.52–0.59	<0.0001
Interval	0.49	0.32–0.74	0.0008
Screen-detected	0.26	0.23–0.29	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Non-screen-detected	0.68	0.64–0.73	<0.0001
Interval	0.64	0.42–0.98	0.0387
Screen-detected	0.35	0.31–0.40	<0.0001

Table 5.4.24: Breast cancer survival for women aged 40 or over diagnosed with breast cancer, by screen detection status and tumour size

Tumour size (mm)		HR	95% CI	*p* value
0–10	Never-screened	1.0	. .	. .
	Interval	1.32	0.74–2.35	0.3526
	Non-screen-detected	0.81	0.66–0.98	0.0328
	Screen-detected	0.43	0.36–0.52	<0.0001
11–15	Never-screened	1.0	. .	. .
	Interval	0.92	0.56–1.51	0.7273
	Non-screen-detected	0.88	0.75–1.02	0.0846
	Screen-detected	0.55	0.48–0.64	<0.0001
16–19	Never-screened	1.0	. .	. .
	Interval	0.84	0.49–1.43	0.5143
	Non-screen-detected	0.79	0.67–0.92	0.0028
	Screen-detected	0.48	0.40–0.57	<0.0001
20–29	Never-screened	1.0	. .	. .
	Interval	0.74	0.52–1.04	0.0801
	Non-screen-detected	0.79	0.72–0.86	<0.0001
	Screen-detected	0.55	0.49–0.61	<0.0001
30+	Never-screened	1.0	. .	. .
	Interval	0.55	0.42–0.72	<0.0001
	Non-screen-detected	0.78	0.73–0.84	<0.0001
	Screen-detected	0.46	0.42–0.51	<0.0001
Unknown/Not applicable	Never-screened	1.0	. .	. .
	Interval	0.54	0.42–0.68	<0.0001
	Non-screen-detected	0.52	0.49–0.55	<0.0001
	Screen-detected	0.15	0.14–0.16	<0.0001

Table 5.4.25: Breast cancer survival for women aged 40 or over diagnosed with breast cancers 20 mm in size or over, by screen detection status

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.52	0.44–0.60	<0.0001
Non-screen-detected	0.59	0.56–0.61	<0.0001
Screen-detected	0.27	0.26–0.29	<0.0001
Breast cancer mortality, adjusted			
Never-screened	1.0	. .	. .
Screening women			
Interval	0.63	0.61–0.66	<0.0001
Non-screen-detected	0.62	0.53–0.73	<0.0001
Screen-detected	0.32	0.30–0.34	<0.0001

6 Breast cancer screening behaviour

Screening behaviour is determined by two factors—screening (women attending BreastScreen Australia) and rescreening (women returning to BreastScreen Australia). Both are required for adequate levels of participation in BreastScreen Australia for breast cancer morbidity and mortality reductions to be maximised.

This chapter examines what may influence a woman's decision to screen, and to rescreen. This chapter also includes a section that looks more closely at special groups of women who choose to screen through BreastScreen Australia.

6.1 Screening in BreastScreen Australia

Association between cervical screening participation and participation in BreastScreen Australia

This section examines if there is an association between screening behaviour in BreastScreen Australia and screening behaviour under the previous National Cervical Screening Program.

Women who had *either* at least one Pap test between the ages of 20 and 69 and between 1 January 2000 and 31 December 2014 *or* at least one screening mammogram through BreastScreen Australia between the ages of 20 to 79 and between 1 January 2000 and 31 December 2014 were included in the following analyses.

In this section, women were categorised differently from how they were categorised in previous analyses—as **regular screeners**, **irregular screeners**, or **non-screeners**. Regular screeners were those who screened at least three times with a mean screening interval of 30 months or less, as previously described (Roder et al. 2008); irregular screeners were those who had screened, but did not conform to this definition. Non-screeners were those who had never had a Pap test (for cervical screening) or a screening mammogram (for breast cancer screening through BreastScreen Australia).

The first analyses examined the screening behaviour of women in BreastScreen Australia according to their previous cervical screening behaviour (since women are eligible for cervical screening around age 20, but are not able to screen through BreastScreen Australia until age 40).

Of the 3,188,110 women who were regular cervical screeners, 838,973 (26.3%) were regular screeners in BreastScreen Australia, and 589,880 (18.5%) were irregular screeners; the remaining 55.2% were non-screeners in BreastScreen Australia. In comparison, of the 3,716,080 women who were irregular cervical screeners, 383,956 (10.3%) were regular screeners in BreastScreen Australia, 543,960 (14.6%) were irregular screeners, and the remaining 75.0% were non-screeners in BreastScreen Australia (Table 6.1.1).

These data show that women who were regular cervical screeners were more likely to participate in BreastScreen Australia, and to become regular screeners in that program too.

Table 6.1.1: BreastScreen Australia screening behaviour, by prior cervical screening behaviour

	BreastScreen Australia screening behaviour					
	Regular screener		Irregular screener		Non-screener	
Cervical screening behaviour	Number	%	Number	%	Number	%
Regular screener	838,973	26.3	589,880	18.5	1,759,257	55.2
Irregular screener	383,956	10.3	543,960	14.6	2,788,164	75.0
Non-screener	484,636	49.9	486,445	50.1	. .	. .

When women aged under 50 at the time of their most recently recorded Pap test (outside of the BreastScreen Australia target age) were excluded from the analysis, the proportion of regular cervical screeners who were also regular screeners in BreastScreen Australia rose to 56.4%, and the proportion who were non-screeners fell to 15.8% (Table 6.1.2).

This suggests that women who are regular cervical screeners at the age at which they are targeted to screen through BreastScreen Australia are not only more likely to screen, but are also more likely to become regular screeners in BreastScreen Australia. Importantly, only a relatively small proportion of these women chose not to screen at all through BreastScreen Australia.

Table 6.1.2: BreastScreen Australia screening behaviour, by prior cervical screening behaviour, aged 50–69 at date of ultimate Pap test

	BreastScreen Australia screening behaviour					
	Regular screener		Irregular screener		Non-screener	
Cervical screening behaviour	Number	%	Number	%	Number	%
Regular screener	777,190	56.4	382,926	27.8	217,386	15.8
Irregular screener	329,199	33.4	353,719	35.9	302,559	30.7

To determine whether cervical screening behaviour affected the age at which women commenced screening through BreastScreen Australia, the age of women at their earliest screening round in the data set was examined across the three cervical screening behaviour groups (regular, irregular, and non-screener).

It was found that the median age at first screen through BreastScreen Australia was lowest for regular cervical screeners at 50.7, followed by irregular cervical screeners at 51.6. Women who did not participate in cervical screening had the highest median age at first screen at 61.3 (Table 6.1.3).

Table 6.1.3: Age at first recorded participation in BreastScreen Australia, by cervical screening behaviour

Cervical screening behaviour	Mean age at first BreastScreen	Median age at first BreastScreen	SD	Minimum	Maximum
Regular screener	51.1	50.7	6.7	30.7	80.0
Irregular screener	53.0	51.6	7.9	33.1	80.0
Non-screener	61.4	61.3	9.6	20.4	80.0

Since BreastScreen Australia data for this project were from 1 January 2000, some women included in this analysis would have had their first screen prior to this date. Therefore, this analysis was repeated to include women who had their first screen after 1 January 2000.

Again, it was found that the median age at first screen through BreastScreen Australia was lowest for regular cervical screeners at 49.6, followed by irregular cervical screeners at 50.5. Women who did not participate in cervical screening had the highest median age at first screen at 54.3 (Table 6.1.4).

Table 6.1.4: Age at first participation in BreastScreen Australia, by cervical screening behaviour

Cervical screening behaviour	Mean age at first BreastScreen	Median age at first BreastScreen	SD	Minimum	Maximum
Regular screener	49.0	49.6	6.1	30.7	80.0
Irregular screener	50.5	50.5	6.8	33.1	80.0
Non-screener	56.6	54.3	9.3	32.8	80.0

Considered together, these results demonstrate that regular participation in screening may be transferred from one screening program to another, with regular participants in cervical screening participating earlier and more regularly in BreastScreen Australia than women who do not participate in cervical screening. This is particularly so when women are regular participants in cervical screening at the age at which they become eligible to participate in BreastScreen Australia.

Women are eligible for cervical screening around 20 years earlier than they are for BreastScreen Australia. Encouraging participation in cervical screening may be seen as not only protecting women from cervical cancers, but also leading to higher participation in BreastScreen Australia in the longer term.

Prior to these analyses, we had described a previously unknown relationship between participation in BreastScreen Australia and cervical screening under the previous National Cervical Screening Program. An unexpected finding of ‘co-screening’ was reported (AIHW 2018a), with many women choosing have their screening mammogram through BreastScreen Australia and their cervical screening Pap test on the same date. There were 72,165 occurrences of this in the cohort examined, with a proportion of these found to be the same woman having her screening mammograms and Pap tests on the same date over many screening rounds. - being more convenient for women to have both tests on the same date and/or it made it easier to remember to have both screening tests, as both screening programs shared a 2-year screening interval, and, from age 50, also shared a target age group.

Irrespective of the reason behind this phenomenon, it is likely that the overall effect was more regular screening participation in both BreastScreen Australia and the National Cervical Screening Program. With the latter now changed from 2-yearly Pap tests to 5-yearly HPV tests, it will be of interest to see if these changes to cervical screening have any effects on participation in BreastScreen Australia over the coming years.

Screening through more than one state or territory program

Linkage of state and territory BreastScreen data allowed us to examine the occurrence of women screening in more than one state or territory.

Overall, just under 4% of women who screened through BreastScreen Australia over the 15 years 2000–2014 accessed screening in more than one state or territory (Table 6.1.5).

Table 6.1.5: Number of women who screened in BreastScreen Australia, by number of state/territory programs accessed

Screening behaviour	Number	%
Women who screened through one state/territory BreastScreen program	3,204,930	96.3
Women who screened through more than one state/territory BreastScreen program	122,920	3.7

To investigate further the 122,920 women who screened through more than one state or territory BreastScreen program, the number of occurrences of a woman attending a subsequent screen in a different state or territory to her previous screen were examined. The results of this are shown in Table 6.1.6.

The statistic of most note in Table 6.1.6 is the relatively high number of subsequent screens that occur in BreastScreen NSW after an original screen in BreastScreen ACT. This is due to BreastScreen ACT previously being BreastScreen ACT & SE NSW, and therefore including New South Wales women, who are now screened through BreastScreen NSW.

Excluding the movement of women from BreastScreen ACT to BreastScreen NSW, the number of screens in each state or territory that were followed by a screen in another state or territory should be considered relative to the number of women who reside and screen in each state or territory.

We have not speculated on the possible factors that influence the movement of women from one jurisdiction to another, other than to note that some proportion of the women will have moved to reside in another state or territory, and that, not unexpectedly, the number of screens is relatively high between states and territories that border one another.

