Benefits and harms of breast cancer screening revisited: a large, retrospective cross-sectional study quantifying treatment intensity in women with screen-detected versus non-screendetected cancer in Australia and New Zealand

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# ABSTRACT

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Correspondence to Dr Kathy Dempsey; kathy.dempsey@sydney.edu.au **Objectives** Non-mortality benefits of breast cancer screening are rarely considered in assessments of benefits versus harms. This study aims to estimate the rate of overdiagnosis in women with screen-detected breast cancer (SDBC) by allocating cases to either possibly overdiagnosed (POD) or not overdiagnosed categories and to compare treatment recommendations for surgery and adjuvant treatments by category, age at diagnosis and cancer stage.

**Methods and analysis** Retrospective secondary analysis of 10 191 women diagnosed with breast cancer in Australia and New Zealand in 2018. Treatment recommendations for 5226 women with SDBC and 4965 women with non-SDBC (NSDBC) were collated and analysed. Descriptive statistics were used to calculate proportions and risk ratios (RRs).

Results The POD rate was 15.8%. Screening detected 66.3% of stage 0 tumours, 59% of stage 1, 40% of stage 2 and 27.5% of stage 3 tumours. Women with SDBC were less likely than their NSDBC counterparts to receive chemotherapy (RR 0.60 Aus/0.53 NZ), immunotherapy (mostly human epidermal growth factor 2 receptor therapy) (RR 0.58 Aus/0.82 NZ), mastectomy (RR 0.55 Aus/0.63 NZ) and axillary lymph node dissection (RR 0.49 Aus/0.52 NZ), or to require both mastectomy and radiotherapy (RR 0.41 Aus/0.34 NZ). Less than 1% of POD women were recommended chemotherapy, 9.5% radiotherapy, 6.4% endocrine therapy, 2.2% mastectomy and 0.5% axillary lymph node dissection. Conclusions Women with SDBCs required less intensive treatment; rates of possible overtreatment of SDBCs are relatively low and may be minimised through multidisciplinary discussion and shared decision-making. Reduced treatment intensity should be

considered when balancing the potential benefits and

harms of screening.

# WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Recent studies of organised national breast cancer screening programmes have focused on estimates of the mortality benefits and overdiagnosis rates.

#### WHAT THIS STUDY ADDS

- ⇒ This study demonstrates that screening detects a significant proportion of high-risk breast cancer phenotypes.
- ⇒ It documents lower treatment intensity in women with screen-detected breast cancer, especially in women who may be considered potentially overdiagnosed (15.8%).
- ⇒ It reveals that concerns about extensive overtreatment of possibly overdiagnosed cancers are likely to be overstated.

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This study establishes that earlier detection of highrisk cancers not only improves a woman's prognosis, but often reduces treatment intensity, and is, therefore, likely to improve post-treatment quality of life, compared with later diagnosis.

# BACKGROUND

Much research and commentary over the last 15 years has focused on overdiagnosis as a major harm of breast cancer screening, although a consensus on the magnitude of the problem is lacking.<sup>1–9</sup> Estimates range widely and there is no agreement on the best method to measure it.<sup>10</sup> In 2013, the Independent UK Panel on Breast Cancer Screening defined overdiagnosis as 'the detection of cancers on screening, which would not have

become clinically apparent in the woman's lifetime in the absence of screening'.<sup>10</sup> The report reviewed the previous literature and estimated a 20% relative risk reduction in mortality for all women invited to screen, offset by a 1% absolute chance that each woman invited to screen may have a cancer diagnosed and treated which would otherwise never have caused her problems.<sup>10</sup> The extent of these estimates has since been challenged.<sup>11-13</sup> A 2021 review of published estimates of breast cancer overdiagnosis noted 'that all the very high estimates were from studies with no individual data on screening exposure, whereas studies with such individual data tended to obtain more modest estimates' (Chaltiel and Hill<sup>14</sup>, p.1). The authors concluded that many estimates of breast cancer overdiagnosis represent 'serious overestimations' (Chaltiel and Hill<sup>14</sup>, p. 1). A 2023 large case-control study of women screened through England's National Health Service (NHS) Breast Screening Programme (NHSBSP) supported this argument, with overdiagnosis estimates of 9.5% without adjustment for self-selection, and 3.7% with adjustment.<sup>15</sup> The authors concluded their results 'showed little if any overdiagnosis, and it is reasonable to conclude that NHSBSP is associated with at worst modest overdiagnosis of breast cancer' (Blyuss *et al*,<sup>15</sup> p. 1886).

The UK Panel report did not take into consideration important non-mortality benefits from breast cancer screening when weighing up the benefits versus harms,<sup>10</sup> although this idea has been considered since 2001.<sup>16-18</sup> The arguments for alerting women to the potential harms of overdiagnosis, and for describing the mortality and the non-mortality related benefits of early detection, are both based on the premise of harm minimisation. Earlystage breast cancer is less likely to require treatment with mastectomy, axillary lymph node dissection (ALND), chemotherapy and postmastectomy radiotherapy and is more likely to be associated with better long-term quality of life than cancer diagnosed at a later stage.<sup>19</sup> The early identification of high-risk cancers also provides the opportunity for higher rates of pathological complete response to neoadjuvant therapy, with excellent clinical outcomes for many women, particularly those with triple negative and human epidermal growth factor receptor (HER) 2 positive phenotypes.<sup>20</sup> This translates into a better prognosis and less adjuvant systemic therapy, and its associated morbidity, for these women.

This study compared and measured the types of breast cancer treatment women were recommended to have based on whether their cancer was diagnosed within or outside a formal screening programme using a large population database. This study has two objectives: to estimate the rate of overdiagnosis in women with screendetected breast cancer (SDBC) by allocating cases to either possibly overdiagnosed (POD) or not overdiagnosed (NOD) based on predetermined criteria; and to compare differences in treatment recommendations for adjuvant treatments and surgery by overdiagnosis category, age at diagnosis, cancer stage and country.

# METHODS Study design

Cross-sectional study quantifying treatment intensity in women with screen-detected versus non-screen-detected breast cancer in Australia and New Zealand.

# Patient and public involvement

There was no involvement from patients or members of the public in the design, or conduct, or reporting of the research. Patient and public involvement will be sought and encouraged in the dissemination of findings stage. This will involve three main avenues of work: (1) codesign with consumers through the Breast Cancer Network Australia's consumer network to write and publish consumer-friendly materials on the additional benefits of screening on the BCNA website and hard copy publications; (2) discussions with key breast cancer screening stakeholders such as BreastScreen Australia and the senior managers in the Australian government's national screening section on updating the breast cancer screening consumer information to include our findings and (3) discussions with UK researchers and NHS Breast Cancer Screening representatives on possible similar updates to their consumer-facing programme information.

# **Definition of terms**

The term SDBC is used to refer to breast cancer detected at the two population-based screening programmes: BreastScreen Australia and BreastScreen Aotearoa (NZ). Data on screening in private centres in these countries are not available. SDBC is assumed to be breast cancer detected prior to the appearance of any signs or symptoms (such as a breast lump, nipple discharge, dimpling or other changes in appearance). 'Early detection' is defined as breast cancer detected through screening. The term 'non-SDBC' (NSDBC) is used to refer to breast cancer that is detected outside the national screening programmes, most often representing cancers detected when a woman presents with symptoms. Interval cancers diagnosed outside the screening programmes are included in this group but cannot be separately identified from the data set, as are asymptomatic cancers identified via private screening or as incidental findings. This project examines phenotypic differences between the two groups and whether SDBC and NSDBC groups differ in the type and extent of surgical and adjuvant treatment (chemotherapy, radiotherapy, endocrine and targeted immunotherapy—mostly HER 2 therapy) they receive.

