



Dataset summary

There were 62,052 cases of newly diagnosed invasive or in situ breast tumours registered in Ireland by the National Cancer Registry for the period 1994–2016, of which 56,366 were invasive (ICD10: C50) and 5,686 were carcinoma in situ (ICD10: D05). Women accounted for the vast majority (61,617) with just 435 cases registered in men in this period.

Based on exclusion criteria discussed below, 54,047 cases of invasive breast cancer (53,642 in women, 405 in men) and 5,062 cases of breast carcinoma in situ (5,038 in women, 24 in men) were considered ‘reportable’ for incidence purposes. These figures exclude second breast tumours of ‘similar’ morphology (for a given behaviour) and in situ tumours following an invasive breast cancer of similar morphology.

Number of diagnoses per woman

There were 58,307 women with 61,617 diagnoses of either invasive breast cancer or carcinoma in-situ or both in the period 1994-2016 (Table 1). Analyses in the remainder of this report are based mainly on the ‘reportable’ 53,642 invasive cases in women (Table 2), with more limited detail on in situ tumours.

Table 1. Total number of female cases (invasive and in situ) in the period 1994-2016

Number of women	Number of registered diagnoses	Total registered diagnoses
55,070	1	55,070
3,167	2	6,334
70	3	213
58,307		61,617

Handling of multiple tumours

We identified multiple tumours on the basis of International Agency for Research on Cancer (IARC) rules [1] which classify tumours as the “same” or “different” based on site and morphology.

Inclusion/exclusion criteria: The first invasive breast cancer of each morphological “type” was counted for each patient. The first in situ breast tumour of each type was also counted for each patient unless it was preceded by or synchronous with an invasive cancer of the same morphological type. In situ cases that occurred before an invasive case of similar morphology were counted as reportable cases and thus figures may differ from previous reports.

Invasive breast cancers in women

Of the 61,617 registered cases in women, the exclusion of multiple tumours from further analysis left 58,680 cases. Of

these, 53,642 cases (91.4%) were recorded as invasive (Table 2) and 5,038 (8.6%) as in situ (see page 8). Considering invasive cancer only, there were 53,540 women with one invasive diagnosis and 51 women with two invasive cancers (i.e. two different breast tumour types based on morphology). Both tumours for these 51 women were counted in the analysis of invasive breast cancer below and all future reference to case counts indicate the number of tumours rather than patients. Also, figures refer to cases in women only, with the exception of the section on male breast cancer at the end of this report.

Table 2. Number of reportable cases in the period 1994-2016

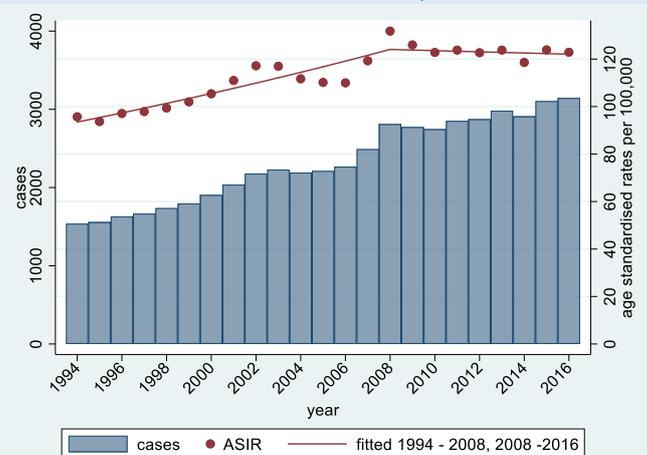
Number of diagnoses	Invasive: Number of women	In situ: Number of women
1	53,540	5,030
2	51	4
No. of cases	53,642	5,038

Time trends in incidence

There was an annual average of 3,053 invasive breast cancer cases diagnosed in Irish women in the period 2014-2016 with an increasing trend in the number of new cases. In particular, greater increases occurred after screening roll-outs in 2000 and 2007.

Age-standardised incidence rates (ASIR), accounting for population changes, increased in the period 1994-2008 with an estimated average annual percentage change (APC) [2] of +2.0% (Figure 1). The trend stabilised in the period 2008-2016 with an APC of -0.2%. The influence of the national screening programme (BreastCheck [3]) can be seen in the ASIRs, with peaks in 2002 and 2008 after successive roll-outs of the programme. BreastCheck offers screening every two years to women aged 50-64 years (50-69 years from 2018); it began in the eastern half of the county in 2000 and was rolled out to other regions from 2007.

Figure 1. Case numbers, age-standardised incidence rates and fitted rate-trends for invasive breast cancer in Irish women, 1994-2016



From	To	APC (%)	95% CI	
1994	2008	+2.0%*	+1.6%	+2.5%
2008	2016	-0.2%	-1.1%	+0.7%

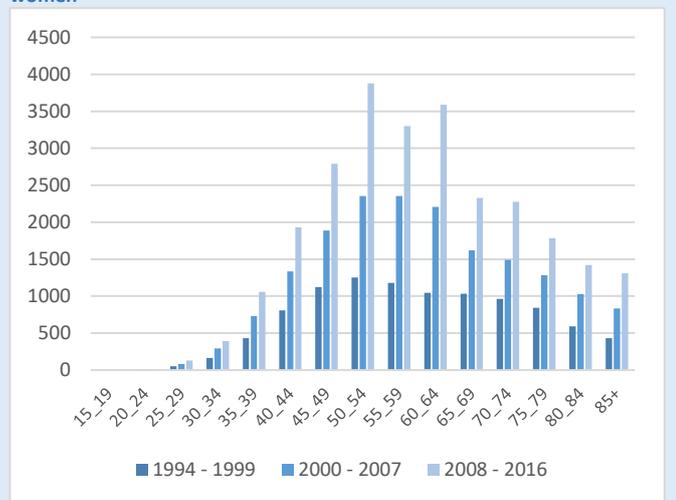
*Statistically significant at the 5% level.

Age profile of invasive breast cancers

The median age at diagnosis for invasive breast cancer in women was 59 years across the three time periods examined. In the periods 1994-1999 and 2008-2016, case numbers peaked in the 50-54 age-group, and in 2000-2007 in the 55-59 age-group (Figure 2).