Table 6.1.6: Number of subsequent screens that occurred in another state or territory program

	State/territory of subsequent screen							
State/territory of original screen	**NSW**	**Vic**	**Qld**	**WA**	**SA**	**Tas**	**ACT**	**NT**
NSW		8,937	19,345	2,053	1,399	1,491	3,730	623
Vic	4,804		7,251	1,642	1,473	1,212	749	458
Qld	12,259	5,877		2,879	1,613	2,062	912	1,268
WA	1,419	1,702	2,444		669	703	197	436
SA	1,340	1,836	2,673	804		418	217	528
Tas	763	1,058	1,552	519	234		143	107
ACT	18,267	1,128	1,924	280	227	208		98
NT	562	513	1,919	554	846	142	105	

Note: BreastScreen ACT was previously BreastScreen ACT & SE NSW, so the large number of women who have moved from screening in the Australian Capital Territory to screening in New South Wales represent New South Wales women who used to be screened by BreastScreen ACT & SE NSW who are now screened by BreastScreen NSW.

Two subgroups of women who undertook interstate screening were examined further.

We first determined whether women were using interstate screening in order to access annual screening. We found that there were indeed a small number of women who crossed state borders multiple times to access more frequent screening. However, this totalled less than 1% of all women screening through the program, so did not appear to be a major issue.

We then determined whether women were using interstate screening in order to access a second screen, presumably because either they were not satisfied with their original screen, or they were seeking a second reassurance that they did not have breast cancer. Characteristics of the screening episode after which women chose to have an early rescreen interstate are shown in Table 6.1.7.

Compared with other screening episodes, women were more likely to rescreen early interstate in the age groups 50–54 and 55–59—the age groups at which many women have their first screen. Women may therefore be screening again interstate to seek further reassurance that they do not have breast cancer. They were also slightly more likely to have a lump or a non-specific breast symptom, so again, may be seeking reassurance.

For most years there were no apparent differences between the two groups of screening episodes; there are a few years, however, for which there was a notably higher proportion of screening episodes followed by an early interstate rescreen. Whether this is just random variation, or these are years in which more women were seeking additional reassurance is not clear.

The strongest effect was a family history of breast cancer, with women with a family history more likely to rescreen early interstate. It is possible that these women are worried that they are at increased risk of breast cancer and—like other groups identified—may be seeking additional reassurance that they do not have breast cancer.

Table 6.1.7: Characteristics of screening episodes followed by an early interstate rescreen

		Screening episodes followed by early interstate rescreen		Other screening episodes	
Characteristic		**Count**	**%**	**Count**	**%**
Age at screen	<40	—	—	38	—
	40–44	168	2.4	24,115	3.7
	45–49	509	7.2	56,517	8.7
	50–54	1,713	24.2	140,083	21.5
	55–59	1,918	27.1	160,771	24.7
	60–64	1,456	20.6	139,083	21.4
	65–69	956	13.5	89,182	13.7
	70–74	269	3.8	30,289	4.7
	75–79	73	1.0	8,146	1.3
	80–84	15	0.2	1,897	0.3
	85+	3	—	345	0.1

(continued)

Table 6.1.7 (continued): Characteristics of screening episodes followed by an early interstate rescreen

Characteristic		Screening episodes followed by early interstate rescreen		Other screening episodes	
		Count	%	Count	%
Year of screen	2000	40	0.6	37,886	5.8
	2001	316	4.5	37,750	5.8
	2002	617	8.7	40,460	6.2
	2003	386	5.5	38,100	5.9
	2004	416	5.9	42,367	6.5
	2005	386	5.5	40,775	6.3
	2006	593	8.4	45,766	7.0
	2007	433	6.1	41,929	6.4
	2008	477	6.7	45,885	7.1
	2009	466	6.6	46,067	7.1
	2010	498	7.0	45,633	7.0
	2011	588	8.3	45,002	6.9
	2012	672	9.5	48,180	7.4
	2013	539	7.6	45,696	7.0
	2014	653	9.2	48,970	7.5
Symptom status	No symptoms	5,504	77.7	358,657	55.1
	Lump	217	3.1	16,998	2.6
	Nipple discharge—clear	12	0.2	1,452	0.2
	Nipple discharge—blood stained	1	—	255	—
	Other breast symptoms	338	4.8	21,563	3.3
	Not stated	1,008	14.2	251,541	38.7
Family history of breast cancer	Not stated	345	4.9	84,248	13.0
	Family history of breast cancer	1,648	23.3	81,360	12.5
	No family history of breast cancer	5,087	71.9	484,858	74.5
Personal history of breast cancer	Not stated	345	4.9	84,248	13.0
	Personal history of breast cancer	214	3.0	7,324	1.1
	No personal history of breast cancer	6,521	92.1	558,894	85.9

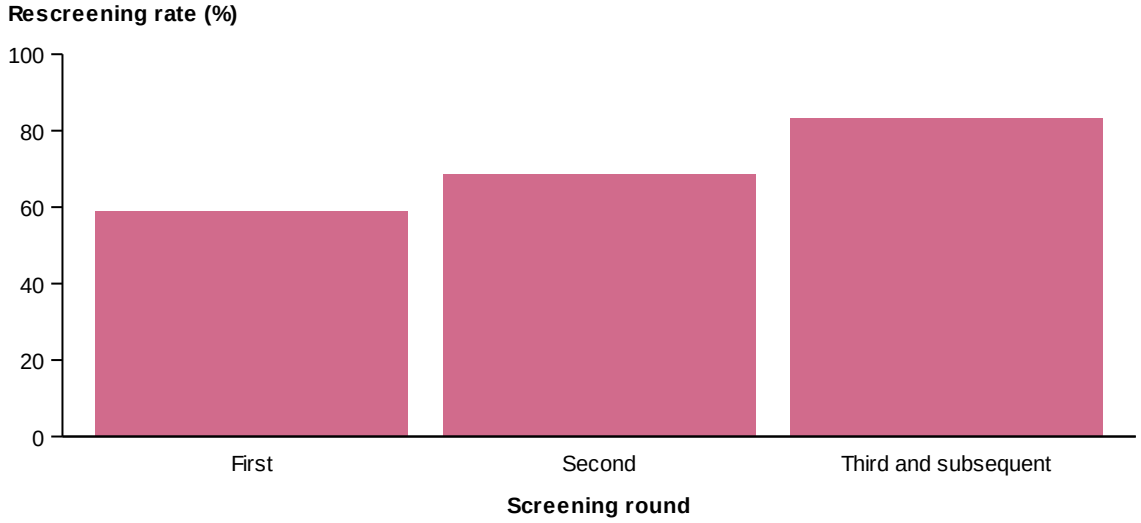
6.2 Rescreening in BreastScreen Australia

Recruiting women to commence screening through BreastScreen Australia is of fundamental importance. However, it is also crucial that a large proportion of women return to screen after their initial screen, and do so regularly (2 years is the recommended screening interval).

There are two concerns with rescreening:

- women who screen once but never return to BreastScreen Australia
- women who rescreen, but do so at longer intervals than recommended. This has been shown to reduce mortality benefits from screening and result in an increase in interval cancers (BreastScreen Australia, 2004), since increased time between screening may allow a tumour to grow to the point where symptoms become evident, thus eliminating the advantage of screening.

It is known from routine monitoring of BreastScreen Australia that rescreening after a woman's first screening round is lowest, with around 60% of women aged 50–67 who screened for the first time rescreening within 27 months (considered to be rescreening within the recommended screening interval); just under 70% rescreen within 27 months after their second screen, and just over 80% rescreen within 27 months after their third or subsequent screen through BreastScreen Australia (Figure 6.2.1).



Source: BreastScreen Australia monitoring report 2014–2015 (AIHW 2017).

Figure 6.2.1: Rescreening by screening round, women aged 50–67 screened during 2013

This suggests that, once women have screened a few times, they are likely to be regular screeners, but that there are a substantial proportion of women who do not return after their first screen, a trend that was only slightly better after a woman's second screen.

Patterns in rescreening

Patterns in rescreening outside the recommended screening interval were examined first, to get a more complete picture of rescreening in BreastScreen Australia.

Women aged 50–69 who screened through BreastScreen Australia between 2000 and 2014 were used in this study, after excluding women who screened annually, had an invasive breast cancer or DCIS detected following a positive screening mammogram, or turned 70 before they were due for their next screen.

Screens in these women were counted, and assessed to determine if (and when) a subsequent screen occurred. This subsequent screen was categorised according to the length of time between the screen and the rescreen, as categorised below, and then became the next screen assessed to determine if (and when) a subsequent screen occurred, and so on. If no subsequent screen occurred, the woman was considered to have not rescreened (these comprise the category *never rescreened*).

A woman's screening round was her screening round in the national program, (which was not necessarily her screening round within a state or territory program).

Categories of rescreening used were:

- rescreened within 27 months
- rescreened between 27 and 36 months
- rescreened between 36 and 48 months
- rescreened after 48 months
- never rescreened.

Consistent with Figure 6.2.1, rescreening within 27 months was lowest for women after their first screening round at about 60%, followed by women after their second screening round at about 70%, and highest for women after their third or subsequent screening round with about 80% rescreening within 27 months.

Looking beyond 27 months, rescreening within 36 months, 48 months and more than 48 months was highest for women after their first screening round, followed by women after their second screening round, and lowest for women after their third or subsequent screening round (Table 6.2.1).

Table 6.2.1: Rescreening within BreastScreen Australia, women aged 50–69

Screening round		≤27 months	27–36 months	36–48 months	>48 months	Never
First screening round	Number	367,615	84,256	31,180	34,946	88,363
	%	60.6	13.9	5.1	5.8	14.6
Second screening round	Number	511,908	95,500	30,934	29,951	60,918
	%	70.2	13.1	4.2	4.1	8.4
Third+ screening round	Number	3,249,388	396,006	100,665	69,844	176,919
	%	81.4	9.9	2.5	1.7	4.4
All screening rounds	**Number**	**4,128,911**	**575,762**	**162,779**	**134,741**	**326,200**
	%	**77.5**	**10.8**	**3.1**	**2.5**	**6.1**

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

These higher values at longer rescreening intervals did not change the overall trend in rescreening rates, however, with 85.4% of women 'ever-rescreening' after their first

screening round, 91.6% of women ‘ever-rescreening’ after their second screening round, and 95.6% of women ‘ever-rescreening’ after their third or subsequent screening round (93.9% after all screening rounds combined).

This indicates that there are two issues at play in the lower rescreening rates after first and second screens—the first is that fewer women rescreen at all, particularly after a first screen, but also after a second screen. That is, women try screening once, or even twice, but then choose not to screen again. The second issue is that, for those women who do choose to rescreen, it appears to take a few screening rounds for them to rescreen within the recommended screening interval.

While the rates of women ‘ever-rescreening’ are high, this does not translate into mortality benefits, because increased time between screening may allow a tumour to grow to the point where symptoms become evident, thus eliminating the advantage of screening. Therefore, the rate at which women rescreen within 27 months is the crucial measure of adequate and appropriate rescreening within BreastScreen Australia.

Further analyses were undertaken on rescreening after first, second and third or subsequent screens to investigate what may influence a woman’s decision not to rescreen after these screening rounds.