To account for possible overdiagnosis arising from screening, the criteria used by Elder *et al*<sup>21</sup> to classify patients were adapted, using our terminology, as POD or NOD. The NOD group comprises phenotypes we believe a consensus opinion of breast cancer experts in Australia and New Zealand would consider required treatment. These are: high-grade ductal carcinoma in situ (DCIS); stage 1, grade 1, 1≥10 mm; stage 1, grades 2 and 3; stage 2 and 3; HER2+ and triple negative invasive cancers. This consensus represents the opinions of very senior, experienced clinicians in the authorship of this paper, supported by the strong opinions expressed in their respective multidisciplinary team (MDT) meeting. These occur throughout Australia and New Zealand. Phenotypes outside this group may or may not be overdiagnosed, depending on patient characteristics including age, comorbidities or frailty. POD phenotypes are: lowgrade and intermediate-grade stage 0 cancers (DCIS) (regardless of receptor status); and stage 1 cancers (grade 1, 1 to <10 mm, excluding triple negative and HER2+ receptor status).

# **Data analysis**

For analyses, 95% confidence intervals are reported. Given the large sample size permits detection of trivial associations, our interpretation focuses on magnitude of effect, most often using risk ratios (RRs). P values of significance are not presented due to the likelihood of misinterpretation. Background on the data source and descriptors is provided in online supplemental appendix A.

# **Primary outcome**

The primary outcome was treatment intensity. Definitive treatments were determined: for breast surgery, this was wide local excision (WLE) or mastectomy; for axillary surgery, this was sentinel lymph node biopsy (SLNB) if the number of nodes examined was between 1 and 7, or ALND if the number of nodes examined was greater than 7. In addition, the type of adjuvant treatment each woman had received was collated: chemotherapy, radio-therapy and Herceptin (classified in the Breast Quality Audit (BQA) as immunotherapy).

# Variables

The variable of primary interest was whether or not breast cancer was detected within a national screening programme. Our data set was extracted from all 2018 entries in the Breast Surgeons of Australia and New Zealand BQA database,<sup>22</sup> which classifies cases according to surgeon referral source. There are four options: (a) referred from Breast Screen Australia; (b) referred from Breast Screen Aotearoa (New Zealand); (c) 'symptomatic' (usually referred from general practitioner) and (d) 'other' (usually referred from a private screening practice or other specialist). For the present analysis, these four categories were merged into two: (1) Breast Screen Australia/Aotearoa (SDBC) and (2) 'symptomatic' and 'other' (NSDBC).

Data extraction and cleaning was conducted during 2022. Treatment recommendations for 5226 women with SDBC and 4965 women with NSDBC were collated and analysed. Descriptive statistics were used to calculate proportions and RRs. Analysis was performed on women of target screening age only (50–74 in Australia; 45–69 in NZ). Age was recorded in years at time of diagnosis. Postcode was used as a proxy for socioeconomic status, using the Socio-Economic Status for Areas codes, which

map Australian postcodes to deciles indicating socioeconomic advantage, where a higher score indicates less disadvantage<sup>23</sup> (equivalent data were unavailable for New Zealand). Cancer stage was coded using the seventh Edition of the American Joint Committee on Cancer's tumour, node, metastases system.<sup>24</sup> Triple negative status and HER2 status were also included as variables.

# RESULTS

# Demographic and tumour variables

Demographic and tumour variables by screening status are shown in table 1. Australian women comprised 76% (n=7746) and New Zealand women 24% (n=2445) of the study cohort, with a mean age of 61 for both the SDBC and NSDBC groups. Not all demographic or tumour variables were available for all women: DCIS grade was missing in 75 women and cancer stage missing in 35 women.

The vast majority identified as non-Indigenous, including 83.2% of Australian and 81% of NZ women; 40.9% of Australian women attended public hospitals, compared with 72.5% of NZ women. Among Australian women, 20.3% resided in low socioeconomic areas, 39.2% in middle and 40.5% in high socioeconomic areas. When comparing the number of SDBC cases as a proportion of the total breast cancers, New Zealand women had a higher rate of SDBC (56.6%) compared with Australian women (49.6%).

Compared with Australian women, NZ women had overall fewer recommendation rates for WLE, and combined WLE and radiotherapy, chemotherapy, radiotherapy and endocrine therapy; and higher recommendation rates for mastectomy alone and mastectomy with radiotherapy. Recommendation rates for other treatments were similar between the two subgroups.

In this study, one-third of all triple negative cancers were screen detected, along with 40% of all HER2 positive tumours, and half of both positive oestrogen receptor (ER) and progesterone receptor (PR) positive cancers. Screening detected two-thirds of DCIS (stage 0) including 63.1% of intermediate-grade and 72.3% of high-grade DCIS tumours, which have the potential to become invasive.<sup>25</sup> Furthermore, 59% of stage 1 tumours, 40% of stage 2 tumours and 27.5% of stage 3 tumours were detected through screening.

# **Overdiagnosis rate**

Applying the allocation rules from table 2, 639 (16.7%) of Australian women and 179 (13.9%) of New Zealand women were POD, making a combined estimated POD rate of 818women (15.8%) within this cohort.

# Surgical and adjuvant treatments

Cross-tabulations for individual treatments by diagnostic pathway and country, for the total cohort, are shown in table 3. Women with SDBC were more likely to undergo WLE (RR 1.30 Aus/1.39 NZ) and re-excision (RR 1.35 Aus/1.27 NZ) than women with NSDBC, but only half