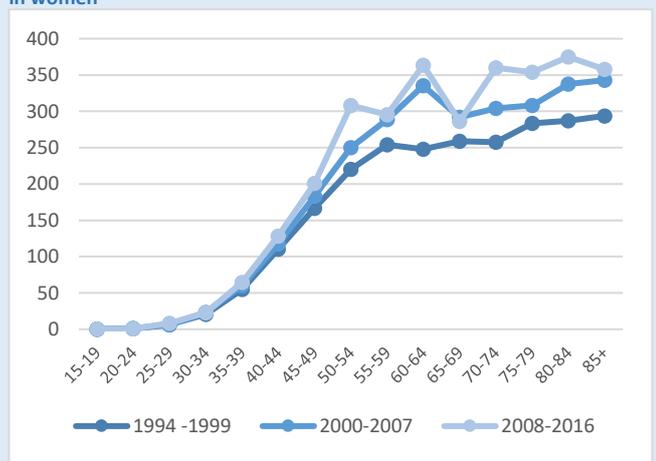
Approximately 40% of cases during 2000-2016 were diagnosed in women aged between 50 and 64 years inclusive, which was the target age for breast screening in Ireland until 2018.

Figure 2. Age-specific case numbers by period for invasive breast cancer in women



The age-specific rates followed a broadly similar pattern across the three time periods, with peak rates in the oldest age group, 80+ years, but with an additional earlier peak (reflecting screening) at ages 60-64 during 2000-2007 and 2008-2016 (Figure 3).

Figure 3. Age-specific rates (per 100,000) by period for invasive breast cancer in women



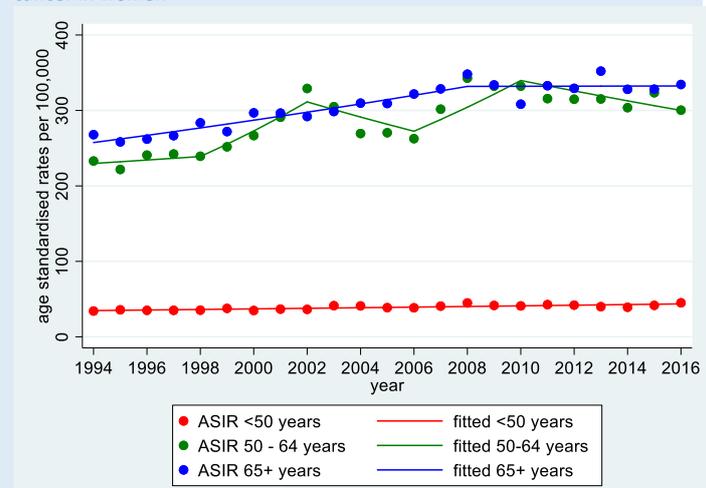
We also present truncated age-standardised rates to monitor any trends in the incidence rates in women in the target age-group for screening (50-64 years) and separately for the women in the pre- and post-screening age-groups.

For women younger than 50 years, rates increased by, on average, 1% per year across the whole period (Figure 4), from 34.2 per 100,000 in 1994 to 45.1 per 100,000 in 2016.

The trends in the screening age group, 50-64 years were quite complex, showing the typical increase and subsequent slight

decline in incidence rates following the roll out of the screening programme. This can be seen in the steep increases from 1998 to 2002 (reflecting roll-out on a regional basis from 2000) and from 2006 to 2010 (reflecting national roll-out from 2008). The rates for the over 65s rose over the period 1994-2008 with an annual percentage change of +1.8%, followed by stabilisation in the period 2008-2016.

Figure 4. Age-standardised incidence rates by age-group for invasive breast cancer in women



Age-group	From	To	APC (%)	95% CI	
<50 years	1994	2016	+1.0%*	+0.7%	+1.3%
50-64 years	1994	1998	+1.0%	-2.9%	+5.0%
	1998	2002	+6.8%*	+0.5%	+13.6%
	2002	2006	-3.3%	-9.0%	+2.8%
	2006	2010	+5.7%	-0.6%	+12.3%
	2010	2016	-2.0%	-4.1%	0.0%
65+ years	1994	2008	+1.8%*	+1.4%	+2.2%
	2008	2016	0.0%	-0.9%	+1.0%

*Statistically significant at the 5% level.

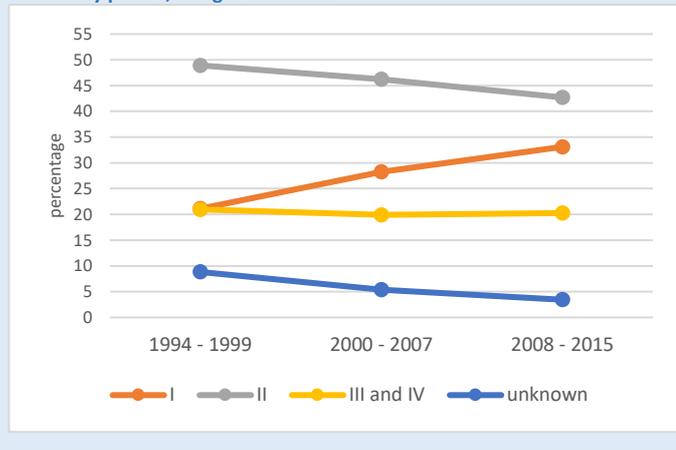
Stage at diagnosis

It is expected that the introduction of organised mammographic screening may contribute to stage shift over time, with an increase in the relative number of early stage cases and a corresponding decrease in late stage cases. However, during prevalence rounds of screening, a local increase may mask the underlying trend. We examined stage distribution across all ages and in the pre-screening, screening eligible and post-screening age-groups.

Across all ages combined, the percentage of stage I cases increased from 21% in 1994-1999 to 33% in 2008-2015 while the percentage of stage II cases decreased from 49% in 1994-1999 to 42% in 2008-2015 (Figure 5). The percentage of late stage (III and IV) cancers remained fairly static at around 20% across the three periods.

The TNM staging criteria applied to these cases changed between 2013 and 2014 but this should not unduly affect these broader comparisons; 2016 stage data were less complete and were excluded.