First screening round

Women who screened once, and did not screen again were compared with women who screened within 27 months of their first screen (women who rescreened after 27 months were not the focus of the comparison but were included here for completeness).

Age was investigated first. It was found that, while the highest proportion of first screens was in the 50–54 age group, this proportion was higher in those that rescreened within 27 months at about 70%, and lower in those that did not rescreen at about 60% (Table 6.2.2).

This indicates that a greater proportion of women who rescreened within 27 months had their first screen at age 50–54 compared with women who did not rescreen (Table 6.2.2).

Table 6.2.2: Rescreening behaviour according to age at first screen

	Age group at first screen			
Rescreening behaviour	**50–54**	**55–59**	**60–64**	**65–69**
Never rescreened (%)	61.3	21.2	13.1	4.4
Rescreened ≤27 months (%)	71.4	16.1	9.6	2.9
Rescreened >27 months (%)	72.4	17.4	8.3	2.0

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Because of the apparent effect of age at first screening on rescreening behaviour, the analysis was rerun to also include women aged 40–49, since women become eligible for BreastScreen Australia at age 40. It was found that including first screens that occurred in these younger women provided more information about women who never rescreened.

The highest proportion of first screens for women who never rescreened after their first screen occurred for the two age groups 40–44 and 50–54, whereas the highest proportion of first screens in women who rescreened within 27 months remained in the 50–54 age group (Figure 6.2.2).

As already indicated, women first become eligible for BreastScreen Australia at age 40 and are first invited at age 50. It appears as though there is a cohort of women who ‘try’ breast cancer screening once—either when they first become eligible or when they are first invited

to screen—but who then never return. Whether this is due to something experienced at their first screen, or because they only even intended to have a single screening experience (for example, for peace of mind due to the presence of a symptom) was not immediately clear. This was investigated in the following analyses.

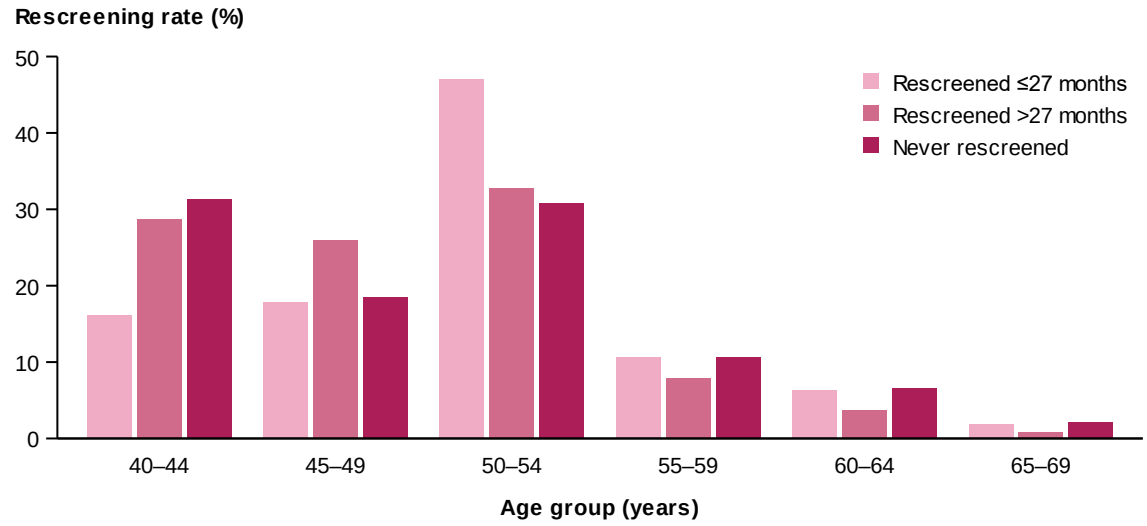


Figure 6.2.2: Rescreening behaviour according to age at first screen

Self-reported characteristics and recall to assessment status were compared for women who did not rescreen and women who rescreened within 27 months of their first screen. Women who did not rescreen after their first screen were found to have a higher occurrence of family history and symptoms at the time of their screen (Table 6.2.3).

This may support the hypothesis that some women who screen once and then never screen again may see themselves to be at risk of having breast cancer and so attend BreastScreen Australia; when this first screen does not detect a breast cancer, they may then have 'peace of mind' and not make further screening a priority.

Table 6.2.3: Rescreening behaviour according to self-reported characteristics and recall to assessment status at first screen

	Self-reported characteristic/recall to assessment status at first screen			
Rescreening behaviour	**Personal history**	**Family history**	**Symptoms**	**Recalled to assessment**
Never rescreened (%)	0.7	6.4	13.1	11.7
Rescreened ≤27 months (%)	0.6	5.2	9.6	11.0
Rescreened >27 months (%)	0.1	4.8	8.3	10.0

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Second screening round

Analyses were repeated for second screens.

Similar to first screening rounds, a greater proportion of women who rescreened within 27 months had their second screening round at age 50–54 compared with women who did not rescreen (Table 6.2.4).

Table 6.2.4: Rescreening behaviour according to age at second screen

	Age group at second screen			
Rescreening behaviour	**50–54**	**55–59**	**60–64**	**65–69**
Never rescreened (%)	49.6	27.2	17.1	6.2
Rescreened ≤27 months (%)	62.5	21.7	12.2	3.7
Rescreened >27 months (%)	61.8	24.4	11.0	2.8

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Self-reported characteristics and recall to assessment status were also compared between women who did not rescreen and women who rescreened within 27 months of a second screening round. The proportion of women who reported a family history of breast cancer or DCIS, or a symptom, at their second screening round was higher among women who did not rescreen (Table 6.2.5).

Unlike the first screening round, a higher proportion of women who did not rescreen were recalled to assessment at their second screening round (Table 6.2.5).

Table 6.2.5: Rescreening behaviour according to self-reported characteristics and recall to assessment status at second screen

	Self-reported characteristic/recall to assessment status at second screen			
Rescreening behaviour	**Personal history**	**Family history**	**Symptoms**	**Recalled to assessment**
Never rescreened (%)	0.6	7.6	9.8	5.6
Rescreened ≤27 months (%)	0.7	6.5	6.0	4.7
Rescreened >27 months (%)	0.1	5.6	8.3	4.6

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Third or subsequent screening rounds

Analyses were repeated for third or subsequent screens.

The only clear difference between age groups was that a slightly higher proportion of women who rescreened had their third or subsequent screen at age 50–54 (Table 6.2.6). Unlike the data for women attending their first or second screen, these data comprise multiple screening rounds for women who screened three or more times.

While lower rescreening of women after a screen at age 65–69 may be due to women reaching the upper end of the target age group, there may also be an effect of co-morbidities in older women contributing to this drop in rescreening.

Table 6.2.6: Rescreening behaviour according to age at third or subsequent screen

	Age group at third or subsequent screen			
Rescreening behaviour	**50–54**	**55–59**	**60–64**	**65–69**
Never rescreened (%)	17.3	32.4	34.5	15.8
Rescreened ≤27 months (%)	21.5	34.8	32.5	11.2
Rescreened >27 months (%)	24.6	37.1	29.4	8.8

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Self-reported characteristics and recall to assessment status were also compared between women who did not rescreen and women who rescreened within 27 months of a third or subsequent screening round.

The two main features noted for women who did not screen after a third or subsequent screening round were a higher proportion of symptoms and a higher proportion recalled to assessment, compared with women who rescreened within 27 months (Table 6.2.7).

Table 6.2.7: Rescreening behaviour according to self-reported characteristics and recall to assessment status at third or subsequent screen

	Self-reported characteristic/recall to assessment status at third or subsequent screen			
Rescreening behaviour	**Personal history**	**Family history**	**Symptoms**	**Recalled to assessment**
Never rescreened (%)	1.0	10.0	7.5	5.1
Rescreened ≤27 months (%)	1.0	9.6	4.7	3.7
Rescreened >27 months (%)	0.2	7.1	6.6	4.0

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

Rescreening after a false positive screening result

It has been shown that women with false positive screening mammograms (that is, those recalled to assessment for further investigation and found not to have breast cancer) are less likely to participate in subsequent screening rounds (Sim et al. 2012).

In the previous analyses, a higher recall to assessment rate was a feature common to women who did not rescreen after a third or subsequent screen. The possibility that false positive screening results may contribute to a woman's decision not to rescreen was therefore deemed important to investigate.

Cohorts and definitions were as for the previous rescreening analyses, which follow the methodology of Sim et al. (2012), with some adaptations.

Women aged 50–69 who screened through BreastScreen Australia between 2000 and 2014 were used in this study, after excluding women who screened annually, had an invasive breast cancer or DCIS detected following a positive screening mammogram, or who turned 70 before they were due for their next screen.

Screens in these women were counted, and assessed to determine if (and when) a subsequent screen occurred. This subsequent screen was categorised according to the rescreening categories below, and then became the next screen assessed to determine if (and when) a subsequent screen occurred, and so on. If no subsequent screen occurred, the woman was considered to have not rescreened (these comprise the category *never rescreened*).

A woman's screening round was her screening round in the national program, (which was not necessarily her screening round within a state or territory program).

Categories of rescreening used were:

- rescreened within 27 months
- rescreened outside 27 months
- never rescreened.

Comparisons were made between screens that were negative (true negatives) and screens that were positive (as assessed by a woman being recalled to assessment) where breast

cancer or DCIS was not detected (false positives). The χ^2 test was used to determine the statistical significance of any differences between the rescreening proportions.

Results were determined for first, second, and third or subsequent screening rounds separately, as well as for all screening rounds.

There was a statistically significant difference (p <0.001) between the proportion of women who rescreened within 27 months of a true negative first screen and the proportion who rescreened within 27 months of a false positive first screen—women whose first screen was a false positive had a higher rescreening rate of 61.8% than women whose first screen was a true negative screen, of whom 59.8% rescreened within 27 months (Table 6.2.8).

In contrast, there was no difference (p = 0.3) between the proportion of women who rescreened within 27 months of a true negative second screen (69.3%) and the proportion who rescreened within 27 months of a false positive second screen (69.5%) (Table 6.2.8).

There was a statistically significant difference (p <0.001) between the proportion of women who rescreened within 27 months of a true negative third or subsequent screen and the proportion of women who rescreened within 27 months of a false positive third or subsequent screen—women whose third or subsequent screen was a false positive had a lower rescreening rate of 79.5% than women whose third or subsequent screen was a true negative, of whom 81.1% rescreened within 27 months (Table 6.2.8).

When all screening rounds were considered together, false positive screens were associated with lower rescreening rates than true negatives (73.6% compared with 77.3%; p <0.001).

This trend was not common to all state and territory BreastScreen programs. Analyses at the state and territory level showed that, while this trend existed in some states and territories, in others there was no difference in rescreening rates.