Table 1         Demographic and tumour variable;	s by diagnosti	c pathway and	d country (scree	ning age; n=1	0191)*				
	Australia n	(%)		New Zealar	(%) u pu		Total n (%)		
Demographic and tumour variables	NSDBC	SDBC	Aus total	NSDBC	SDBC	NZ total	NSDBC	SDBC	<b>Cohort Total</b>
Participants									
	3904 (50.4)	3842 (49.6)	7746 (100.0)	1061 (43.4)	1384 (56.6)	2445 (100.0)	4965 (48.7)	5226 (51.3)	10 191 (100.0)
Age (years)									
Mean	62.1	62.9	62.5	59.3	58.0	58.6	61.5	61.6	61.6
Range	50-74	50-74	50-74	45-69	45-69	45–69	45-74	45-74	45-74
SEIFA decile†‡									
Low (1–3)	731 (19.0)	825 (21.6)	1556 (20.3)	I	I	I	731 (19.0)	825 (21.6)	1556 (20.3)
Medium (4–7)	1479 (38.4)	1527 (40.0)	3006 (39.2)	I	I	I	1479 (38.4)	1527 (40.0)	3006 (39.2)
High (8–10)	1640 (42.6)	1467 (38.4)	3107 (40.5%)	I	I	I	1640 (42.6)	1467 (38.4)	3107 (40.5)
Indigenous status									
Not indigenous	3251 (83.4)	3190 (83.1)	6441 (83.2)	879 (83.2)	1101 (79.6)	1980 (81.1)	4130 (83.4)	4291 (82.1)	8421 (82.7)
Aboriginal	25 (0.6)	26 (0.7)	51 (0.7)	0 (0.0)	0 (0.0)	0 (0.0)	25 (0.5)	26 (0.5)	51 (0.5)
Torres Strait Islander	4 (0.1)	4 (0.1)	8 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	4 (0.1)	4 (0.1)	8 (0.1)
Both Aboriginal and Torres Strait Islander	1 (0.0)	3 (0.1)	4 (0.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.0)	3 (0.1)	4 (0.0)
Māori	0 (0.0)	2 (0.1)	2 (0.0)	111 (10.5)	165 (11.9)	276 (11.3)	111 (2.2)	167 (3.2)	278 (2.7)
Pacific peoples	4 (0.1)	3 (0.1)	7 (0.1)	32 (3.0)	68 (4.9)	100 (4.1)	36 (0.7)	71 (1.4)	107 (1.1)
Unknown	613 (15.7)	613 (16.0)	1226 (15.8)	34 (3.2)	50 (3.6)	84 (3.4)	647 (13.1)	663 (12.7)	1310 (12.9)
Hospital admission status									
Public patient	1415 (37.6)	1635 (44.3)	3050 (40.9)	728 (68.6)	1044 (75.4)	1772 (72.5)	2143 (44.4)	2679 (52.8)	4822 (48.7)
Private patient	2347 (62.4)	2053 (55.7)	4400 (59.1)	333 (31.4)	340 (24.6)	673 (27.5)	2680 (55.6)	2393 (47.2)	5073 (51.3)
Oestrogen receptor									
Positive	2943 (82.5)	2859 (89.7)	5802 (85.9)	810 (84.5)	996 (90.8)	1806 (87.8)	3753 (82.9)	3855 (90.0)	7608 (86.4)
Negative	624 (17.5)	327 (10.3)	951 (14.1)	149 (15.5)	101 (9.2)	250 (12.2)	773 (17.1)	428 (10.0)	1201 (13.6)
Progesterone receptor									
Positive	2547 (71.6)	2559 (80.5)	5106 (75.8)	692 (72.4)	894 (81.6)	1586 (77.3)	3239 (71.7)	3453 (80.8)	6692 (76.1)
Negative	1012 (28.4)	621 (19.5)	1633 (24.2)	264 (27.6)	201 (18.4)	465 (22.7)	1276 (28.3)	822 (19.2)	2098 (23.9)
HER2 receptor									
Positive	488 (14.0)	290 (9.5)	778 (11.9)	129 (13.8)	130 (12.4)	259 (13.1)	617 (14.0)	420 (10.2)	1037 (12.2)
Negative	2999 (86.0)	2778 (90.5)	5777 (88.1)	803 (86.2)	916 (87.6)	1719 (86.9)	3802 (86.0)	3694 (89.8)	7496 (87.8)
Triple negative									
Yes	399 (11.2)	193 (6.1)	592 (8.8)	98 (10.2)	48 (4.4)	146 (7.1)	497 (11.0)	241 (5.6)	738 (8.4)
									Continued

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Table 1 Continued									
	Australia n	(%)		New Zeala	(%) u pu		Total n (%)		
Demographic and tumour variables	NSDBC	SDBC	Aus total	NSDBC	SDBC	NZ total	NSDBC	SDBC	<b>Cohort Total</b>
No	3169 (88.8)	2994 (93.9)	6163 (91.2)	861 (89.8)	1050 (95.6)	1911 (92.9)	4030 (89.0)	4044 (94.4)	8074 (91.6)
TNM stage									
0	399 (10.3)	754 (19.7)	1153 (15.0)	73 (6.9)	175 (12.6)	248 (10.1)	472 (9.5)	929 (17.8)	1401 (13.8)
-	1416 (36.4)	1855 (48.5)	3271 (42.4)	449 (42.3)	827 (59.8)	1276 (52.2)	1865 (37.7)	2682 (51.3)	4547 (44.8)
N	1663 (42.8)	1062 (27.8)	2725 (35.3)	426 (40.2)	333 (24.1)	759 (31.0)	2089 (42.2)	1395 (26.7)	3484 (34.3)
ი	412 (10.6)	150 (3.9)	562 (7.3)	113 (10.7)	49 (3.5)	162 (6.6)	525 (10.6)	199 (3.8)	724 (7.1)
DCIS grade§									
Low	54 (14.7)	73 (10.0)	127 (11.5)	9 (15.5)	22 (13.2)	31 (13.8)	63 (14.8)	95 (10.6)	158 (12.3)
Intermediate	136 (37.0)	226 (30.8)	362 (32.9)	23 (39.7)	46 (27.5)	26 (30.7)	159 (37.3)	272 (30.2)	388 (30.2)
High	178 (48.4)	434 (59.2)	612 (55.6)	26 (44.8)	99 (59.3)	125 (55.6)	204 (47.9)	533 (59.2)	737 (57.4)
Percentages may not add to 100% due to decin *In 2018, population breast cancer screening ag †SEIFA is an Australian Bureau of Statistics indi (SES) information. ±SFIFA deciles: 1=lowest SFS: 10=hinbest SFS	nal rounding. le was 50–74 in Au cation. SEIFA infoi	istralia and 45– mation based (	69 in NZ. on postcode is no	ot available in N	ew Zealand, wh	iere full residenti	ial address is rec	quired to obtain	socioeconomic

Control decises in the combination of low-grade, intermediate-grade and high-grade DCIS because the level of grade was not always provided (n=39).
Australia; DCIS, ductal carcinoma in situ; NSDBC, non-SDBC; NZ, New Zealand; SDBC, screen-detected breast cancer; SEIFA, Socio-Economic Indexes for Areas; TNM, tumour, node, metastases.

Table 2         Allocation of SDBC cases to possibly overdiagnose	ed (POD) and not overdiagnosed (NOD) categories*
POD n=818	NOD n=4365
<ul> <li>Low and medium grade stage 0 cancers (DCIS)† (regardless of receptor status)‡</li> <li>Stage 1 cancers (grade 1, 1 to &lt;10 mm,§ excluding triple negative and HER2+ receptor status)</li> </ul>	<ul> <li>High-grade DCIS (regardless of receptor status)‡</li> <li>Stage 1 cancers (grade 1, ≥10 mm;§ grade 2 and grade 3)</li> <li>All stage 2 cancers</li> <li>All stage 3 cancers</li> <li>All HER2+ invasive cancers</li> <li>All triple negative invasive cancers</li> </ul>

\*Total SDBC patients (5183) differs from table 1 (5226), as not all cases included information required to allocate them to either POD or NOD categories (n=43).

†Ductal carcinoma in situ.

‡HER2 testing was not routinely available for DCIS in 2018, so it is not possible to derive HER2 status or triple negative status.

§We have conservatively defined small, possibly overdiagnosed cancers as less than 10 mm.

DCIS, ductal carcinoma in situ; HER2, human epidermal growth factor receptor; SDBC, screen-detected breast cancer.

as likely to undergo more extensive surgical treatments including mastectomy (RR 0.55 Aus/0.63 NZ) and ALND (RR 0.49 Aus/0.52 NZ). In terms of adjuvant treatments, women with SDBC were less likely than the NSDBC group to be recommended for chemotherapy (RR 0.60 Aus/0.53 NZ) and immunotherapy (RR 0.58 Aus/0.82 NZ), as likely to be recommended for endocrine therapy in Australia but less likely in NZ (RR 0.99 Aus/0.86 NZ) and slightly more likely to have radiotherapy recommended (RR 1.09 Aus/1.04 NZ). The SDBC group were also far less likely to have both chemotherapy and radiotherapy recommended (RR 0.54 Aus/0.37 NZ).