Figure 5. Stage percentage breakdown of invasive breast cancer cases in women by period, all ages combined



For younger women, the percentage with a stage I diagnosis increased from 22% in 1994-1999 to 26% in 2008-2015 (Figure 6a). However, the percentage with a late stage (III or IV) diagnosis increased from 18% in 1994-1999 to 22% in 2008-2015, while the percentage with a stage II diagnosis decreased from 53% in 1994-1999 to 48% in 2008-2015.

As would be anticipated, there was a large increase in the percentage presenting with stage I cancer for women in the screening age-group (50-64 years), from 23% in 1994-1999 to 44% in 2008-2015 (Figure 6b). The percentage with a stage II diagnosis showed a related but not as steep decline, from 50% in 1994-1999 to 38% in 2008-2015. The percentage of late stage cancer declined from 20% in the earliest period to 16% in 2008-2015. This suggests that there has been some stage replacement in the women who are eligible for screening, although this may comprise some 'extra' cases diagnosed at early stages in addition to cases that would otherwise have been detected at late stage. (Note: Women diagnosed in the 50-64 age-group comprise both participants and non-participants of the screening programme.)

The percentage of cases with stage II or Stage III/IV remained fairly static over all periods for the over 65s (Figure 6c), while the increase in percentage with stage I cases was offset by a decrease in the percentage of non-staged cases.

Figure 6a. Stage percentage breakdown of invasive breast cancer cases by period, <50 years

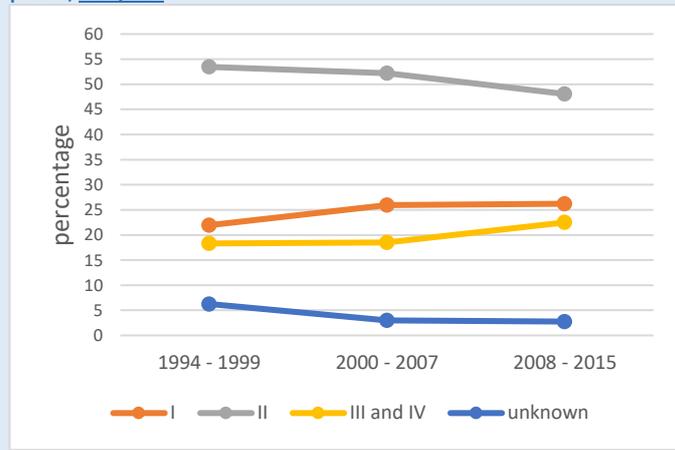


Figure 6b. Stage percentage breakdown of invasive breast cancer cases by period, 50-64 years

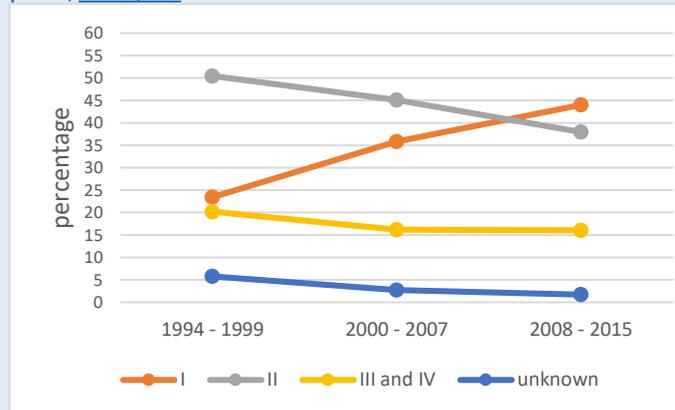
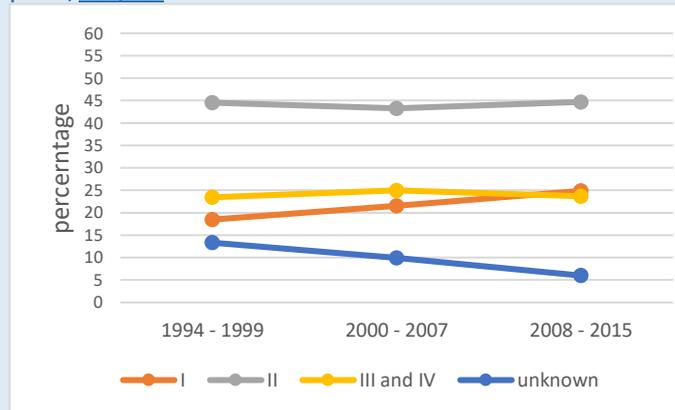


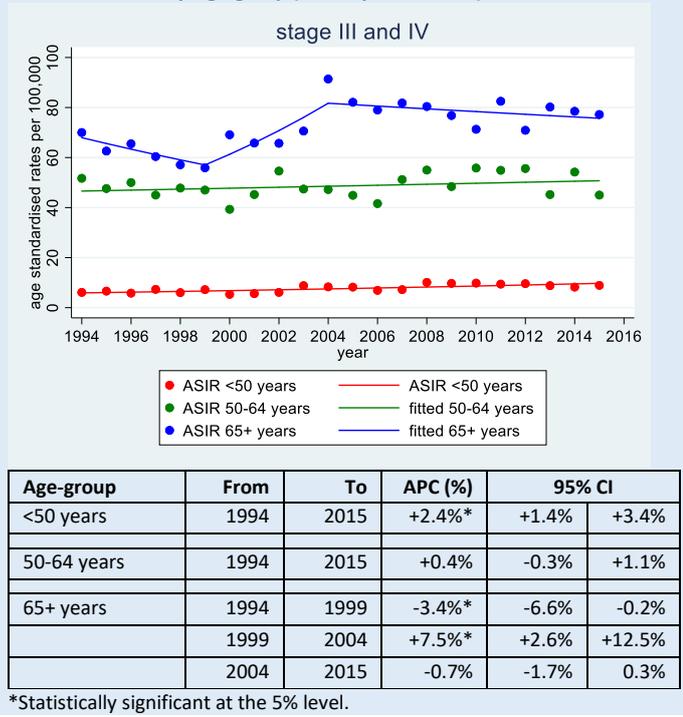
Figure 6c. Stage percentage breakdown of invasive breast cancer cases by period, 65+ years



Overall and in each age-group, there was an increase in the percentage of stage I cases over the three periods.