Table 6.2.8: Rescreening after a true negative or false positive screen, women aged 50–69

Screening round			Never rescreened	Rescreened ≤27 months	Rescreened >27 months
First screening round	True negative	Number	74,485	297,713	126,032
		%	14.9	59.8	25.3
	False positive	Number	8,443	34,553	12,874
		%	15.1	61.8	23.0
Second screening round	True negative	Number	54,466	432,751	137,610
		%	8.7	69.3	22.0
	False positive	Number	2,723	20,170	6,108
		%	9.4	69.5	21.1
Third + screening round	True negative	Number	167,172	2,947,777	517,964
		%	4.6	81.1	14.3
	False positive	Number	7,077	103,522	19,589
		%	5.4	79.5	15.0
All screening rounds	True negative	Number	296,123	3,678,240	781,604
		%	6.2	77.3	16.4
	False positive	Number	18,243	158,248	38,572
		%	8.5	73.6	17.9

Note: Insufficient time had passed since screens performed in later years to know if women had rescreened within the longer time intervals, so some rescreened values will be slight underestimates. However, all groups were affected equally by this, so no biases were introduced.

6.3 Special groups

Younger women who screen through BreastScreen Australia

In this section, women aged 40–49 are examined. These women are able to access BreastScreen Australia, but are not actively targeted until they turn 50.

The first question of interest for women aged 40–49, was *Why do these women screen*? Are they just 'good screeners' who want to participate in breast cancer screening as soon as they are able? Are there other drivers, such as being at higher risk of breast cancer, or accessing breast cancer screening in *Remote* and *Very remote* areas where BreastScreen Australia is the only service available?

Characteristics of women who screen in the 40–49 age group are shown in Table 6.3.1, along with those of women whose first screen is in the 50–69 age group for comparison.

Women who commenced screening early were more likely to have a family history of breast cancer than those who commenced screening when they reached the target age group. Women who commenced screening early were also more likely to have symptoms, including a lump, nipple discharge, and other non-specific symptoms. This points to women who commence screening in the 40–49 age group having a higher risk, or a higher perceived risk, of breast cancer than women who commence screening when they reach the target age group. Since women aged 40–49 are not invited to either screen or rescreen through BreastScreen Australia, these women are actively seeking breast cancer screening.

Women who commenced screening early were less likely to reside in *Major cities* and more likely to reside in *Remote* and *Very remote* areas than women who commenced screening when they reached the target age group. This suggests that BreastScreen Australia may be providing services in younger women in these more remote areas that would otherwise be unavailable to them.

Table 6.3.1: Characteristics of women aged 40–49 and 50–69

		Age at first recorded screen			
		40–49		50–69	
Characteristic		**Number**	**%**	**Number**	**%**
Personal history of breast cancer	Personal history of breast cancer	1,842	0.2	13,853	0.7
	No personal history of breast cancer	999,731	97.2	1,955,437	96.3
	Personal history not stated	26,801	2.6	60,581	3.0
Family history of breast cancer	Family history of breast cancer	102,404	10.0	130,459	6.4
	No family history of breast cancer	899,169	87.4	1,838,831	90.6
	Family history not stated	26,801	2.6	60,581	3.0
Symptoms reported at screen	No symptoms	554,115	53.9	1,341,408	66.1
	Lump	58,756	5.7	50,850	2.5
	Nipple discharge—clear	6,499	0.6	3,935	0.2
	Nipple discharge—blood stained	845	0.1	732	—
	Other symptoms	56,311	5.5	73,707	3.6
	Symptoms not stated	351,848	34.2	559,239	27.6

(continued)

Table 6.3.1 (continued): Characteristics of women aged 40–49 and 50–69

		Age at first recorded screen			
		40–49		50–69	
Characteristic		**Number**	**%**	**Number**	**%**
Remoteness area	Major cities	485,596	47.2	1,108,494	54.6
	Inner regional	140,900	13.7	336,007	16.6
	Outer regional	61,696	6.0	132,822	6.5
	Remote	11,024	1.1	14,844	0.7
	Very remote	4,642	0.5	5,871	0.3
	Unknown remoteness	324,516	31.6	431,833	21.3
Socioeconomic group	1 (most disadvantage)	136,486	13.3	338,084	16.7
	2	137,927	13.4	327,163	16.1
	3	127,703	12.4	287,303	14.2
	4	129,381	12.6	295,841	14.6
	5 (least disadvantage)	170,823	16.6	346,638	17.1
	Socioeconomic group unknown	326,054	31.7	434,842	21.4

The second question of interest for women aged 40–49, was *What is their screening experience*? To answer this, false positive and false negative screens for women who screened at age 40–49 were compared with those for women who screened at age 50–69.

Women aged 40–49 were less likely to have a false positive screen than women aged 50–69 (Table 6.3.2). In contrast, false negative screens were slightly higher in women aged 40–49 (although the number or false negative screens was small in both age groups) (Table 6.3.3).

Table 6.3.2: False positive screening tests in women aged 40–49 and 50–69

	Age at screen			
	40–49		50–69	
Screening round	**Number**	**%**	**Number**	**%**
First screening round	57,899	6.9	80,402	8.0
Second screening round	17,288	3.5	42,514	3.6
Third screening round	9,658	3.1	41,976	3.2
Subsequent screening rounds	7,607	2.7	161,504	2.5
Total	**92,452**	**4.8**	**326,396**	**3.3**

Table 6.3.3: False negative screening tests in women aged 40–49 and 50–69

	Age at screen			
	40–49		50–69	
Screening round	**Number**	**%**	**Number**	**%**
First screening round	182	0.02	153	0.02
Second screening round	139	0.03	135	0.01
Third screening round	76	0.03	192	0.02
Subsequent screening rounds	80	0.03	949	0.02
Total	**477**	**0.03**	**1,429**	**0.02**

The third question of interest for women aged 40–49, was *What are the implications for later screening*? If women start screening early are they more inclined to screen at age 50–54, and/or are they more likely to become regular screeners?

Women who screened at age 50–54 in the 5 years 2010–2014 were divided into two groups—those who had screened at age 40–49 in the 10 years between 2000 and 2009, and those who had not. It was found that just under half (46.7%) of women who screened at age 50–54 had previously screened at age 40–49 (Table 6.3.4).

Table 6.3.4: Proportion of women who screened at age 50–54 who also screened at age 40–49

	Screened at age 50–54 during 2010–2014	
Screened at age 40–49 during 2000–2009	**Number**	**%**
No	358,930	53.3
Yes	314,865	46.7

An adjusted proportional hazard regression was then performed to determine the likelihood of women aged 40–49 screening for a second time after a first screen. It was found that, compared with women who commenced screening at age 50–54, women who commenced screening at age 40–49 were slightly more likely to return for a second screen, with a hazard ratio of 1.12 (1.12–1.13) (Table 6.3.5).

Table 6.3.5: Likelihood of returning for second screen in women who commenced screening at age 40–49 compared with women who commenced screening at age 50–69, 2000–2012

Age commenced screening	Number	Relative likelihood of returning for second screen (hazard ratio)	CI	*p* value
40–49	896,059	1.12	1.12–1.13	<0.0001
50–69	861,675	1.0	. .	. .

This suggests that women who screen at age 40–49 may be more motivated to screen; this may be because of a perceived higher risk of breast cancer due to the presence of a symptom or a family history of breast cancer, as noted earlier.

The screening behaviour of women who commenced screening at age 40–49 was then compared with women who commenced screening at age 50–59. It was found that, compared with women who commenced screening at age 50–69, a lower proportion of women who commenced screening at age 40–49 screened once or became regular screeners, with this group of women being more likely to be irregular screeners (Table 6.3.6).

Table 6.3.6: Screening behaviour of women who commenced screening at age 40–49 compared with that of women who commenced screening at age 50–69, 2000–2006

	Age commenced screening			
	40–49		50–69	
Screening behaviour	**Number**	**%**	**Number**	**%**
Regular screener	346,439	58.7	301,354	62.2
Irregular screener	201,041	34.1	123,800	25.6
Screened once only	42,761	7.2	59,461	12.3

Together, these results indicate that women who commence screening at age 40–49 are quite a unique group that are different to women who commence screening at age 50–69.

Higher risk women who screen through BreastScreen Australia

In this section, higher risk women are examined. Higher risk women are those who have a personal history, family history or symptoms of breast cancer. The first question of interest for higher risk women is *How many screen*? The second question of interest is *What proportion of screens in higher risk women result in the detection of an invasive breast cancer or DCIS*? Data relevant to these analyses are shown in tables 6.3.7–6.3.9.

Overall 1.2% of screens had a personal history reported, 11.8% had a family history reported, and 5.6% had a symptom reported. All differed by age. Screens at which a personal or family history or a symptom was reported were slightly more likely to have an invasive breast cancer or DCIS detected.

Table 6.3.7: Number of screens in which a personal history was reported, and proportion in which an invasive breast cancer or DCIS was detected, by 5-year age group

	Personal history reported				Personal history not reported			
Age group	Number	% of screens	Number detected	% detected	Number	% of screens	Number detected	% detected
40–44	1,219	0.2	25	2.1	714,574	99.8	2,555	0.4
45–49	4,272	0.4	50	1.2	1,204,251	99.6	5,832	0.5
50–54	13,196	0.5	169	1.3	2,781,946	99.5	14,529	0.5
55–59	22,937	0.8	255	1.1	2,686,441	99.2	15,068	0.6
60–64	31,285	1.3	419	1.3	2,373,171	98.7	16,566	0.7
65–69	34,070	1.8	434	1.3	1,871,140	98.2	14,803	0.8
70–74	24,736	2.7	318	1.3	897,754	97.3	8,221	0.9
75–79	17,201	5.0	231	1.3	324,477	95.0	3,455	1.1
80–84	9,188	9.7	132	1.4	85,882	90.3	1,075	1.3
85+	3,534	16.5	42	1.2	17,947	83.5	257	1.4
Total	**161,638**	**1.2**	**2,075**	**1.3**	**12,957,583**	**98.8**	**82,361**	**0.6**

Table 6.3.8: Number of screens in which a family history was reported, and proportion in which an invasive breast cancer or DCIS was detected, by 5-year age group

	Family history reported				Family history not reported			
Age group	Number	% of screens	Number detected	% detected	Number	% of screens	Number detected	% detected
40–44	100,327	14.0	470	0.5	615,466	86.0	2,110	0.3
45–49	160,060	13.2	1,002	0.6	1,048,463	86.8	4,880	0.5
50–54	285,805	10.2	2,035	0.7	2,509,337	89.8	12,663	0.5
55–59	302,958	11.2	2,435	0.8	2,406,420	88.8	12,888	0.5
60–64	276,126	11.5	2,790	1.0	2,128,330	88.5	14,195	0.7
65–69	231,498	12.2	2,568	1.1	1,673,712	87.8	12,669	0.8
70–74	121,355	13.2	1,601	1.3	801,135	86.8	6,938	0.9
75–79	52,063	15.2	756	1.5	289,615	84.8	2,930	1.0
80–84	16,938	17.8	284	1.7	78,132	82.2	923	1.2
85+	4,103	19.1	65	1.6	17,378	80.9	234	1.3
Total	**1,551,233**	**11.8**	**14,006**	**0.9**	**11,567,988**	**88.2**	**70,430**	**0.6**

Table 6.3.9: Number of screens in which a symptom was reported, and proportion in which an invasive breast cancer or DCIS was detected, by 5-year age group

	Symptom reported				Symptom not reported			
Age group	Number	% of screens	Number detected	% detected	Number	% of screens	Number detected	% detected
40–44	83,164	11.6	797	1.0	632,629	88.4	1,783	0.3
45–49	107,462	8.9	1,416	1.3	1,101,061	91.1	4,466	0.4
50–54	176,058	6.3	2,338	1.3	2,619,084	93.7	12,360	0.5
55–59	132,233	4.9	2,048	1.5	2,577,145	95.1	13,275	0.5
60–64	100,115	4.2	1,960	2.0	2,304,341	95.8	15,025	0.7
65–69	70,113	3.7	1,480	2.1	1,835,097	96.3	13,757	0.7
70–74	36,173	3.9	900	2.5	886,317	96.1	7,639	0.9
75–79	16,197	4.7	548	3.4	325,481	95.3	3,138	1.0
80–84	5,374	5.7	264	4.9	89,696	94.3	943	1.1
85+	1,358	6.3	82	6.0	20,123	93.7	217	1.1
Total	**728,247**	**5.6**	**11,833**	**1.6**	**12,390,974**	**94.4**	**72,603**	**0.6**

There is also interest in assessing the impact of women with symptoms who are not recalled to assessment and are later diagnosed with an interval breast cancer.