When comparing women with NSDBC, with those in the NOD group, the former is more likely to be recommended for chemotherapy (RR 1.45 Aus/1.68 NZ), immunotherapy (RR 1.50 Aus/1.08 NZ) and chemotherapy plus radiotherapy (RR 1.61 Aus/2.42 NZ), as well as mastectomy (RR 1.69 Aus/1.50 NZ) and ALND (RR 1.80 Aus/1.74 NZ). In contrast, they have approximately the same risk of undergoing endocrine therapy (RR 0.94 Aus/1.10 NZ) and a lower risk of radiotherapy (RR 0.88 Aus/0.95 NZ) and WLE (RR 0.78 Aus/0.73 NZ).

The largest between-group differences were found in women with NSDBC and those screened in the POD group. Surgical treatments were more intensive: women with NSDBC were less likely to be recommended for WLE (RR 0.73 Aus/0.67 NZ), up to three times more likely to require mastectomy (RR 3.21 Aus/2.34 NZ), over 45 times more likely to be recommended for mastectomy plus radiotherapy (RR 48.53 Aus/4.89 NZ) and seven times more likely to have ALND recommended (RR 7.13 Aus/7.79 NZ). No women in the POD group were recommended to have chemotherapy plus radiotherapy, or immunotherapy, and only four Australian women were recommended to have chemotherapy (RR 55.17 Aus). Women with NSDBC were also more likely to require endocrine therapy (RR 1.56 Aus/1.78 NZ), while recommendations for radiotherapy alone were similar in both the NSDBC and POD groups (RR 1.09 Aus/1.10 NZ).

Finally, among those screened, women in the POD group were far less likely than those in the NOD group

to undergo invasive treatments. For surgical procedures, POD women were much less likely to be recommended for ALND (RR 0.25 Aus/0.22 NZ) and mastectomy (RR 0.53 Aus/0.64 NZ), but slightly more likely to receive WLE (RR 1.07 Aus/1.08 NZ). They were also less likely to receive radiotherapy alone (RR 0.81 Aus/0.86 NZ) and endocrine therapy (RR 0.60 Aus/0.62 NZ).

# Age distribution and cancer stage by overdiagnosis category and country

Table 4 shows the distribution of SDBC cases per age group, country, cancer stage and overdiagnosis category. Those in the 45–49 age group (NZ only) comprised 231 (16.8%) NZ women, of which 20 (8.7%) cases were categorised as POD. The majority of cases (4063) were diagnosed in the 50–69 age group: 478 Australian women (16.2%) and 154 New Zealand women (13.9%) were categorised as POD. Women in the 70–74 age group (Australia only) comprised 845 cases, of which 156 (18.5%) were classified as POD.

Of the 808 women with SDBC classified as POD, 11.5% had low-grade DCIS, 32.9% had intermediate-grade DCIS and 55.6% had lower risk stage 1 (grade 1, <10 mm, HER2 negative and ER and/or PR positive) breast cancer. Women classified as NOD (n=4331) had 12.2% high-grade DCIS, 51.1% higher risk stage 1 (grade 1,  $\geq$ 10 mm, with any receptor status), 32.1% stage 2 and 4.6% stage 3 breast cancers.

# Age distribution, cancer stage and recommended treatments by overdiagnosis category

Table 5 shows the proportion of SDBC women, divided into the same three age groups as table 4, in POD versus NOD categories who received each type of treatment. More intensive surgical options were less likely for POD women: 2.2% were recommended for mastectomy and only 0.5% for ALND. In terms of adjuvant treatments, less than 1% of women in the POD categories were recommended to have chemotherapy, 9.5% to have radiotherapy and 6.4% to have endocrine therapy. No POD women required chemotherapy and radiotherapy. HER2

Table	3 Cross-	-tabulatic	ons for a	djuvant ti	reatmen	ts and sı	urgery by	diagnost	tic pathv	vay, ovei	rdiagnosis	catego	ry (NOD	vs POD)	and cou	ntry			
Breact	cancer	SDBC   n=4365	*OD	SDBC I n=818	POD†	SDBC‡ (NOD+I n=5183	(OOc	NSDBC n=4965	0.0	Total (SDBC+ n=10148	-NSDBC) B§	RR tot SDBC NSDB (95% (	call Cls)	RR NSDBC NOD** (95% C	vs (s)	RR NSDBC POD†† (95% CI	sv (s	RR POD vs NOD# (95% CI	(s
treatm	ents	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ
Adjuva	nt treatmen	ts n (%)																	
CT11	No§§	1876 (65.2)	863 (76.8)	432 (99.1)	139 (100.0)	2308 (69.7)	1002 (79.3)	1777 (49.4)	620 (61.0)	4085 (59.1)	1622 (71.1)	0.60 (0.56,	0.53 (0.46,	1.45 (1.37,	1.68 (1.47,	55.17 (20.79,	I	0.03 (0.01,	0.00
	Yes	1001 (34.8)	261 (23.2)	4 (00.9)	0 (00.0)	1005 (30.3)	261 (20.7)	1821 (50.6)	397 (39.0)	2826 (40.9)	658 (28.9)	0.64)	0.6)	1.54)	1.92)	146.41)		0.07)	
	Missing	364/43(	35 (8.3)	243/81	3 (29.7)**	* 607/518	33 (11.7)	350/490	65 (7.0)	957/10	148 (9.3)								
	Total	4001 (9	1.7)	575 (70	.3)	4576 (8	8.3)	4615 (9	13.0)	9191 (90	0.6)								
RT	No†††	735 (23.3)	441 (37.0)	240 (37.7)	82 (45.8)	975 (25.7)	523 (38.1)	1248 (32.1)	427 (40.3)	2223 (28.9)	950 (39.1)	1.09 (1.06,	1.04 (0.97,	0.88 (0.86,	0.95 (0.89,	1.09 (1.02,	1.10 (0.95,	0.81 (0.76,	0.86 (0.75,
	Yes	2425 (76.7)	752 (63.0)	397 (62.3)	97 (54.2)	2822 (74.3)	849 (61.9)	2637 (67.9)	633 (59.7)	5459 (71.1)	1482 (60.9)	1.13)	1.11)	0.91)	1.01)	1.16)	1.27)	0.87)	0.99)
	Missing	12/436	5 (0.3)	2/818 ((	0.2)	14/5183	3 (0.3)	20/496	5 (0.4)	34/10 14	48 (0.3)								
	Total	4353 (9	9.7)	816 (99	(8)	5169 (9:	9.7)	4945 (9	(9.6)	10114 (	99.7)								
Ш	10###	912 (29.0)	527 (44.2)	364 (57.3)	117 (65.4)	1276 (33.7)	644 (46.9)	1291 (33.4)	408 (38.5)	2567 (33.5)	1052 (43.3)	0.99 (0.96,	0.86 (0.81,	0.94 (0.91,	1.10 (1.03,	1.56 (1.42,	1.78 (1.44,	0.60 (0.55,	0.62 (0.50,
	Yes	2236 (71.0)	666 (55.8)	271 (42.7)	62 (34.6)	2507 (66.3)	728 (53.1)	2580 (66.6)	652 (61.5)	5087 (66.5)	1380 (56.7)	1.03)	0.92)	0.97)	1.18)	1.71)	2.18)	0.66)	0.76)
	Missing	24/436	5 (0.5)	4/818 ((	<b>J.5</b> )	28/5183	3 (0.5)	34/496	5 (0.7)	62/10 14	48 (0.6)								
	Total	4341 (9	9.5)	814 (99	.5)	5155 (9:	9.5)	4931 (9	19.3)	10 086 (	99.4)								
F	No§§§	2640 (92.1)	1016 (90.4)	435 (100.0)	139 (100.0)	3075 (93.2)	1155 (91.4)	3159 (88.1)	911 (89.6)	6234 (90.5)	2066 (90.6)	0.58 (0.49,	0.82 (0.64,	1.50 (1.29.	1.08 (0.84,	I	I	0.00	0.00
	Yes	226 (7.9)	108 (9.6)	0 (0.0)	0 (0.0)	226 (6.8)	108 (8.6)	425 (11.9)	106 (10.4)	651 (9.5)	214 (9.4)	0.67)	1.06)	1.75)	1.40)				
	Missing	375/43(	35 (8.6)	244/81	3 (29.8)**	* 619/518	33 (11.9)	364/49(	65 (7.3)	983/10	148 (9.7)								
	Total	3990 (9	1.4)	574 (70	.2)	4564 (8	8.1)	4601 (9	12.7)	9165 (90	0.3)								
CT+RT	ILLON .	2713 (91.2)	1093 (97.2)	435 (100.0)	139 (100.0)	3148 (95.1)	1232 (97.5)	3267 (90.9)	949 (93.3)	6415 (92.9)	2181 (95.7)	0.54 (0.45,	0.37 (0.24,	1.61 (1.35,	2.42 (1.60,	I	I	0.00	0.00
	Yes	162 (8.8)	31 (2.8)	0 (0.0)	0 (0.0)	162 (4.9)	31 (2.5)	327 (9.1)	68 (6.7)	489 (7.1)	99 (4.3)	0.65)	0.56)	1.94)	3.68)				
	Missing	366/43(	35 (8.4)	244/81	3 (29.8)***	* 610/518	33 (11.8)	354/49	65 (7.1)	964/10	148 (9.5)								
	Total	3999 (9	1.6)	574 (70	.2)	4573 (8	8.2)	4611 (9	12.9)	9184 (90	0.5)								
Open t	viopsy	115 (3.6)	24 (2.0)	47 (7.4)	10 (5.6)	162 (4.3)	34 (2.5)	219 (5.6)	39 (3.7)	381 (6.4)	73 (4.7)	0.76 (0.62, 0.92)	0.67 (0.43, 1.06)	1.55 (1.24, 1.93)	1.83 (1.11, 3.02)	0.76 (0.56, 1.03)	0.66 (0.33, 1.29)	2.03 (1.46, 2.82)	2.78 (1.35, 5.71)
																			ontinued

