National Cancer Registry Ireland

Cancer Trends

Female breast cancer

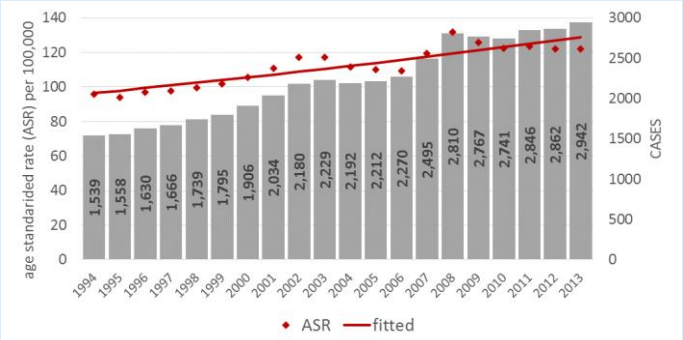
SUMMARY STATISTICS

Table 1. Female breast cancer incidence, mortality & prevalence

	Invasive	in situ
new cases per year: 2011-2013 average	2,883	360
incidence rate per 100,000/year ~	122.6	16.4
cumulative lifetime risk to age 74	9.6%	1.3%
% of all invasive cancers in females*	30.3%	
rank among most common cancers*	1st	
deaths per year: 2011-2012 average	690	
mortality rate (per 100,000 per year)	26.7	
cumulative lifetime risk of death (to age 74)	2.0%	
% of all cancer deaths in females	16.7%	
rank among most common cancer deaths	2nd	
20 year prevalence‡	29,828	3,798

~ rate age-standardised to 1976 European standard population [1]
* invasive cancers in females, excluding non-melanoma skin cancer
‡ patients diagnosed since 1994 who were still alive at end of 2013

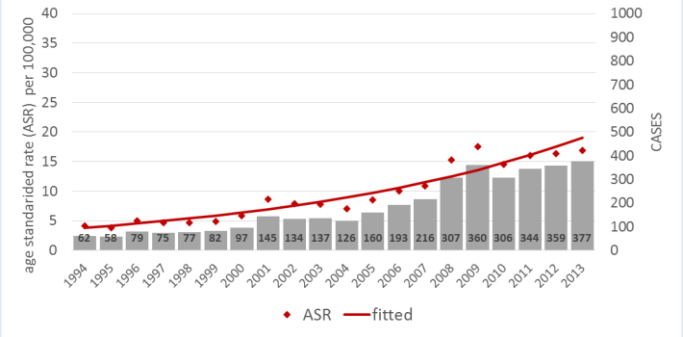
Figure 1. Female invasive breast cancer incidence trend: 1994-2013



from-to	annual percentage change (APC)	95%CI	trend
1994-2013	+1.5%	[1.1%, 1.9%]	↑

On average, 2,883 new cases of invasive breast cancer were registered per year during 2011-2013 – an age-standardised rate of 123 per 100,000 per year. The rate increased significantly by 1.5% annually from 1994 to 2013 (Figure 1). Against the overall upward trend, the influence of the national screening programme (BreastCheck) is evident from two peaks in incidence in 2002 and 2008 (see also Figure 7 below).

Figure 2. Female *in situ* breast cancer incidence trend: 1994-2013

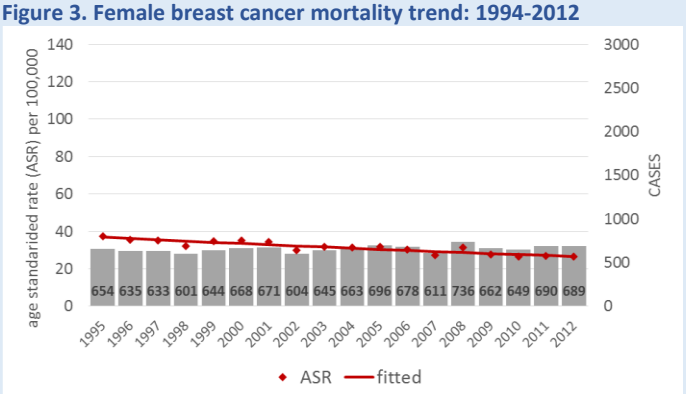


from-to	annual percentage change (APC)	95%CI	trend
1994-2013	+8.8%	[7.4%, 10.2%]	↑

During the period 2011-2013, the average number of in situ breast cancer cases was 360 per year. The incidence rate increased significantly by c.9% annually during 1994-2013 (Figure 2). The influence of the national screening programme can again be seen, in peaks around 2001 and 2009, and the overall trend in in situ cases was probably more strongly influenced by screening than was the trend in invasive cases.

Breast cancer mortality rates were obtained from the Central Statistics Office (CSO) for the years 1994-2012 [2]. During 2011-2012, on average 690 deaths were attributable to breast cancer - an age-standardised rate of 27 deaths per 100,000 per year. The mortality rate declined significantly at almost 2% annually during the period 1994-2012 (Figure 3). The number of deaths was more static, reflecting population increase and ageing.