Analyses revealed that this occurred in a very small number of women. Over the entire period 2000–2014, this occurred just 125 times—13 times within 1 month of the screen at which a symptom was reported, an additional 15 times between 1 and 2 months, and 97 times 2 months or more after the screen at which a symptom was reported (Table 6.3.10).

Table 6.3.10: Number of women with a symptom who were not recalled to assessment and were later diagnosed with an interval breast cancer

Time since screen	Number
Within 1 month	13
Between 1 and 2 months	15
After 2 months	97
Total	**125**

7 Discussion

This is the second in a series of reports to present results from a major data linkage project that linked data from the eight state and territory BreastScreen registers, the eight state and territory cervical screening registers, the National Bowel Cancer Screening Program Register, the Australian Cancer Database, the National Death Index, and the National HPV Vaccination Program Register.

The project had three main objectives, these being to:

1. determine key cancer outcomes in screening and non-screening individuals to determine whether screen-detected cancers are less likely to result in death than cancers detected outside screening programs
2. gain an understanding of the screening behaviour of participants, such as who screens, in which programs, and whether this is influenced by common factors such as socioeconomic status, history of positive test results, or other events
3. use the linked data to enhance currently available screening data, such as analysis of linked cervical screening and HPV vaccination data to look at the effect of HPV vaccination on cervical abnormalities, cancers and participation in cervical screening.

The first report from this Australian-first data linkage project (AIHW 2018a) presented initial results on the lower risk of death associated with breast cancers detected through BreastScreen Australia compared with breast cancers diagnosed in women who had never screened through BreastScreen Australia.

This second report, which has breast cancer and BreastScreen Australia as its focus, expanded on these findings to provide a more comprehensive picture of the survival from breast cancer detected through BreastScreen Australia. This report also includes results from analyses designed to elucidate the screening behaviour of women who participate in BreastScreen Australia, which would not have been possible without linkage across the other cancer screening programs and a national BreastScreen Australia data set. These results provide answers that may allow those who manage these programs to provide a better service, which will ultimately benefit all women who participate in this national breast cancer screening program.

In this respect, this report wholly fulfils the first and second objectives for this project for breast cancer.

7.1 Objective 1: Cancer outcomes

This report examined survival outcomes of breast cancer diagnosed in all women eligible to screen through BreastScreen Australia to more fully explore the previously-determined survival benefits of detecting a cancer as a result of screening in women aged 50–69.

Screening history from state and territory BreastScreen registers was used to categorise breast cancers in the Australian Cancer Database diagnosed in women aged 40 and over in the period 2002–2012 according to screen detection status. Data from the National Death Index to the end of 2015 were used to determine if death (due to breast cancer, or to any cause) followed these breast cancer diagnoses. Screen detection status groups for breast cancer were ‘screen-detected cancers’, ‘non-screen-detected cancers in screened women’, ‘interval cancers’ and ‘non-screen-detected cancers in never-screened women’.

Survival from breast cancer in women in the target age group for BreastScreen Australia

As reported previously (AIHW 2018a), and reported again here, for women aged 50–69, breast cancers detected through BreastScreen Australia had a 69% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia. This indicates that it is more beneficial for a breast cancer to be detected through screening mammography than by being symptomatic.

This may be due to breast cancers detected through BreastScreen Australia being at an earlier stage than breast cancers that have become symptomatic. Although it was not possible to know the stage of the breast cancers diagnosed in this study, tumour size (one of the three factors that determine stage, along with lymph node involvement and presence of distant metastases) was recorded for most breast cancers. In this study, it was found that 55.3% of breast cancers detected through BreastScreen Australia were small, compared with 27.6% of breast cancers diagnosed in women who had never screened through BreastScreen Australia.

Although not the focus of the study, interval breast cancers and non-screen-detected breast cancers in screened women were also included in the analyses. These breast cancers were also less likely to cause death than breast cancers diagnosed in women who had never screened, but the difference in risk of death was half that of screen-detected breast cancers (both had a 35% lower risk of breast cancer death than never-screened breast cancers).

These results indicate the importance of screening according to the recommended screening interval to reap the full benefits of breast cancer screening, but also show that there is still some benefit to having had a previous screen, even if the breast cancer is not screen-detected. This may be because cancers can develop only in the time since a woman's previous screen, so may be more likely to be smaller than breast cancers diagnosed in women who have never been screened. Data from this project support this; while the proportion of small breast cancers was found to be highest in screen-detected breast cancers at 55.3%, the proportion in interval cancers and non-screen-detected breast cancers in screened women was about 34%, markedly higher than that in never-screened breast cancers, of which only 27.6% were small.

Survival for the 5-year age groups within the 50–69 age group were also examined. The risk of breast cancer death in screen-detected breast cancers compared with those diagnosed in women who had never screened was the same across all 5-year age groups between ages 50–54 and 65–69, ranging between a 68% and 70% lower risk.

Screen-detected breast cancers may be subject to lead-time bias—that is, when a cancer is detected earlier, but leads to no increase in life span. In this case, an individual lives with cancer for longer, but does not live for longer than they would have had the cancer been diagnosed later. Adjustments were therefore made to account for any lead-time bias. In addition to the mean lead time of 40 months that was used to correct for lead-time bias in data previously reported for this study (AIHW 2018a), corrections were also made based on lead times of 2 years and 4 years. Lead times of 40 months and 4 years are likely to be the most appropriate for women aged 50–69, since 40 months is a mean lead time that has received a level of consensus (Duffy & Parmar 2013), and 4 years aligns with the estimated mean sojourn time for women aged 50–69 (Duffy et al. 1997).

After correcting for lead-time bias using these two lead times, screen-detected breast cancers still had a 54% to 57% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

It has further been suggested that screen-detected breast cancers may be subject to screening selection bias, which is when women who choose to screen may have lower breast cancer mortality for non-screening reasons. In this case, women who choose to

screen may be more ‘well’ and therefore may have lived longer after a breast cancer diagnosis than women who choose not to screen, even if the breast cancer had not been screen-detected.

Previous investigations of the correction for any screening selection bias in this study demonstrated the importance of using the appropriate correction factor for the analysis data. It was concluded that an Australian-specific screening selection correction factor derived from these linked study data should be investigated to determine if this could enable appropriate correction for this potential bias (AIHW 2018a). An Australian-specific correction factor of 0.91—derived using data from this study—was compared with two published correction factors: a correction factor of 1.36, previously determined to over-correct for screening selection bias in Australian data, and a correction factor of 1.17, a more appropriate correction factor than 1.36, but likely also an over-correction.

After correcting for screening selection bias using these three correction factors, screen-detected breast cancers had a 41% to 73% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

However, the derived correction factor for Australia of 0.91—which may be a slight underestimate due to treatment improvements over time—is indicative of screening selection bias having only a minor or no effect in Australia. Research by Roder et al. (2008) supports this. Their survey of South Australian women determined that women who participated in BreastScreen Australia were more likely to have a family history of breast cancer, a history of breast surgery, and to have previously used hormone replacement therapy. This indicates that women who participate in BreastScreen Australia may have a higher background risk for breast cancer than women who do not participate.

Therefore, while a range of possible corrections have been presented here, those that use the Australian correction factor of 0.91, and those that are uncorrected, are likely to be the most appropriate to use when estimating the risk of breast cancer deaths in screen-detected breast cancers compared with breast cancers diagnosed in women who have never screened.

After correcting for lead-time bias and screening selection bias using lead times and correction factors deemed most appropriate for Australian women aged 50–69, breast cancers detected through BreastScreen Australia had a 54% to 63% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

These estimates of lower risk for screen-detected breast cancers align with the findings from a full review of available high quality observational studies undertaken by the International Agency for Research on Cancer that determined that women aged 50–69 who attended breast cancer screening using screening mammography had about a 40% reduction in the risk of death from breast cancer (Lauby-Secretan et al. 2015). Several Australian studies, at the jurisdictional and national level, also found a reduction in mortality in screening participants (DoHA 2009; Morrell et al. 2012; Nickson et al. 2012; Roder et al. 2008; Taylor et al. 2004).

Overall, these findings are consistent with the finding that breast cancers detected through BreastScreen Australia had better survival outcomes.

Note that, while it has been recognised that a small number of breast cancers detected by screening mammography would not have become clinically apparent within a woman’s lifetime, it is not currently possible to predict which breast cancers will fall into this category.

Presence of these cancers cannot be adjusted for in these analyses, but effects have been minimised through the inclusion of only invasive breast cancers—and not DCIS, which may

be less likely to progress to be clinically apparent within a woman's lifetime—and appropriate adjustments made to correct for lead-time bias and screening selection bias.

Molecular and genomic research may in future develop the means to identify breast cancers that are unlikely to progress, which would see a change in best practice to allow these breast cancers to be managed more conservatively (Cancer Australia 2017).

Survival from breast cancer in women outside the target age group for BreastScreen Australia

Women aged 40–49 and 70 and over, for the years of data analysed, were eligible to attend BreastScreen Australia, but were not actively targeted. These women were not sent invitation or reminder to screen correspondence (note that this changed from July 2013, from which time the target age group was widened to ages 50–74). Not included in the first report, these age groups were analysed in this report to provide a more comprehensive assessment of breast cancer survival across all age groups that screen through BreastScreen Australia.

It was found that, for both these additional age groups, screen-detected breast cancers were less likely to cause death than breast cancers diagnosed in women who had never screened through BreastScreen Australia. For women aged 40–49, risk of death for screen-detected breast cancers was 55% lower, and for women aged 70 and over, risk of death for screen-detected breast cancers was 64% lower, compared with breast cancers diagnosed in women who had never screened.

Lower risk was found to align with the proportion of screen-detected breast cancers that were small, with 47.1% of screen-detected breast cancers in women aged 40–49 small, and 54.5% of screen-detected breast cancers in women aged 70 and over small. These data lend further support to the premise that the better survival of breast cancers detected through BreastScreen Australia may be due to screen-detected breast cancers being found (and treated) at an earlier stage than breast cancers that have become symptomatic, and are diagnosed outside BreastScreen Australia.