Dempsey K, et al. BMJ Oncology 2023;2:e000100. doi:10.1136/bmjonc-2023-000100

Table 3 Conti	nued																	
Breast cancer	SDBC N n=4365		SDBC F n=818	op†	SDBC‡ (NOD+P n=5183	(DO)	NSDBC n=4965		Total (SDBC+l n=10148	NSDBC)	RR tot SDBC NSDBC (95% C	al Vs (1s)	RR NSDBC NOD** (95% C	; vs Is)	RR NSDBC POD†† (95% CI	vs (s	RR POD vs NOD‡‡ (95% CI	(6
treatments	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ	Aus	NZ
WLE	2580 (81.3)	826 (69.2)	554 (86.7)	134 (74.9)	3134 (82.2)	960 (70.0)	2465 (63.1)	533 (50.2)	5599 (93.6)	1493 (95.3)	1.30 (1.27, 1.34)	1.39 (1.30, 1.49)	0.78 (0.75, 0.80)	0.73 (0.68, 0.78)	0.73 (0.70, 0.76)	0.67 (0.60, 0.74)	1.07 (1.03, 1.10)	1.08 (0.99, 1.19)
Re-excision	422 (13.3)	133 (11.1)	83 (13.0)	16 (8.9)	505 (13.3)	149 (10.9)	382 (9.8)	91 (8.6)	887 (27.7)	240 (20.0)	1.35 (1.19, 1.53)	1.27 (0.99, 1.62)	0.74 (0.65, 0.84)	0.77 (0.60, 0.99)	0.75 (0.60, 0.94)	0.96 (0.58, 1.59)	0.98 (0.78, 1.22)	0.80 (0.49, 1.31)
Mastectomy	726 (22.9)	395 (33.1)	77 (12.1)	38 (21.2)	803 (21.1)	433 (31.6)	1509 (38.7)	528 (49.8)	2312 (72.3)	961 (80.0)	0.55 (0.51, 0.59)	0.63 (0.57, 0.70)	1.69 (1.57, 1.82)	1.50 (1.36, 1.66)	3.21 (2.59, 3.97)	2.34 (1.76, 3.13)	0.53 (0.42, 0.66)	0.64 (0.48, 0.86)
Breast surgery plu	us RT n (%	-																
WLE+RT	2209 (69.6)	674 (56.5)	382 (59.8)	88 (49.2)	2591 (68.0)	762 (55.5)	2016 (51.6)	428 (40.3)	4607 (84.7)	1190 (80.3)	1.32 (1.28, 1.35)	1.38 (1.31, 1.45)	0.74 (0.72, 0.76)	0.71 (0.68, 0.75)	0.86 (0.81, 0.92)	0.82 (0.72, 0.93)	0.86 (0.81, 0.91)	0.87 (0.77, 0.99)
Mx+RT	235 (7.4)	82 (6.9)	2 (0.3)	7 (3.9)	237 (6.2)	89 (6.5)	593 (15.2)	203 (19.1)	830 (15.3)	292 (19.7)	0.41 (0.36, 0.46)	0.34 (0.27, 0.42)	2.05 (1.81, 2.32)	2.78 (2.23, 3.47)	48.53 (12.34, 190.84)	4.89 (2.48, 9.64)	0.04 (0.01, 0.17)	0.57 (0.28, 1.14)
Axillary surgery n	(%)																	
SLNB	2385 (75.2)	852 (71.4)	384 (60.1)	121 (67.6)	2769 (72.7)	973 (70.9)	2551 (65.3)	684 (64.5)	5320 (79.0)	1657 (78.2)	1.11 (1.09, 1.14)	1.10 (1.06, 1.14)	0.87 (0.85, 0.89)	0.90 (0.87, 0.94)	1.09 (1.02, 1.16)	0.95 (0.86, 1.06)	0.80 (0.75, 0.85)	0.95 (0.86, 1.05)
ALND	432 (13.6)	179 (15.0)	22 (03.4)	6 (3.4)	454 (11.9)	185 (13.5)	958 (24.5)	277 (26.1)	1412 (21.0)	462 (21.8)	0.49 (0.44, 0.54)	0.52 (0.44, 0.61)	1.80 (1.63, 2.00)	1.74 (1.47, 2.05)	7.13 (4.73, 10.74)	7.79 (3.54, 17.12)	0.25 (0.17, 0.38)	0.22 (0.10, 0.49)
																	0	ontinued