As percentages are constrained to sum to 100, it is also illuminating to consider the age-standardised rates, in particular for late-stage cancers. This avoids possible artefactual trends in proportions which could occur if late stage diagnoses remained constant (adjusted for population) while early stage diagnoses increased. We present the results for the pre-screening, screening-eligible and post-screening age-groups (Figure 7).

Figure 7. Truncated age-standardised rates for late-stage invasive breast cancer in women by age-group (at first presentation)

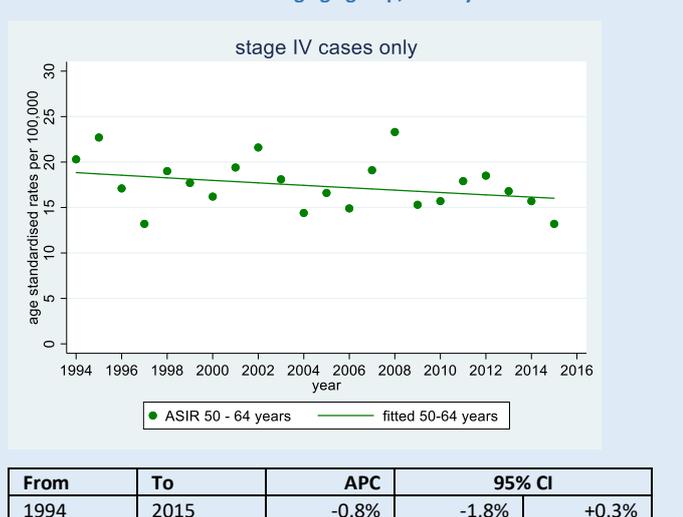


In younger women (less than 50 years), the truncated age-standardised rates of late stage (III and IV) invasive breast cancer displayed an increasing trend, with an APC of 2.4% over the period 1994-2015 (Figure 7). In contrast, for women aged 50-64 years, the rates remained fairly flat throughout the period 1994-2015, with some evidence of temporary increases (circa 2002 and 2008) in late-stage cases around the time of the screening rollouts. It may be too early to see any screening related reduction in late-stage cases. The rates for late-stage cancers in women aged 65 and over were more variable, but have stabilised since 2004.

Factors influencing the increases seen in both the proportion and the rate of late-stage cancers in women under 50 are not clear, but could include improvements in the quality or scope of diagnostic or staging investigations.

To explore the trends in late stage cancer further, we also plotted the age-standardised incidence rates for stage IV cancer only, for the screening age-group.

Figure 8. Age-standardised incidence rates, stage IV (at first presentation) cases for women in the screening age group, 50-64 years



Here we see a small downward trend with an average reduction of 0.8% per year, though this is not significant at the 5% level (Figure 8). Currently, there is no direct evidence that the downward trend in this age group is related to the introduction of screening, as there was no significant change in the trend around the roll-out years of the national screening programme, but screening may have contributed to the continuation of this trend.

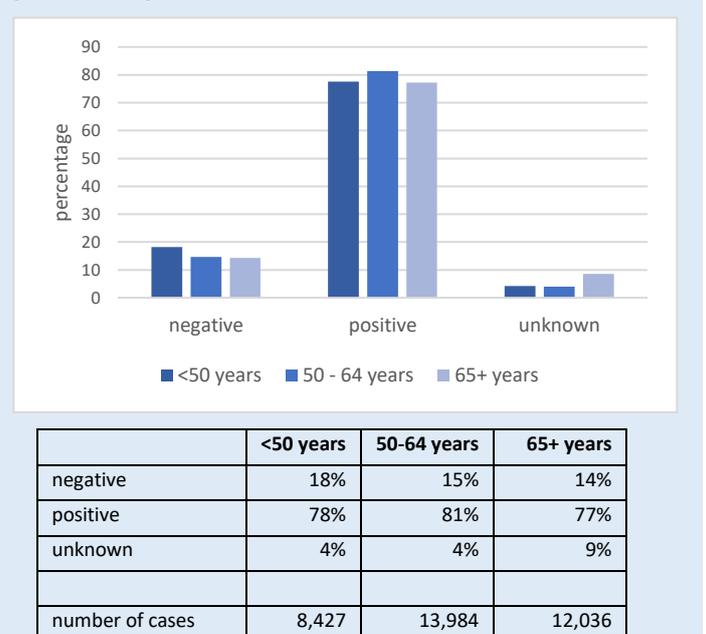
Receptors for breast cancer

Breast cancers with receptors for the hormone oestrogen are termed oestrogen-receptor positive or ER positive breast cancers. Similarly, progesterone-receptor positive (PR) breast cancers are those with receptors for the hormone progesterone. Some breast cancers have high numbers of receptors for the protein HER2 (human epidermal growth factor 2). They are termed HER2 positive breast cancers. If a breast cancer does not have receptors for either HER2 or the hormones oestrogen and progesterone, it is described as triple-negative breast cancer.

Having hormone and/or HER2 receptors can affect the treatment course and potentially the outcome of the disease. Some previous work has been done to examine the distribution of ER/PR/HER2 positive breast cancers by screening status in the Irish context [4].

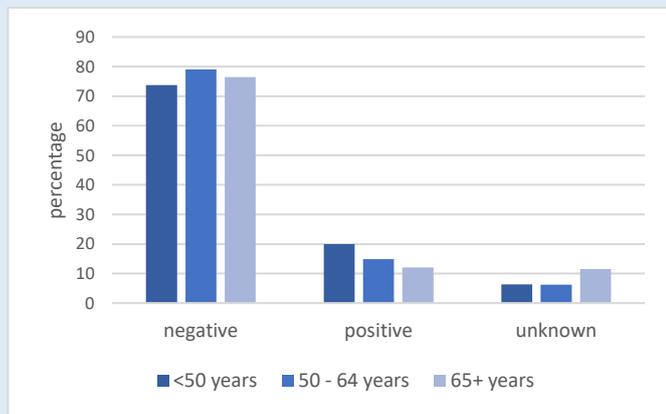
In the period 2003-2015, 79% of women had cancers which were ER or PR positive, with women in the screening-eligible (50-64) age-group having the highest proportion at 81% (Figure 9).