Survival for the 5-year age groups within the 40–49 and 70 and over age groups was also examined. Women aged 70–74 had a similar risk profile as those aged 50–69, with a 69% lower risk of breast cancer death in screen-detected breast cancers compared with those diagnosed in women who had never screened. This difference in risk decreased as 5-year age groups moved further from the target age group. Women aged 45–49 and 75–79 had a 61% and 64% lower risk, respectively, and women aged 80–84 and 85 and over had a 60% and 59% lower risk, respectively. Women aged 40–44 had the smallest difference in this risk, with a 42% lower risk of breast cancer death.

After correcting for lead-time and screening selection bias using lead times and correction factors deemed most appropriate for Australian women aged 40–49, breast cancers detected through BreastScreen Australia had a 34% to 51% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

After correcting for lead-time and screening selection bias using lead times and correction factors deemed most appropriate for Australian women aged 70 and over, breast cancers detected through BreastScreen Australia had a 55% to 62% lower risk of causing death than breast cancers diagnosed in women who had never screened through BreastScreen Australia.

7.2 Objective 2: Screening behaviour

Screening behaviour is determined by two factors—screening (women attending BreastScreen Australia) and rescreening (women returning to BreastScreen Australia). Both are required for adequate levels of participation in BreastScreen Australia for breast cancer morbidity and mortality reductions to be maximised.

This report used linked BreastScreen Australia and cervical screening data to determine if there was an association being regular participation in cervical screening and participation in BreastScreen Australia, as well as using the linked national BreastScreen Australia data set to better understand patterns of screening and rescreening in BreastScreen Australia participants.

Analyses of linked BreastScreen Australia and cervical screening data demonstrated that women who are regular participants in cervical screening are not only more likely to participate in BreastScreen Australia, but are more likely to also become regular screeners in that program. This effect was strongest in women who were participants in cervical screening at age 50—the age at which women are first invited to screen through BreastScreen Australia.

Women who were participants in cervical screening—either regularly or irregularly—were also more likely to commence participation in BreastScreen Australia earlier, with both regular and irregular cervical screening participants having a mean commencement age of about 50. In contrast, non-participants in cervical screening had a mean commencement age 5 to 10 years later than this.

Being aged 50 or over is one of the greatest risk factors for developing breast cancer, and earlier in this report the mortality benefits of having a breast cancer detected through screening mammography rather than due to the breast cancer being symptomatic were demonstrated to be high from age 50. Since participating regularly in cervical screening appears to be a strong influencing factor on a woman's decision to screen—and to screen from the time she is in the target age group—this behaviour has the potential to decrease mortality from breast cancer.

A factor found to influence whether a woman rescreened through BreastScreen Australia was the number of times she had been previously screened. Rescreening data suggest that, once women have screened three or so times, they are likely to be regular screeners. However, there are a significant proportion of women who do not return after their first screen, a trend that was only slightly better after a woman's second screen.

Further investigation determined that there were two issues at play in the lower rescreening rates after first and second screens. Firstly, fewer women rescreened at all, particularly after a first screen, but also after a second screen (so some women screened once or even twice but then chose not to screen again). Secondly, for those who do chose to rescreen, it appeared to take three or so screening rounds for women to rescreen within the recommended screening interval. Increased time between screening may allow a tumour to grow to the point where symptoms become evident, thus eliminating the advantage of screening. Therefore, the rate at which women rescreen within 27 months is a crucial measure of adequate and appropriate rescreening within BreastScreen Australia.

Factors associated with a woman not rescreening varied by screening round. Women who did not rescreen after their first screen were more likely to report symptoms, whereas women who did not rescreen after a third or subsequent screen were more likely to have been recalled to assessment for further investigation.

It has been shown that, in one jurisdictional BreastScreen program, women with false positive screening mammograms (that is, those recalled to assessment for further investigation and found not to have breast cancer) are less likely to participate in subsequent screening rounds (Sim et al. 2012). This was investigated as a possible reason for the rescreening patterns observed using these study data.

Overall, it was found that when all screening rounds were combined, there was a trend of lower rescreening rates in women who had a false positive screen compared with women who had a true negative screen. However, this differed across screening rounds—after a woman's first screen, rescreening was found to be higher in women with a false positive screen compared with women with a true negative screen, with no difference in the rescreening rate after a woman's second screen. Only third and subsequent screening rounds aligned with the overall trend.

It is also of note that, while the overall trend was true at the national level, there was variation at the jurisdictional level. Some state and territory BreastScreen programs were consistent with this overall trend, and some showed no difference in the rescreening rates between women who had a false positive screen and those who had a true negative screen.

7.3 Project limitations and areas for improvement

This project had several limitations and areas where additional or improved data would provide more enriched outcome data.

- Cancer outcomes and screening behaviour were not explored for Aboriginal and Torres Strait Islander people. This is a major omission, given that it is known that Aboriginal and Torres Strait Islander people have poorer outcomes and lower participation in BreastScreen Australia. Indigenous status is available on the cancer and BreastScreen registers included in this study, and it is a priority to include specific analyses by Indigenous status for this project in future if the opportunity arises. At the time of preparation of this report, Phase 2 of this data linkage project is currently in the scoping stage, and—if it goes ahead—would include capturing Indigenous status to allow these important analyses to be undertaken.
- The Australian Cancer Database, the source of cancer data for this project, does not currently include data on cancer stage or spread. Staging data would greatly enhance this project, as it would allow the lower mortality of screen-detected cancers to be better understood and explored.
- Breast cancers in this project were restricted to invasive breast cancers; inclusion of DCIS in future analyses would be of value.
- For screening behaviour analyses, only women who appeared on a BreastScreen register could be included. Women who have never screened were invisible in these analyses, which limits our understanding of why these women choose not to screen.

7.4 Where to from here?

This is the second report to present results from this Australian-first data linkage project. While the first report fulfilled the first and second objectives, and partly fulfilled the third objective of this project, this report wholly fulfils the first and second objectives for breast cancer. Future releases and products are planned to enhance the objectives already fulfilled for cervical cancer, and to completely fulfil the third objective. At the time of report production, one final AIHW report is planned to achieve this.

The final report planned is specific to the previous National Cervical Screening Program (that ceased on 30 November 2017), that, in addition to further cancer outcome and screening behaviour analyses, will enable investigation of the relationship between HPV vaccination and cervical screening and cervical cancer. It will also look at lessons learned from that program that may be relevant to the current National Cervical Screening Program.

Along with a report specific to bowel cancer screening outcomes released earlier in 2018, the three reports from this project will collectively provide a comprehensive picture of cancer outcomes and screening behaviour across BreastScreen Australia, the National Cervical Screening Program and the National Bowel Cancer Screening Program.

Appendix A: Additional data tables

Table A1: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 50–69 diagnosed with breast cancer, with screen-detected cancers as the reference group

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.61	2.18–3.12	<0.0001
Non-screen-detected	2.63	2.46–2.80	<0.0001
Never-screened	4.42	4.16–4.70	<0.0001
Breast cancer mortality, adjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.07	1.73–2.47	<0.0001
Non-screen-detected	2.07	1.94–2.21	<0.0001
Never-screened	3.20	3.00–3.40	<0.0001

Table A2: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 40–49 diagnosed with breast cancer, with screen-detected cancers as the reference group

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.12	1.49–3.00	<0.0001
Non-screen-detected	1.33	1.11–1.59	0.0018
Never-screened	2.71	2.33–3.15	<0.0001
Breast cancer mortality, adjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	1.85	1.31–2.63	0.0005
Non-screen-detected	1.14	0.95–1.36	0.1591
Never-screened	2.25	1.93–2.62	<0.0001

Table A3: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 70 and over diagnosed with breast cancer, with screen-detected cancers as the reference group

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.42	1.63–3.60	<0.0001
Non-screen-detected	2.75	2.48–3.04	<0.0001
Never-screened	5.53	5.03–6.07	<0.0001
Breast cancer mortality, adjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	1.77	1.19–2.63	0.0045
Non-screen-detected	2.07	1.86–2.29	<0.0001
Never-screened	2.82	2.55–3.11	<0.0001

Table A4: Unadjusted (crude) and adjusted hazard ratios for breast cancer mortality for women aged 40 and over diagnosed with breast cancer, with screen-detected cancers as the reference group

	HR	95% CI	*p* value
Breast cancer mortality, unadjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.41	2.08–2.79	<0.0001
Non-screen-detected	2.62	2.49–2.76	<0.0001
Never-screened	4.72	4.50–4.94	<0.0001
Breast cancer mortality, adjusted			
Screening women			
Screen-detected	1.00	. .	. .
Interval	2.04	1.76–2.36	<0.0001
Non-screen-detected	1.99	1.88–2.09	<0.0001
Never-screened	2.98	2.84–3.13	<0.0001

Table A5: Results of sensitivity analysis, by 5-year age group

	Breast cancer diagnosis years included			
	2002–2012		2000–2012	
Age group	HR	95% CI	HR	95% CI
50–54	0.32	0.28–0.37	0.36	0.32–0.40
55–59	0.31	0.28–0.35	0.34	0.31–0.38
60–64	0.30	0.27–0.34	0.31	0.28–0.35
65–69	0.32	0.28–0.36	0.33	0.29–0.37
50–69	**0.31**	**0.29–0.33**	**0.33**	**0.32–0.35**

Appendix B: Positive predictive value of screening mammography

The screening test used in BreastScreen Australia, like other screening tests, is not intended to be diagnostic, but aims to identify individuals who are more likely to have cancer or cancer precursors, and therefore require further investigation from diagnostic tests. The positive predictive value (PPV) of a screening test is the probability that individuals with a positive screening test have cancer (or a precursor to cancer).

The screening test of BreastScreen Australia is the mammogram, with two views performed on each breast. The images are reviewed, and if there are features that may be indicative of breast cancer, the woman is recalled to an assessment centre for diagnostic testing.

The PPV is the proportion of screening mammograms for which the recommendation is recall to assessment that lead to an invasive breast cancer diagnosis, as previously described (Kavanagh et al. 2000). Because recall to assessment rates and invasive breast cancer detection rates are higher for a woman's first screening round and differ by age, the PPV has been calculated separately for first and subsequent screening rounds, as well as for all screening rounds combined, for all 5-year age groups (Table B1).

Table B1: Positive predictive value of mammography, by 5-year age group

Year	First screening round PPV (%)	Subsequent screening rounds PPV (%)	All screening rounds PPV (%)
40–44	3.4	4.7	3.7
45–49	5.0	6.7	5.9
50–54	5.8	8.1	7.1
55–59	9.4	11.6	11.2
60–64	12.9	15.3	15.1
65–69	14.6	17.9	17.6
70–74	17.5	21.1	20.9
75–79	23.1	22.7	22.8
80–84	26.6	25.6	25.7
85+	26.8	24.7	25.2
Total	**6.5**	**13.3**	**11.3**

Appendix C: Classifications

Classification of population groups

Cancer and screening data were analysed by remoteness area and socioeconomic status. Remoteness area was classified into areas according to the 2011 Australian Bureau of Statistics (ABS) Australian Statistical Geography Standard, while socioeconomic status quintiles were classified using the 2011 ABS Index of Relative Socioeconomic Disadvantage.