8

treatments     Aus     NZ     Aus     NZ     Aus     NZ       Blank cells have a denominator of 0, so it is not possible to calculate an RR.       Cells containing a figure of 0.0 have a numerator of 0, so it is not possible to call       Percentages may not add to 100% due to decimal rounding.       *NOD: high-grade DCIS (regardless of receptor status) and stage 1 cancers (grainegative invasive cancers.       *POD=possibly vorcidianosed: low and medium grade stage 0 cancers (DCIS)	Aus NZ culate an RR.	Aus NZ	Aus NZ	Aus NZ	A M7	
Blank cells have a denominator of 0, so it is not possible to calculate an RR. Cells containing a figure of 0.0 have a numerator of 0, so it is not possible to cal Percentages may not add to 100% due to decimal rounding. *NOD: high-grade DCIS (regardless of receptor status) and stage 1 cancers (gra negative invasive cancers. †POD=possibly overdiagnosed: low and medium grade stage 0 cancers (DCIS).	culate an RR.				AUS NZ	Aus
*NOD: high-grade DCIS (regardless of receptor status) and stage 1 cancers (grad negative invasive cancers. POD=possibly overdiadnosed: low and medium grade stage 0 cancers (DCIS)						
+POD=possibly overdiagnosed: low and medium grade stage 0 cancers (DCIS) /	lde 1, ≥rumm;u yra	tde 2 and grade 3) and	d all stage 2 and s	tage 3 cancers and	All HER2+ invasive c	ancers and all tr
status).	(regardless of rece	otor status) and stage	1 cancers (grade	1, <10mm, excludit	וק triple negative and	HER2+ recepto
‡Total SDBC patients (5183) differs from table 1 figure (5226), as not all cases in §Total cohort numbers (10 148) differs from table 1 (10 191), as not all SDBC cas	Icluded information ses included (n=43,	required to allocate the see point 3).	hem to either POD	or NOD categories	(n=43).	
TRR, ratio of proportions of individuals receiving treatment for NSDBC compare	d with SDBC (inclu	ding not overdiagnose	ed plus possibly o	verdiagnosed).		
**RR, ratio of proportions of individuals receiving treatment for NSDBC compare ††RR, ratio of proportions of individuals receiving treatment for NSDBC compare	ed with the not over ed with the possibl	diagnosed componen v overdiagnosed com	nt of SDBC. ponent of SDBC.			
##RR, ratio of proportions of individuals receiving treatment for SDBC (possibly \$5'No' cases include 771 women where CT was recommended but not used.	overdiagnosed) co	mpared with SDBC (n	ot overdiagnosed)			
Thincludes 895 neoadjuvant cases.						
***These figures represent overestimates of the missing POD data. An unknown, was a minimum data set that did not include CT or IT treatment categories. The,	, but likely substant maiority of this mis	ial, proportion of POD sing data belongs in t	) women had data	entered into the D( out was not recorde	SIS short form of the days as a voi because	3QA audit. This it was never offe
Women who required CT or IT would have their data entered into the full dataset	بن	)				
TTT No cases include 50/ women where KI was recommended but not used. ±±± No' cases include 832 women where FT was recommended but not used.						
§§§'No' cases include 122 women where IT was recommended but not used.						
111. No' cases include 102 women where CT+RT were recommended but not us	sed.					
****Most extensive type of breast surgery per person.						
TTTTWOST extensive type of axiliary surgery per person.		di estre de serencia de la compactica de la	E	the second se		
ZLND, axiliary lympn node dissection, Aus, Australia; C.1, chemotherapy; DOG, Zealand: OD, overdiagnosed: RR, risk ratio; RT, radiotherapy: SDBC, screen-det	tected breast cance	n situ; E.I, endocrine tr ar: SI NB: sentinel lymi	nerapy; II, immunc nh node hionsv: V	virierapy; ivix, mastr VI E_wide local exci	ctomy; Noubu, non sion	-SUBU; NZ, Nev

Table 4 Diagnosis of SDBC\* by age, breast cancer stage, overdiagnosis category and country (n=5139)†

			Age						
Overdiagnosis			45–49	50–69		70–74	Total pe	r country	Total
category	Description	ı	NZ only	Aus	NZ	Aus only	Aus	NZ	Aus and NZ
Possibly	Stage 0‡	Low grade	5	57	15	16	73	20	93§
overdiagnosed	Stage 0‡	Intermediate grade	5	183	37	41	224	42	266§
(POD)	Stage 1¶	See footnote**	10	238	102	99	337	112	449§
Not	Stage 0‡	High grade	18	340	76	94	434	94	528
overdiagnosed	Stage 1¶	See footnote††	103	1176	592	342	1518	695	2213
(NOD)	Stage 2¶	All	79	837	250	225	1062	329	1391
	Stage 3¶	All	11	122	38	28	150	49	199
Total per country			231	2953	1110	845	3798	1371	5139

NZ screening age only; NZ and Australian screening age; Australian screening age only. \*Screen-detected breast cancer.

†Total SDBC patients (5139) differs from table 1 figure (5226), as not all cases included information required to allocate them to either POD or NOD categories (n=87).

‡Ductal carcinoma in situ.

Stable 4 has fewer POD cases (808) than tables 2 and 3 (both 818) because data is not available on 10 POD cases (5 missing stage data; 5 missing grade data).

¶Invasive cancer.

\*\*Grade 1, 1 to <10 mm; not HER2+ or Triple negative.

††Grade 1, ≥10 mm; any receptor 2 status.

Aus, Australia; HER2, human epidermal growth factor receptor; NZ, New Zealand; SDBC, screen-detected breast cancer.

positivity was an exclusion criterion for classification as POD, so none of these women required immunotherapy.

In terms of treatments by age, younger women (45–49, NZ only) were recommended to have the highest rates of mastectomy (41.1%) and ALND (15.6%), chemotherapy (28.1%) and immunotherapy (11.3%), and the lowest rates of chemotherapy plus radiotherapy (2.6%), radiotherapy (54.5%), endocrine therapy (52.9%), WLE (59.7%) and SLNB (68.8%). Older women (70-74, Aus only) had the lowest rates of recommendations for mastectomy (21.1%), ALND (10.1%) and immunotherapy (4.6%), and the highest rates for SLNB (76%)recommendations. Compared with the older group, the majority of women (50-69, Aus plus NZ) were recommended for higher rates of WLE (79.3%), chemotherapy only (25.5%) and slightly higher rates for radiotherapy (72%), chemotherapy and radiotherapy (3.9%) and endocrine therapy (62.7%).

# DISCUSSION

This analysis of 10191 women quantified the differences in diagnoses and recommended treatments (a proxy for treatment-related morbidity) for women with SDBC versus NSDBC. Our results demonstrate that breast cancer screening detects both low- and higher-risk cancers before they become symptomatic. Furthermore, earlier detection results in fewer invasive treatments for women with SDBC compared with women with NSDBC.

Overdiagnosis is recognised as a potential harm of breast cancer screening, and therefore, we assessed the

proportion of cases that may have been overdiagnosed. The POD rate was calculated to be 15.8% and was shown to vary with age.

Women with NSDBC were up to three times more likely to require mastectomy, over 45 times more likely to be recommended for mastectomy plus radiotherapy, and seven times more likely to have ALND recommended. This suggests that detection (or overdetection) of lowrisk cancers may lead to minimal harm if they are treated appropriate to their stage and size at time of detection. For example, many of the tumours in the POD group may be managed with surveillance rather than surgery,<sup>26</sup> <sup>27</sup> and/or endocrine therapy,<sup>27 28</sup> or radiotherapy.<sup>27 29-34</sup> This de-escalation of treatment for some early-stage disease needs to be balanced against growing evidence that intermediate-grade and high-grade DCIS may progress to invasive cancer and should be treated, rather than monitored, to prevent progression.<sup>25 35-37</sup>

# Strengths and weaknesses

This robust study design comprised secondary analysis of data collected at a single time point (2018), on over 10000 women diagnosed with primary breast cancer, from approximately 320 breast surgeons across Australia and New Zealand. The analysis is based on recommended treatments for women who did and did not have their breast cancer diagnosed through their national screening programmes.