Figure 9. Proportion of female breast cancer cases which were ER or PR positive in the period 2003-2015



The percentage of women with HER2 positive breast cancer was 15% overall, with the highest percentage in women aged less than 50 years at around 20% (Figure 10).

Figure 10. Proportion of female breast cancer cases which were HER2 positive in the period 2006–2015



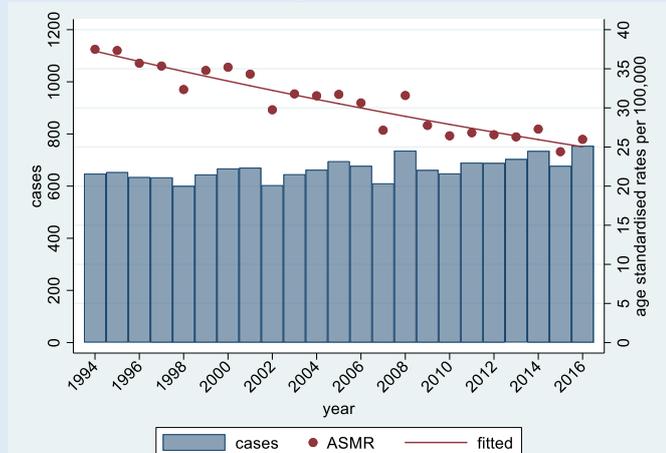
	<50 years	50-64 years	65+ years
negative	74%	79%	76%
positive	20%	15%	12%
unknown	6%	6%	12%
number of cases	6,713	11,405	9,694

These receptor results are broadly consistent with previous findings, including in Ireland [4], that mammography screening preferentially detects ER/PR positive and HER2 negative tumours, which are typically slower growing.

Mortality

Numbers of deaths per year due to breast cancer have remained relatively stable over the period 1994-2016, with an annual average of 723 deaths in the period 2014-2016. Age-standardised mortality rates for breast cancer have been declining fairly steadily (-1.8% annual percentage change) over the period 1994-2016 (Figure 11), including a decline from 35.2 per 100,000 in 2000 (the year the screening programme was introduced) to 25.9 per 100,000 in 2016.

Figure 11. Case numbers (deaths) and age-standardised mortality rates for invasive breast cancer in women, 1994-2016



From	To	APC (%)	95% CI	
1994	2016	-1.8%*	-2.1	-1.5

*Statistically significant at the 5% level.

While Joinpoint software was used to assess overall trends in the period 1994 -2016 (Figure 11) and found that the best

model was one linear fit through the data, we also examined trends for the periods 1994-2000, 2000-2008 and 2008-2016. (These models are not data-driven but user-specified, based on the timing of the two main phases of BreastCheck rollout, from 2000 and 2008.) Average APCs for these periods were:

- 1994-2000: -1.5% (95%CI -3.4%, +0.5%);
- 2000-2008: -1.7% (95%CI -3.6%, +0.2%);
- 2008-2016: -1.75% (95%CI -3.2%, -0.3%).

This further analysis likewise does not provide any strong evidence that mortality trends have changed within the wider period 1994-2016 or in relation to the introduction of screening. The detailed trends are likely to reflect, in large part, improvements in treatment quality or specificity, and in proportions of patients treated, over time (cf. Treatment section below), in addition to any screening benefits.

However, previous work [5] has shown that breast cancer mortality rates in screening-eligible women in the eastern half of the country (where screening was rolled out first) were 9% (95% CI -20%, +4%) lower than in the rest of the country in the period 2000-2013. This lower rate was interpreted as a conservative estimate of the benefit (in mortality reduction) of the screening-eligible women in the eastern population having had access to organized mammographic screening up to eight years earlier than elsewhere.

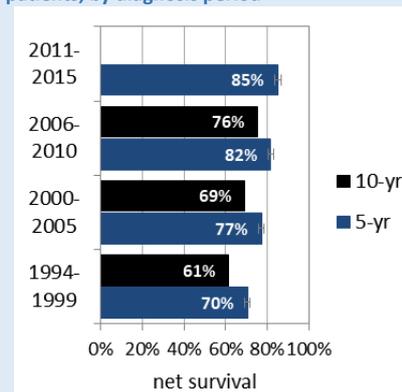
Truncated age-standardised mortality rates in the under-50 and 50+ age-groups both decreased across the period 1994-2016: from 8.4 per 100,000 in 1994 to 4.5 per 100,000 in 2016 (under 50), and from 109 per 100,000 to 79 per 100,000 (50+). Average APCs for these periods involved ongoing declines (statistically significant for both age-groups, but with no significant differences in trend between age-groups):

- Age <50 1994-2016: -2.6% (95%CI -3.5%, -1.7%);
- Age 50+ 1994-2016: -1.6% (95%CI -1.9%, -1.4%).

Survival

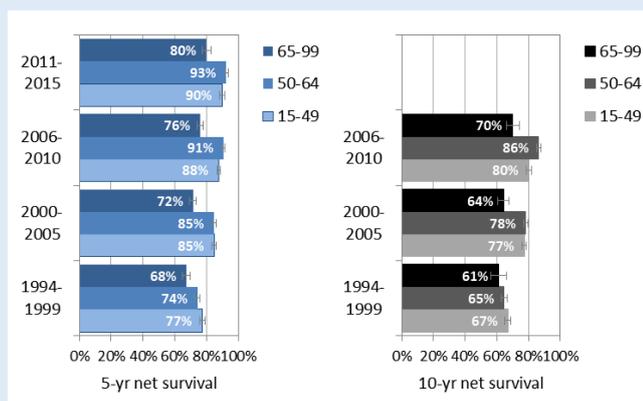
Five-year net survival [6] for female breast cancer patients as a whole has improved markedly over time, from an average (age-standardised) of 70% for diagnosis period 1994-1999 to 85% for 2011-2015 (Figure 12). This represents, on average, approximately a halving of 5-year mortality risk over this time. Ten-year survival has also improved markedly, from an average of 61% for diagnosis period 1994-1999 to 76% for 2006-2010 (not yet available for 2011-2015 cases).