Geographical classification

The ability to access and provide a wide range of services is influenced by the distance between clients and providers, be it for the clients to travel to the service providers or for the providers to travel to deliver services close to a person's home. The geographical location of areas is therefore an important concept in planning and analysing the provision of services.

As previously stated, geographical location was classified according to the ABS Australian Statistical Geography Standard Remoteness Structure (ABS 2011), which groups geographical areas into 6 remoteness categories, using the Accessibility/Remoteness Index for Australia. This index is a measure of the remoteness of a location from the services provided by large towns or cities. Accessibility is judged purely on distance to one of the metropolitan centres. A higher score on this index denotes a more remote location. Further information is available on the ABS website at <http://www.abs.gov.au/websitedbs/D3310114.nsf/home/geography>.

Residential address postcodes (at time of screen for BreastScreen Australia participants) were mapped to the 2011 Remoteness Structure, classified to five main areas: *Major cities*, *Inner regional*, *Outer regional*, *Remote* and *Very remote*. The sixth area, *Migratory*, is not used in this project. The category *Major cities* includes Australia's capital cities, except Hobart and Darwin, which are classified as *Inner regional*. Participants whose postcodes were not available in the remoteness correspondence were included in an 'Unknown' geographical location grouping.

Socioeconomic classification

Socioeconomic classifications were based on the 2011 ABS Index of Relative Socioeconomic Disadvantage (IRSD) (ABS 2013). The IRSD is one of four Socioeconomic Indexes for Areas developed by the ABS and is based on factors such as average household income, education levels and unemployment rates. The IRSD is not a person-based measure; rather, it is an area-based measure of socioeconomic status in which small areas of Australia are classified on a continuum from most to least disadvantaged. This information is used as a proxy for the socioeconomic status of people living in those areas and may not be correct for each person in that area.

People were assigned to socioeconomic groups (quintiles) according to the IRSD of their residential postcode as per the geographical classification. Socioeconomic groups (based on IRSD rankings) were calculated with a 2011 Census postal area correspondence (previously called a concordance) using a population-based method at the Australia-wide level.

The first socioeconomic group (labelled '1') corresponds to geographical areas containing the 20% of the population with the most disadvantage according to the IRSD, and the fifth group (labelled '5') corresponds to the 20% of the population with the least disadvantage.

Classification of cancer groups

Morphology refers to the histological characteristics of tumours, defined by the type of cell they involve. A tumour that involves skin cells, internal organ tissue, or lining cells is called a carcinoma, and a tumour that involves connective or supportive tissue (muscle cells, bone cells) is called a sarcoma. Each of these broad cellular types can be categorised further by their microscopic properties. The histological type of cancer is associated with different risk factors, natural behaviour history and responsiveness to therapeutic interventions.

Histological types of breast cancer are shown in Table C.1, grouped into 10 higher level groups. In this project, breast cancers were not grouped any further.

Table C1: Breast cancer histology groupings

Breast cancer group	Type of breast cancer (ICD-O-3 codes)
Invasive ductal carcinoma	Pleomorphic carcinoma (8022)
	Carcinoma with osteoclast-like giant cells (8035)
	Basaloid carcinoma (8123)
	Scirrhous adenocarcinoma (8141)
	Carcinoma simplex (8231)
	Infiltrating duct carcinoma, not otherwise specified (8500)
	Duct carcinoma, desmoplastic type (8514)
	Infiltrating ductular carcinoma (8521)
	Infiltrating duct and lobular carcinoma (8522)
	Infiltrating duct mixed with other types of carcinoma (8523)
	Paget disease and infiltrating duct carcinoma of breast (8541)
	Paget disease and intraductal carcinoma of breast (8543)
Invasive lobular carcinoma	Pleomorphic lobular carcinoma, not otherwise specified (8519)
	Lobular carcinoma, not otherwise specified (8520)
	Infiltrating lobular mixed with other types of carcinoma (8524)
Medullary carcinoma and atypical medullary carcinoma	Medullary carcinoma, not otherwise specified (8510)
	Atypical medullary carcinoma (8513)
	Medullary carcinoma with lymphoid stroma (8512)
Tubular carcinoma and invasive cribriform carcinoma	Tubular adenocarcinoma (8211)
	Cribriform carcinoma, not otherwise specified (8201)
Mucinous carcinoma	Mucinous adenocarcinoma (8480)
	Mucin-producing adenocarcinoma (8481)
	Signet ring cell carcinoma (8490)
Invasive papillary carcinoma	Intraductal papillary adenocarcinoma with invasion (8503)
	Papillary adenocarcinoma, not otherwise specified (8260)
	Intracystic (papillary) adenocarcinoma (8504)
	Papillary carcinoma, not otherwise specified (8050)
	Solid papillary carcinoma (8509)
	Invasive micropapillary carcinoma (8507)

(continued)

Table C1 (continued): Breast cancer histology groupings

Breast cancer group	Type of breast cancer (ICD-O-3 codes)
Inflammatory carcinoma	Inflammatory carcinoma (8530)
Mesenchymal	Sarcoma, not otherwise specified (8800)
	Spindle cell sarcoma (8801)
	Giant cell sarcoma (8802)
	Epithelioid sarcoma (8804)
	Undifferentiated sarcoma (8805)
	Fibrosarcoma (8810)
	Fibromyxosarcoma (8811)
	Solitary fibrous tumour, malignant (8815)
	Low grade myofibroblastic sarcoma (8825)
	Malignant fibrous histiocytoma (8830)
	Liposarcoma, not otherwise specified (8850)
	Well differentiated liposarcoma, not otherwise specified (excluding superficial soft tissue) (8851)
	Myxoid liposarcoma (8852)
	Pleomorphic liposarcoma (8854)
	Leiomyosarcoma (8890)
	Angiomyosarcoma (8894)
	Myosarcoma (8895)
	Rhabdomyosarcoma (8900)
	Alveolar rhabdomyosarcoma (8920)
	Stromal sarcoma, not otherwise specified (8935)
	Haemangiosarcoma (9120)
	Haemangioendothelioma, malignant (9130)
	Haemangiopericytoma, malignant (9150)
	Lymphangiosarcoma (9170)
	Osteosarcoma, not otherwise specified (9180)
	Chondrosarcoma, not otherwise specified (9220)
Other—specified	Metaplastic carcinoma, not otherwise specified (8575)
	Adenocarcinoma with squamous differentiation (8570)
	Adenocarcinoma with spindle cell metaplasia (8572)
	Squamous cell carcinoma, not otherwise specified (8070)
	Squamous cell carcinoma, keratinising, not otherwise specified (8071)
	Squamous cell carcinoma, large cell nonkeratinising, not otherwise specified (8072)
	Squamous cell carcinoma, spindle cell (8074)
	Spindle cell carcinoma, not otherwise specified (8032)
	Carcinosarcoma, not otherwise specified (8980)
	Adenocarcinoma with cartilaginous and osseous metaplasia (8571)

(continued)

Table C1 (continued): Breast cancer histology groupings

Breast cancer group	Type of breast cancer (ICD-O-3 codes)
	Pseudosarcomatous carcinoma (8033)
	Malignant myoepithelioma (8982)
	Adenocarcinoma, not otherwise specified (8140)
	Phyllodes tumour, malignant (9020)
	Paget disease, mammary (8540)
	Adenocarcinoma with apocrine metaplasia (8573)
	Apocrine adenocarcinoma (8401)
	Neuroendocrine carcinoma, not otherwise specified (8246)
	Small cell carcinoma, not otherwise specified (8041)
	Carcinoma with neuroendocrine differentiation (8574)
	Large cell neuroendocrine carcinoma (8013)
	Carcinoid, not otherwise specified (8240)
	Atypical carcinoid tumour (8249)
	Adenocarcinoma with mixed subtypes (8255)
	Mixed cell adenocarcinoma (8323)
	Secretory carcinoma of breast (C50_) (8502)
	Acinar cell carcinoma (8550)
	Mucoepidermoid carcinoma (8430)
	Lipid-rich carcinoma (C50_) (8314)
	Glycogen-rich carcinoma (8315)
	Clear cell adenocarcinoma, not otherwise specified (8310)
	Sebaceous carcinoma (8410)
	Mixed tumour, malignant (8940)
	Lymphoepithelial carcinoma (8082)
	Basal cell adenocarcinoma (8147)
	Trabecular carcinoma (8190)
	Solid carcinoma, not otherwise specified (8230)
	Adenomyoepithelioma, malignant (8983)
	Adenoid cystic carcinoma (8200)
	Epithelial-myoepithelial carcinoma (8562)
	Peripheral neuroectodermal tumour, not otherwise specified (9364)
	Granular cell tumour, malignant (9580)
	Adenocarcinoma in adenomatous polyp (8210)
	Sweat gland adenocarcinoma (8400)
	Papillary cystadenocarcinoma NOS (8450)
	Adenosquamous carcinoma (8560)
	Comedocarcinoma, not otherwise specified (C50_) (8501)

(continued)

Table C1 (continued): Breast cancer histology groupings

Breast cancer group	Type of breast cancer (ICD-O-3 codes)
Unspecified	Neoplasm, malignant (8000)
	Tumour cells, malignant (8001)
	Malignant tumour, spindle cell type (8004)
	Malignant tumour, clear cell type (8005)
	Carcinoma, not otherwise specified (8010)
	Large cell carcinoma, not otherwise specified (8012)
	Carcinoma, undifferentiated (8020)
	Carcinoma, anaplastic (8021)
	Giant cell and spindle cell carcinoma (8030)
	Giant cell carcinoma (8031)

Notes

1. Breast cancer histology types have been categorised by the Australasian Association of Cancer Registries.
2. Codes were sourced from the International Classification of Diseases for Oncology, Third Edition.

Appendix D: Additional statistical methods

Correction for lead-time bias

The following method from Duffy et al. (2008) was used to correct for estimated lead-time bias for breast cancers. For those with a breast cancer diagnosis who are known to be alive at time *t*:

$$E(s) = \frac{1 - e^{-\lambda t}}{\lambda}$$

For those with a breast cancer diagnosis and a breast cancer death at time *t*:

$$E(s) = \frac{1 - e^{-\lambda t} - \lambda t e^{-\lambda t}}{\lambda(1 - e^{-\lambda t})}$$

where:

- *E*(*s*) equals the estimated sojourn time (lead time)—the period during which the breast cancer is asymptomatic but screen-detectable
- *t* equals the time from screen-detected breast cancer diagnosis to breast cancer death (or loss to follow-up); that is, the uncorrected 'survival' time
- *λ* equals the rate of transition from asymptomatic but screen-detectable to symptomatic breast cancer.

Three lead time estimates were used in this report to compare the effects on the hazard ratio of each estimate. These estimates were based on mean sojourn time of 2 years, 40 months, and 4 years.