A major strength is the unique methodology, which enabled the calculation of an overdiagnosis rate in women with breast cancer using a fixed, a priori definition of

Table 5 Treatment of SDB	כ by age, c	ancer stage and o	verdiagnosis ca	ategory (n=5169) <sup>-</sup>	ř	
			Age n (%)			Total % of each
Treatment	Stage	OD category	45–49 n=231	50–69 n=4063	70–74 n=875	treatment in women with SDBC
Chamatharany	O		0	0	0	
(POD=0.08%)	0	POD	0	0	0	0
(1 0 0 - 0.00 / 0)	-	NODS	1	2	0	3
	I	POD¶	0	4	0	4
		NOD	12	341	52	405
	2	NOD††	43	541	89	673
	3	NOD††	9	147	25	181
	CT % per	age group <sup>a</sup>	28.1	25.5	19.0	24.5
Radiotherapy (POD=9.5%)	0	POD	0	136	31	167
		NOD	5	238	55	298
	1	POD	4	259	61	324
		NOD	62	1326	265	1653
	2	NOD	46	824	175	1045
	3	NOD	9	141	28	178
	RT % per	age group <sup>a</sup>	54.5	72.0	70.3	70.9
Chemotherapy+	0	POD	0	0	0	0
radiotherapy (POD=0/193)		NOD	0	0	0	0
	1	POD	0	0	0	0
		NOD	2	74	16	92
	2	NOD	4	69	8	81
	3	NOD	0	17	3	20
	CT+RT%	per age group <sup>a</sup>	2.6	3.9	3.1	3.7
Endocrine therapy	0	POD	1	42	6	49
(POD=6.4%)		NOD	3	51	6	60
	1	POD	4	218	60	282
		NOD	39	1225	269	1533
	2	NOD	65	878	195	1138
	3	NOD	10	135	25	170
	ET % per	age group <sup>a</sup>	52.9	62.7	61.8	62.5
Immunotherapy	0	POD	0	0	0	0
(POD=0/324)		NOD	0	3	0	3
	1	POD	0	0	0	0
		NOD	7	137	18	162
	2	NOD	17	111	20	138
	3	NOD	2	17	2	21
	IT % per a	age group <sup>a</sup>	11.3	6.6	4.6	6.3
WLE	0	POD	5	234	0	239
(POD=12.3%)		NOD	10	303	74	387
	1	POD	7	300	89	396
		NOD	75	1501	319	1895
	2	NOD	37	803	180	1020
	3	NOD	4	82	14	100
	WLE % p	er age group <sup>a</sup>	59.7	79.3	77.3	78.1
		0.0.0				

Continued

Table 5 Continued

			Age n (%)			Total % of each
Treatment	Stage	OD category	45–49 n=231	50–69 n=4063	70–74 n=875	treatment in women with SDBC
Mastectomy	0	POD	2	52	11	65
(POD=2.2%)		NOD	10	135	32	177
	1	POD	3	35	12	50
		NOD	28	290	44	362
	2	NOD	44	346	68	458
	3	NOD	8	98	18	124
	Mx % pe	er age group <sup>a</sup>	41.1	23.5	21.1	23.9
SLNB (POD=9.8%)	0	POD	2	68	16	86
		NOD	12	150	39	201
	1	POD	9	312	98	419
		NOD	77	1572	327	1976
	2	NOD	58	798	182	1038
	3	NOD	1	18	3	22
	SLNB % per age group <sup>a</sup>		68.8	71.8	76.0	72.4
ALND (POD=0.5%)	0	POD	0	8	1	9
		NOD	1	7	2	10
	1	POD	0	16	2	18
		NOD	4	62	15	81
	2	NOD	21	279	43	343
	3	NOD	10	142	25	177
	ALND %	per age group <sup>a</sup>	15.6	12.7	10.1	12.3

Percentages may not add to 100% due to decimal rounding.

NZ screening age only; NZ and Australian screening age; Australian screening age only

<sup>a</sup>Number of treatments received per age group, divided by the total number in each age group.

\*Screen-detected breast cancer.

†Total SDBC patients (5169) differs from table 1 figure (5226), as not all cases included information required to allocate them to either POD or NOD categories (n=57).

‡Low and intermediate grade ductal carcinoma in situ.

§High grade ductal carcinoma in situ.

¶Grade 1,1 to<10 mm; not HER2+ or triple negative.

\*\*Grade 1,  $\geq$ 10mm; any receptor status.

††Invasive cancer.

ALND, axillary lymph node dissection; CT, chemotherapy; ET, endocrine therapy; HER2, human epidermal growth factor receptor 2; IT, immunotherapy; Mx, mastectomy; NOD, not overdiagnosed; OD, overdiagnosis; POD, possibly overdiagnosed; RT, radiotherapy; SDBC, screen-detected breast cancer; SLNB, sentinel lymph node biopsy; WLE, wide local excision.

overdiagnosis. This enabled correction for overdiagnosis in our analyses by separating the most favourable SDBC diagnoses (POD) from those more high-risk/advanced tumours that, on medical consensus, would not be considered overdiagnosed (NOD). We believe this approach provides a clearer assessment of treatment-related quality of life than previous epidemiological estimates based on intention to screen data linked to mortality outcomes; such approaches did not measure the additional benefits of screening related to reduced treatment intensity and the positive impact this may have on women's quality of life.<sup>10</sup> Our estimate of 15.8% is at the lower end of most overdiagnosis estimates<sup>1–15</sup> and we believe it is a legitimate method.

Importantly, this approach has allowed for direct linkage between diagnostic pathway and treatment recommendations, demonstrating that overdiagnosis does not necessarily lead to overtreatment. However, relatively small numbers of POD women were recommended for adjuvant treatment; this may be explained by either inexperienced clinicians or factors that were not analysed, such as family history of breast cancer or BRCA1 or BRCA2 status. In both Australia and NZ, the vast majority of breast cancer cases are discussed at multidisciplinary

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meetings where treatment decisions are matched not only to the histopathology, but also to the individual women; factors such as age, comorbidities, suitability for surgery, potential side effects of treatment, family history, mutation carrier status and the women's preferences are all considered when making treatment recommendations. Footnotes from Table 3 demonstrate that recommendations for treatment for all breast cancers, however detected, are not always accepted. Women may decline treatments and clinicians may opt for less intensive treatments according to the individual's circumstances.

The cross-sectional design did not track screening episodes over time and data on interval cancers (those that arise between screening rounds) was not available. However, it does provide a clear and accurate snapshot of the impact of diagnostic pathways on diagnosis and recommended treatments. One inherent limitation is the loose boundaries for allocation of women to either screen-detected or non-screen-detected categories, as outlined in online supplemental appendix A. This is a confounding variable beyond our control.

#### **Clinical implications**

This study has three major clinical implications:

- Breast cancer screening detects both low-risk and higher-risk tumours. Earlier detection of high-risk cancers not only improves a woman's prognosis but often reduces treatment intensity and is therefore likely to improve post-treatment quality of life, compared with later diagnosis.
- Women with NSDBC have substantially higher rates of more serious/advanced types of breast cancer than SDBC women, associated with higher rates of treatment intensity.
- Detection of low-risk tumours that are POD does not lead to extensive treatment of these cancers in the vast majority of cases.

## CONCLUSION

A reduction in breast cancer mortality is not the only screening outcome of importance. Reduced intensity of recommended treatment is also a key benefit. Women contemplating breast cancer screening must be informed about both sides of the harm minimisation argument so that they can make an informed, value-based and personalised decision. Any women considering breast cancer screening must be fully informed of both risks (including overdiagnosis) and benefits (including the option of less harmful treatments) before making the decision to screen or not screen.