Figure 12. Age-standardised five-year and ten-year net survival of female breast cancer patients, by diagnosis period



Substantial improvements in survival are also evident for each age-group (15-49, 50-64, and 65+) (Figure 13). However, the extent of the improvement, comparing diagnosis period 2011-2015 with 1994-1999, has been highest for the screening-eligible age-group (50-64). For this age-group, the survival improvement is equivalent to an average reduction in five-year mortality risk by about 70%, compared with a 55% reduction in the mortality risk in the under-50 group and a 40% reduction in the 65+ group. However, the extent of the survival improvement (mortality reduction) in the 50-64 group is likely to be exaggerated somewhat by ‘lead-time’ bias, i.e. an artefactual improvement in measured survival time reflecting earlier diagnosis through screening, in addition to any ‘real’ improvement reflecting diagnosis at a more treatable stage.

Figure 13. Age-specific five-year and ten-year net survival of female breast cancer patients, by diagnosis period



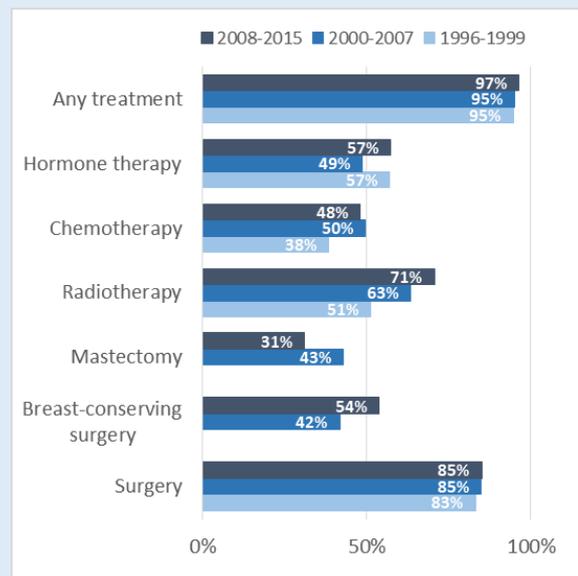
Treatment

Overall, 97% of female breast cancer patients diagnosed during 2008-2015 received tumour-directed treatment for their initial diagnosis, i.e. treatment that removes or prevents tumour growth (whether for curative or palliative purposes). Surgery was the most frequent modality, followed by radiotherapy, hormone therapy and chemotherapy (including immunotherapy or ‘targeted’ therapy) (Figure 14).

There has been little change over time, across the period 1996-2015, in the proportion of patients having surgery (83-85%) or any relevant treatment (95-97%). However, the proportion of patients having breast-conserving surgery increased from 42% during 2000-2007 to 54% 2008-2015, with a corresponding decrease in the proportion having mastectomy, i.e. complete breast-removal (from 43% 2000-2007 to 31% 2008-2015).

There have also been large increases in the proportions of patients having radiotherapy (from 51% of 1996-1999 patients to 71% for 2008-2015) or chemotherapy (38% 1996-1999 to 50% 2000-2007, then stabilising or falling slightly to 48% 2008-2015) (Figure 14). Trends in hormone therapy use are unclear, but data on hormonal therapy are more difficult to collect and figures may be incomplete.

Figure 14. Percentages of female breast cancer patients receiving tumour-directed treatment (up to 12 months after diagnosis), by diagnosis period



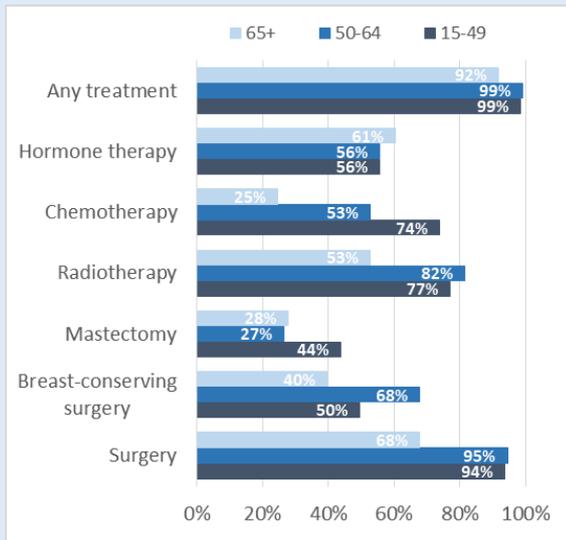
Note: Treatment data for patients diagnosed in 1994, 1995 or 2016 may be less complete and are not presented, likewise pre-2000 data by surgical subtype

In the most recent period, similar proportions of patients in the under-50 and the 50-64 age-groups had surgery (94-95%), any tumour-directed treatment (99%) or hormone therapy recorded in NCRI records (56%) (Figure 15).

The proportion of patients having breast-conserving surgery was highest, and having mastectomy lowest (27%), in the 50-64 group (68%). A slightly higher proportion of patients in the 50-64 (screening-targeted) group had radiotherapy (82%) than in the under-50 group (77%), while chemotherapy use in the 50-64 group was substantially lower (53%) than in the under-50s (74%). The chemotherapy difference likely reflects a higher proportion of more aggressive cancers in the younger group, compared with post-menopausal and screening-detected cancers.

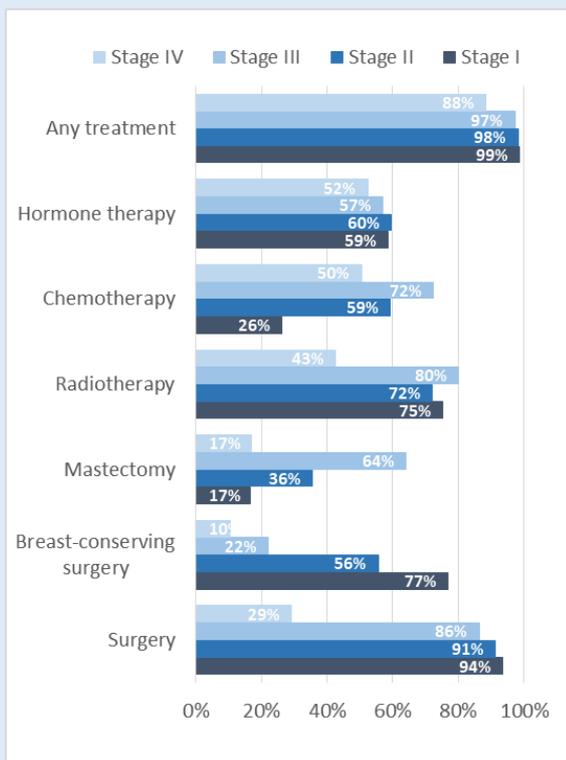
With the exception of hormonal therapy, treatment percentages for patients aged 65 or over were markedly lower than for younger patients (Figure 15), although differences would be more extreme if presented for patients aged 75 or more.