The transition rate λ is the reciprocal of the mean sojourn time. In these calculations, λ values were 0.5 (based on a lead time of 2 years), 0.3 (based on a lead time of 40 months), and 0.25 (based on a lead time of 4 years).

This simple method relies on strong assumptions and generalisations but provides a way to take lead time into account in the mortality estimates of Objective 1. See the relevant papers for further information on correction for lead-time bias.

Correction for screening selection bias

The following method from Duffy and Cuzick (2002) was used to correct for estimated screening selection bias for breast cancers. The correction was applied to the hazard ratios following any other relevant corrections.

$$RR_{corrected} = \frac{P \times RR_1 \times D_r}{1 - (1 - P) \times D_r}$$

where:

- RR_1 equals the original hazard ratio before correction for self-selection bias
- *P* equals the participation rate in breast cancer screening
- D_r equals the correction factor.

A participation rate of 56.2% was used, which is the mean (and median) participation rate for women aged 50–69 in BreastScreen Australia over the years used in this study.

Three correction factors were used. A correction factor of 1.36 was used, as published by Duffy & Cuzick (2002). This correction factor was the most conservative option from several in the literature, and is likely to be an over-estimate for Australian data. A correction factor of 1.17 was also used, as published by the Swedish Organised Service Screening Evaluation Group (2006), and as used by Morrell and others (2017). A third correction factor of 0.91 was used, derived from the study data in this current report. This correction factor was derived using methodology adapted to an Australian context. As screening is available to all women, not only those invited to screen, the uninvited control group was women diagnosed in the pre-screening epoch, between 1986–1988. The non-participant group was unscreened women diagnosed in the screening epoch, between 2000–2002.

Glossary

Aboriginal or Torres Strait Islander: A person of Aboriginal and/or Torres Strait Islander descent who identifies as an Aboriginal and/or Torres Strait Islander. See also **Indigenous**.

adenocarcinoma: The malignant progression of a benign **adenoma**.

asymptomatic: Describes the situation where a person has a particular disease but experiences no symptoms of it.

Australian Statistical Geography Standard (ASGS): Common framework defined by the Australian Bureau of Statistics for collection and dissemination of geographically classified statistics. The ASGS replaced the Australian Standard Geographical Classification (ASGC) in July 2011.

benign: Not malignant.

biopsy: Small sample of tissue that is taken to obtain a definitive diagnosis of an abnormality.

bowel cancer: Comprises cancer of the **colon** and cancer of the rectum, collectively known as colorectal cancer.

breast cancer: Cancer most commonly originating in the ducts of the breast (which carry milk from the lobules to the nipple) but can also originate in the lobules (small lobes of the breast that produce milk), or more rarely in the connective tissue of the breast.

BreastScreen assessment: Further investigation of a mammographic abnormality or symptom reported at screening at a BreastScreen service.

cancer: Cancer, also called malignancy, is a term for diseases in which abnormal cells divide without control and can invade nearby tissues. Cancer cells can also spread to other parts of the body through the blood and lymph systems.

cervical cancer: Cancer affecting the cells of the uterine cervix, which is the lower part (or 'neck') of the uterus where it joins the upper end of the vagina.

cervical cytology test: Cytology means 'study of cells' and, in the context of cervical screening, refers to cells from the cervix that are collected and examined for abnormalities. Cervical cytology using the Pap test was the primary screening tool of the National Cervical Screening Program prior to 1 December 2017.

cervical histology test: Examination of tissue from the cervix through a microscope, collected by a biopsy, which was the primary screening tool of the National Cervical Screening Program prior to 1 December 2017.

cervical HPV test: Assessment of the presence of oncogenic HPV types in a sample, which was used as part of 'test of cure' under the National Cervical Screening Program prior to 1 December 2017, although was also used by some practitioners where it was not indicated.

cervix: The uterine cervix is the 'neck' of the uterus, connecting the vagina to the uterus.

colon: (also called large intestine). Lower part of the digestive system that reabsorbs water, salt and some nutrients from digested food, forming faeces that are later passed out of the body. In this report, the bowel consists of the colon and rectum.

confidence interval: A range determined by variability in data, within which there is a specified (usually 95%) chance that the true value of a calculated parameter lies.

ductal carcinoma in situ (DCIS): A non-invasive tumour of the mammary gland (breast) arising from cells lining the ducts.

eligible population: People who are eligible to participate in a cancer screening programs—for bowel this comprises people registered as an Australian citizen or migrant in the Medicare enrolment file, or registered with a Department of Veterans' Affairs gold card, who reach one of the target ages; for BreastScreen Australia this comprises Australian women aged 40 and over; for cervical screening this comprises sexually active women with an intact cervix.

endocervical: Glandular.

false negative: A test that has incorrectly indicated that the disease is not present.

false positive: A test that has incorrectly indicated that the disease is present.

hazard ratio: Generated from Cox proportional hazards regression, which is used for person-time multivariable modelling, a hazard ratio is essentially the same as a rate ratio. A hazard ratio indicates how many times as high the probability of an event is in one group of people with a particular characteristic as in another group of people without that characteristic, after adjusting for other factors in the model.

HPV: Human papillomavirus, a virus that affects both males and females. There are around 100 types of HPV, with around 40 types known as 'genital HPV', which are contracted through sexual contact. Persistent infection with oncogenic HPV types can lead to cervical cancer, whereas infection with non-oncogenic types of HPV can cause genital warts.

iFOBT: Immunochemical faecal occult blood test—specific type of FOBT test that requires no dietary or medicinal changes before the test. FOBTs are used to detect tiny traces of blood in a person's faeces that may be a sign of **bowel cancer**. The immunochemical FOBT is a central part of Australia's National Bowel Cancer Screening Program.

iFOBT result: The iFOBT results are classified by pathologists as:

positive (blood is detected in at least 1 of 2 samples)

negative (blood is not detected)

inconclusive (the participant is asked to complete another kit).

incidence: The number of new cases (of an illness or event, and so on) occurring during a given period.

Indigenous: A person of Aboriginal and/or Torres Strait Islander descent who identifies as an Aboriginal and/or Torres Strait Islander. See also **Aboriginal or Torres Strait Islander**.

in situ: A Latin term meaning 'in place or position'; undisturbed.

interval cancer: Defined in this report as a cancer diagnosed after a negative screening test. Refer to Methods for definitions for breast, cervical and bowel cancers used in this report.

invasive cancer: A **tumour** whose cells have spread locally and have the potential to spread to nearby healthy or normal tissue or to more distant parts of the body.

invitee: A person who has been invited to participate in the National Bowel Cancer Screening Program.

lead-time bias: Involves the amount of time a diagnosis of **asymptomatic** cancer is brought forward by screening. A concern with some cancers diagnosed earlier through screening is that this earlier diagnosis may make no difference to the outcome of the disease (that is, the date of death). The earlier diagnosis could therefore artificially increase (bias) survival time from that if the cancer were detected symptomatically later.

malignant: Abnormal changes consistent with **cancer**.

mammogram: A radiographic depiction of the breast.

metastasis: The process by which cancerous cells are transferred from one part of the body to another to form a secondary cancer; for example, via the lymphatic system or the bloodstream.

morbidity: Illness.

mortality: The number of deaths occurring during a given period.

National HPV Vaccination Program: This program was first introduced on 1 April 2007 as a program for females. At its inception, it comprised an ongoing vaccination program for females aged 12–13, administered through schools, and a catch-up program for females aged 13–26 between 2007 and 2009, with females aged 13–17 vaccinated through schools and females aged 18–26 vaccinated through the community. From February 2013, the current school-based program for females aged 12–13 was extended to males aged 12–13, with a catch-up program in 2013 and 2014 for males aged 14–15.

negative cytology: A satisfactory cervical cytology test in which no abnormal cells are found.

neoplasm: An abnormal ('neo', new) growth of tissue. Can be benign (not a **cancer**) or malignant (a cancer). Same as **tumour**.

non-responder: A person who was sent an invitation from the National Bowel Cancer Screening Program but did not return their screening kit for analysis.

oncogenic: Cancer-causing.

Pap test: Papanicolaou smear, a procedure to detect cancer and precancerous conditions of the female genital tract, which was the screening test of the National Cervical Screening Program until 1 December 2017. During a Pap test, cells are collected from the transformation zone of the cervix, the area of the cervix where the squamous cells from the outer opening of the cervix and glandular cells from the endocervical canal meet. This is the site where most cervical abnormalities and cancers are detected. For conventional cytology, these cells are transferred onto a slide, and sent to a pathology laboratory for assessment. Collected cells are then examined under a microscope to look for abnormalities.

participant: A person who participated in 1 of the 3 national cancer screening programs.

positive predictive value: The probability that individuals with a positive screening test have cancer (or a precursor to cancer).

positive screening test: In this project defined as a screening test that triggers diagnostic assessment—for bowel screening this is the presence of blood (even microscopic amounts) in a completed screening kit, for BreastScreen this is the identification of a suspicious area on a screening mammogram, for cervical screening this is a Pap test results of possible or definite high-grade abnormality or cervical cancer.

screen-detected cancer: Defined in this report as a cancer diagnosed as a result of a **positive screening test**. Refer to Methods for definitions for breast, cervical and bowel cancers used in this report.

screening: The application of a test to a population which has no overt signs or symptoms of the disease in question, to detect disease at a stage when treatment is more effective. The screening test is used to identify people who require further investigation to determine the presence or absence of disease, and is not primarily a diagnostic test.

sensitivity: A measure of how good a screening test is in identifying people with **cancer**.

socioeconomic status: A measure of socioeconomic status in which small areas of Australia are classified on a continuum from disadvantaged to affluent. See Appendix C for details.

specificity: A measure of how good a screening test is in correctly identifying those who do not have **cancer**.

tumour: See **neoplasm**.

underlying cause of death: The disease or injury that initiated the train of events leading directly to death, or the circumstances of the accident or violence that produced the fatal injury.

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Related publications

The following AIHW publications provide further information and data from BreastScreen Australia, as well as cancers diagnosed in Australia, and may be of interest:

- AIHW 2018. BreastScreen Australia monitoring report 2018. Cancer series no. 112. Cat. no. CAN 116. Canberra: AIHW.
- AIHW 2018. Analysis of cancer outcomes and screening behaviour for national cancer screening programs in Australia. Cancer series no. 111. Cat. no. CAN 115. Canberra: AIHW.
- AIHW 2017. Cancer in Australia 2017. Cancer series no. 101. Cat. no. CAN 100. Canberra: AIHW.
- AIHW 2017. Australian Cancer Incidence and Mortality (ACIM) books: cervical cancer. Canberra: AIHW. Viewed 11 December 2017, <http://www.aihw.gov.au/acim-books>.

This is the second report from an Australian-first project combining data from BreastScreen Australia, the National Cervical Screening Program and the National Bowel Cancer Screening Program, focusing on breast cancer outcomes and screening behaviour in BreastScreen Australia. It was found that screen-detected breast cancers were less likely to cause death than never-screened breast cancers for all age groups eligible to screen in BreastScreen Australia, with analyses giving new insights into screening behaviour.

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