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#### REFERENCES

- 1 Barratt A. Overdiagnosis in mammography screening: a 45 year journey from shadowy idea to acknowledged reality. *BMJ* 2015;350:h867.
- 2 Zackrisson S, Andersson I, Janzon L, et al. Rate of over-diagnosis of breast cancer 15 years after end of Malmö mammographic screening trial: follow-up study. *BMJ* 2006;332:689–92.
- 3 Jørgensen KJ, Gøtzsche PC. Overdiagnosis in publicly organised mammography screening programmes: systematic review of incidence trends. *BMJ* 2009;339:b2587.
- 4 Morrell S, Barratt A, Irwig L, et al. Estimates of overdiagnosis of invasive breast cancer associated with screening mammography. Cancer Causes Control 2010;21:275–82.

# **Original research**

- 5 Carter SM, Barratt A. What is overdiagnosis and why should we take it seriously in cancer screening? *Public Health Res Pract* 2017;27:2731722.
- 6 Welch HG. Overdiagnosis and mammography screening. *BMJ* 2009;339:b1425.
- 7 Raffle AE. Informed participation in screening is essential. BMJ 1997;314:1762–3.
- 8 National Health Service. Benefits and risks. Breast cancer screening. Available: https://www.nhs.uk/conditions/breast-cancer-screening/ why-its-offered/ [Accessed 14 Jan 2021].
- 9 Lauby-Secretan B, Scoccianti C, Loomis D, et al. Breast-cancer screening--viewpoint of the IARC Working Group. N Engl J Med 2015;372:2353–8.
- 10 Marmot MG, Altman DG, Cameron DA, et al. The benefits and harms of breast cancer screening: an independent review. Br J Cancer 2013;108:2205–40.
- 11 Roder DM, Buckley E. Overdiagnosis of cancer in Australia: the role of screening. *Med J Aust* 2020;212:159–60.
- 12 Bulliard J-L, Beau A-B, Njor S, et al. Breast cancer screening and overdiagnosis. Int J Cancer 2021;149:846–53.
- 13 Njor SH, Garne JP, Lynge E. Over-diagnosis estimate from the independent UK panel on breast cancer screening is based on unsuitable data. J Med Screen 2013;20:104–5.
- 14 Chaltiel D, Hill C. Estimations of overdiagnosis in breast cancer screening vary between 0% and over 50%: why? *BMJ Open* 2021;11:e046353.
- 15 Blyuss O, Dibden A, Massat NJ, et al. A case–control study to evaluate the impact of the breast screening programme on breast cancer incidence in England. *Cancer Med* 2023;12:1878–87.
- 16 Spillane AJ, Kennedy CW, Gillett DJ, et al. Screen-detected breast cancer compared to symptomatic presentation: an analysis of surgical treatment and end-points of effective mammographic screening. ANZ J Surg 2001;71:398–402.
- 17 Barth RJ, Gibson GR, Carney PA, et al. Detection of breast cancer on screening mammography allows patients to be treated with lesstoxic therapy. AJR Am J Roentgenol 2005;184:324–9.
- 18 Nickson C, Velentzis LS, Brennan P, et al. Improving breast cancer screening in Australia: a public health perspective. Public Health Res Pract 2019;29:2921911.
- 19 Arndt V, Stegmaier C, Ziegler H, et al. Quality of life over 5 years in women with breast cancer after breast-conserving therapy versus mastectomy: a population-based study. J Cancer Res Clin Oncol 2008;134:1311–8.
- 20 Read RL, Flitcroft K, Snook KL, et al. Utility of neoadjuvant chemotherapy in the treatment of operable breast cancer. ANZ J Surg 2015;85:315–20.
- 21 Elder K, Nickson C, Pattanasri M, et al. Treatment intensity differences after early-stage breast cancer (ESBC) diagnosis depending on participation in a screening program. *Ann Surg Oncol* 2018;25:2563–72.

- 22 Breast Surgeons of Australia and New Zealand Inc. Breastsurganz quality audit. Available: https://www.breastsurganz.org/members/ breastsurganz-quality-audit/ [Accessed 22 Jan 2022].
- 23 Australian Bureau of Statistics. Socio-economic indexes for areas (SEIFA). n.d. Available: https://www.abs.gov.au/websitedbs/ censushome.nsf/home/seifa
- 24 American Joint Committee on Cancer (AJCC) breast cancer staging. 7th edition. 2009. Available: https://cancerstaging.org/referencestools/quickreferences/Documents/BreastMedium.pdf [Accessed 22 Jan 2022].
- 25 Farshid G, Sullivan T, Downey P, et al. Independent predictors of breast malignancy in screen-detected early breast microcalcifications: biopsy results in 2545 cases. Br J Cancer 2011;105:1669–75.
- 26 The LORIS trial. A phase III trial of surgery versus active monitoring for low risk Ductal carcinoma in situ (DCIS) [UK]. Available: https:// www.birmingham.ac.uk/research/activity/mds/trials/crctu/trials/loris/ index.aspx [Accessed 30 Aug 2023].
- 27 The LORD trial. Management of low-risk DCIS (LORD). Available: https://clinicaltrials.gov/ct2/show/NCT02492607 [Accessed 30 Aug 2023].
- 28 The COMET (comparing operative to monitoring and endocrine therapy for low risk DCIS) trial. Available: https://clinicaltrials.gov/ct2/ show/NCT02926911 [Accessed 30 Aug 2023].
- 29 Shah C, Bremer T, Cox C, et al. Correction to: the clinical utility of DCISionRT<sup>®</sup> on radiation therapy decision making in patients with Ductal carcinoma in situ following breast-conserving surgery. Ann Surg Oncol 2021;28:878.
- 30 The EXPERT trial. Available: https://www.breastcancertrials.org.au/ trials/expert/ [Accessed 30 Aug 2023].
- 31 Mann B, Rose A, Hughes J, et al. Primary results of ANZ 1002: postoperative radiotherapy omission in selected patients with early breast cancer trial (PROSPECT) following pre-operative breast MRI. JCO 2022;40:572.
- 32 Whelan TJ, Smith S, Parpia S, *et al*. Omitting radiotherapy after breast-conserving surgery in Luminal A breast cancer. *N Engl J Med* 2023;389:612–9.
- 33 Kirwan CC, Coles CE, Bliss J, et al. It's PRIMETIME. postoperative avoidance of radiotherapy: biomarker selection of women at very low risk of local recurrence. Clin Oncol (R Coll Radiol) 2016;28:594–6.
- 34 White JR, Anderson SJ, Harris EE, *et al.* NRG-BR007: a phase III trial evaluating de-escalation of breast radiation (DEBRA) following breast-conserving surgery (BCS) of stage 1, hormone receptor+, Her2-, RS ≤18 breast cancer. *JCO* 2022;40:TPS613.
- 35 Duffy SW, Dibden A, Michalopoulos D, *et al.* Screen detection of Ductal carcinoma in situ and subsequent incidence of invasive interval breast cancers: a retrospective population-based study. *Lancet Oncol* 2016;17:109–14.
- 36 Narod SA, Iqbal J, Giannakeas V, et al. Breast cancer mortality after a diagnosis of Ductal carcinoma in situ. JAMA Oncol 2015;1:888–96.
- 37 Farshid G, Walters D. Molecular subtypes of screen-detected breast cancer. *Breast Cancer Res Treat* 2018;172:191–9.