Figure 15. Percentages of female breast cancer patients receiving tumour-directed treatment (up to 12 months after diagnosis), by age at diagnosis: diagnosis period 2008-2015



Proportions of patients treated were highest for overall treatment (97-99%) at TNM stages I-III (97-99%); overall surgery (94%) and breast-conserving surgery (77%) at stage I; mastectomy (64%), radiotherapy (80%) and chemotherapy (72%) at stage III (Figure 16). Use of hormone therapy varied less by stage (at least 52%-59%) than use of other modalities. Treatment percentages were, in general, lowest for stage IV patients, but substantial proportions of stage IV patients had radiotherapy (43%), chemotherapy (50%) or hormone therapy (at least 52%).

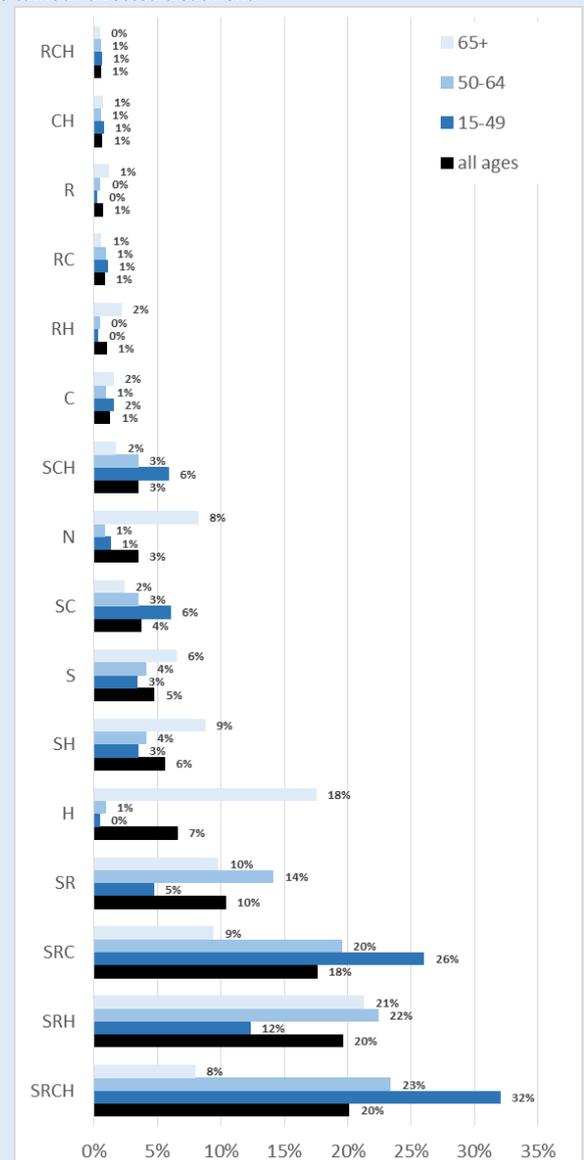
Figure 16. Percentages of female breast cancer patients receiving tumour-directed treatment (up to 12 months after diagnosis), by stage at diagnosis: diagnosis period 2008-2015.



Note: different TNM staging criteria applied to 2014-2015 cases but are not considered to have markedly affected these findings.

The relative use of different treatment modalities in combination or singly during 2008-2015 is summarised by age-group (and overall) in Figure 17. The most frequent combinations in most age-groups were surgery + radiotherapy + chemotherapy/immunotherapy + hormone therapy (SRCH) (20% of all patients), SRH (also 20%) and SRC (18%). Hormone therapy was the most frequent single-modality treatment overall (at least 7% of all patients and at least 18% of those aged 65+).

Figure 17. Combinations of tumour-directed treatment modalities received by female breast cancer patients diagnosed 2008-2015, overall and by age S = surgery, R = radiotherapy, C = chemotherapy, H = hormone therapy – single modality (e.g. “S”) or in combination with other modalities (e.g. “SRCH”); N = no tumour-directed treatment.



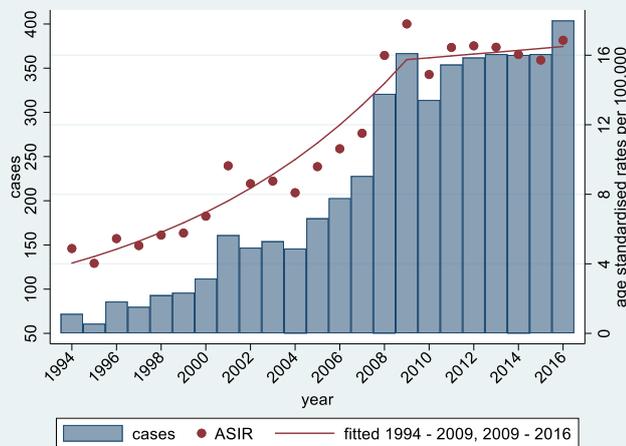
Breast carcinoma in situ

There were 5,657 breast carcinoma in-situ diagnoses in the dataset for women for the period 1994-2016. Of these, 619 were classed as multiple tumours and thus had the same morphological grouping as a prior invasive breast cancer or in situ breast carcinoma. These 619 tumours were dropped from the analysis. There were 5,038 in situ diagnoses remaining in the dataset, for 5,034 women (Table 2).

This represented an annual average of 378 cases diagnosed in the period 2014-2016. Peaks in the annual number of new cases were observed after screening roll-outs in 2000 and in 2008/9 (Figure 18).

The age-standardised incidence rates (ASIR) increased in the period 1994-2009 with an annual percentage change (APC) of 9.5%, after which the trend stabilised with an APC of 0.7%. As with invasive breast cancers, the influence of the national screening programme (BreastCheck) can be seen in the ASIRs for carcinoma in situ, with peaks in 2001 and 2009 after successive roll-outs of the programme (Figure 18).

Figure 18. Case numbers and age-standardised incidence rates, breast carcinoma in situ, 1994-2016



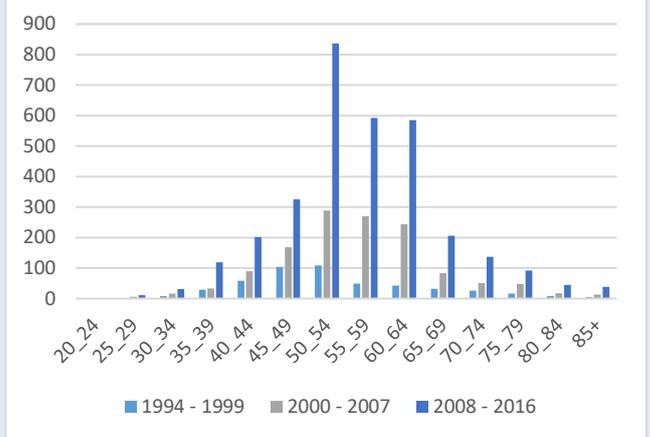
From	To	APC (%)	95% CI	
1994	2009	+9.5%*	+7.8%	+11.2%
2009	2016	+0.7%	-2.2%	+3.7%

*Statistically significant at the 5% level.

Age profile of in situ breast cancers

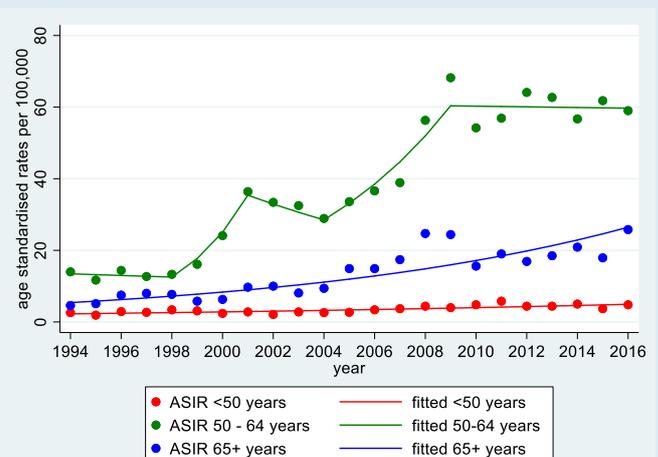
The median age at diagnosis for breast carcinoma in situ was 52 years during 1994-1999 and 56 years during both 2000-2007 and 2008-2016. The greatest numbers of cases occurred in the 50-54 year age group in all three periods (Figure 19).

Figure 19. Age-specific case numbers by period, breast carcinoma in-situ



The truncated age-standardised incidence rates for breast carcinoma in situ show rising trends for all age-groups but with more volatility for the screening age-group 50-64 years (Figure 20). The rates indicate that there was some opportunistic screening occurring in the population as carcinoma in situ does not generally present symptomatically but is found through opportunistic/organised screening or as an incidental finding.

Figure 20. Truncated age-standardised rates, per 100,000, breast carcinoma in-situ



Age-group	From	To	APC (%)	95% CI	
<50 years	1994	2016	+3.6%*	+2.4%	+4.8%
	1994	1998	-1.7%	-10.2%	+7.6%
50-64 years	1998	2001	+41.3%*	+6.2%	+88.1%
	2001	2004	-7.0%	-30.1%	+23.9%
	2005	2009	+16.2%*	+6.1%	+27.2%
65+ years	2009	2016	-0.2%	-3.9%	+3.7%
	1994	2016	+7.5%*	+5.9%	+9.1%

*Statistically significant at the 5% level.

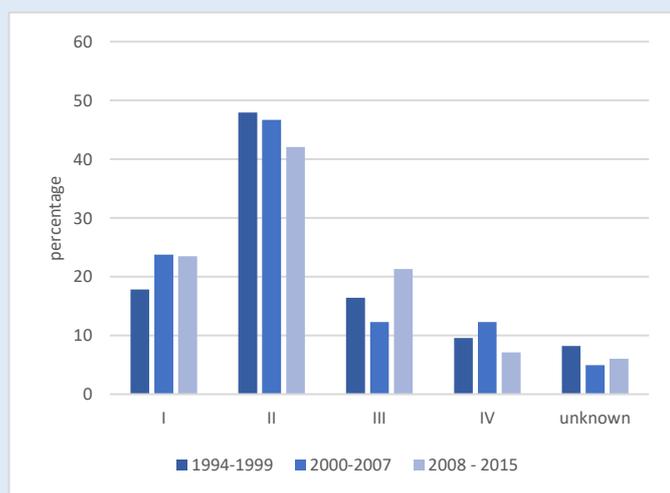
Male breast cancer

There were 435 breast tumours registered in men in the period 1994-2016, with 6 of these cases considered to be multiple diagnoses (thus removed from the analysis dataset). Of the 429 cases remaining, 405 (94.4%) were invasive breast cancer, while 24 (5.6%) were breast carcinoma in situ. In the period 2014-2016 there was an annual average of 25 cases of invasive male breast cancer diagnosed per year.

The median age at diagnosis was 68 years, with 50% of all men aged between 52 and 74 years at diagnosis.

For the invasive cases, the highest proportion (45%) comprised stage II breast cancer, though this has declined in the most recent period (Figure 21).

Figure 21. Stage distribution for male breast cancer by period



	1994-1999	2000-2007	2008-2015
I	18%	24%	24%
II	48%	47%	42%
III	16%	12%	21%
IV	10%	12%	7%
unknown	8%	5%	6%
number of cases	73	122	183

Conclusion

Incidence rates for female invasive breast cancer have stabilised following initial rises after rollouts of the organised screening programme. It is encouraging to see that mortality rates showed a consistent downward trend over the past 20+ years. Further work needs to be done to examine the effect of screening on incidence, stage, receptor status and mortality using combined data from the National Cancer Registry and the National Screening Service.

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