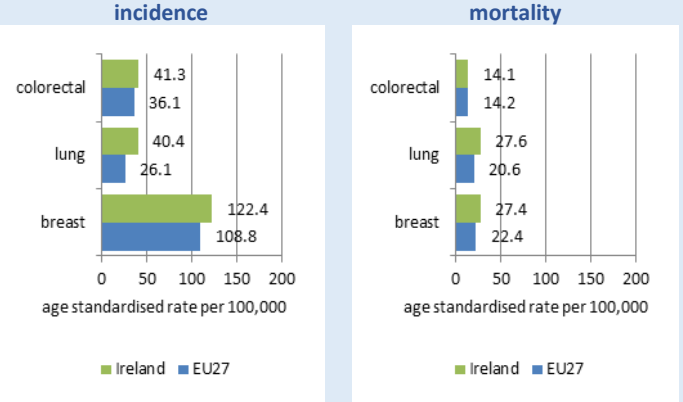
Figure 3. Female breast cancer mortality trend: 1994-2012



from-to	annual percentage change (APC)	95%CI	trend
1994-2013	-1.9%	[-2.3%, -1.5%]	↓

INCIDENCE AND MORTALITY COMPARISONS WITH EUROPE

Figure 4. Comparison of estimated incidence and mortality rates in Ireland with EU(27) average rates in 2012 [3][4]



invasive cancers of breast, lung and colorectum in females

The age-standardised incidence rate for breast cancer in Irish females was estimated to be 122/100,000 in 2012, higher than the EU average (109/100,000) (Figure 4). It cannot be excluded that this difference might reflect completeness of case registration. Almost half of Europe falls outside the coverage of cancer registration - some countries have regional registries with incomplete coverage of the whole country, and some countries have no official registry. Ireland's national registry has an estimated completeness of registration of 98% [5].

By way of comparison with other common cancers, Irish females also had higher incidence rates than the EU average for lung and colorectal cancer, particularly for lung cancer (Figure 4).

In 2012, the mortality rate in Ireland for breast cancer was 27.4/100,000, which was again higher than the EU average (22.4/100,000) (Figure 4).

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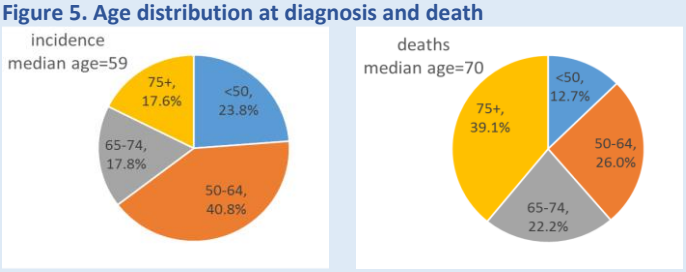
AGE AT DIAGNOSIS

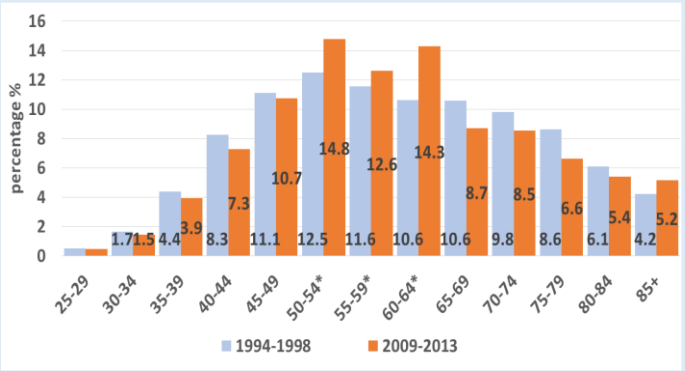
Figure 5. Age distribution at diagnosis and death



incidence (invasive cases) : 2011-2013, deaths: 2011-2012

The median age of diagnosis for invasive breast cancer was 59 years for the period 2011-2013. 41% of patients during this period were diagnosed at ages 50-64, which is the target group of the national screening programme. Almost a quarter of women were under 50 years of age. The median age at death was 70 years and 39% of those that died during the period 2011-2012 were 75+ years and 13% were < 50 years (Figure 5).

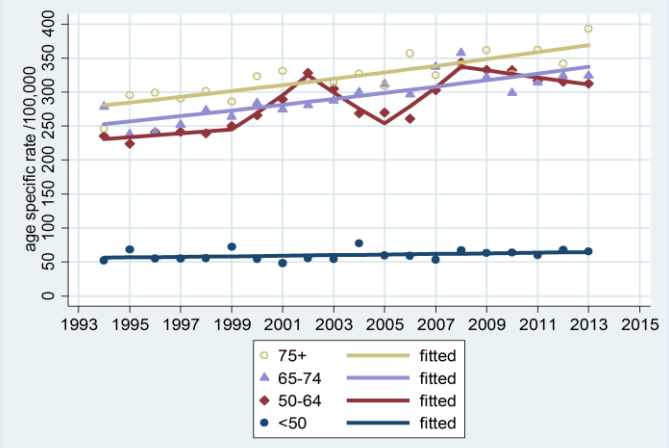
Figure 6. Comparison of age distribution at diagnosis



*identifies age groups covered by the screening programme (2000 onwards)

During 1994-1998, 35% of cases were diagnosed within the 50-64 age range, whereas in the more recent 5-year period 2009-2013 this proportion increased to 42% after full implementation of the national screening programme (Figure 6).

Figure 7. Age specific incidence trends: invasive breast cancer

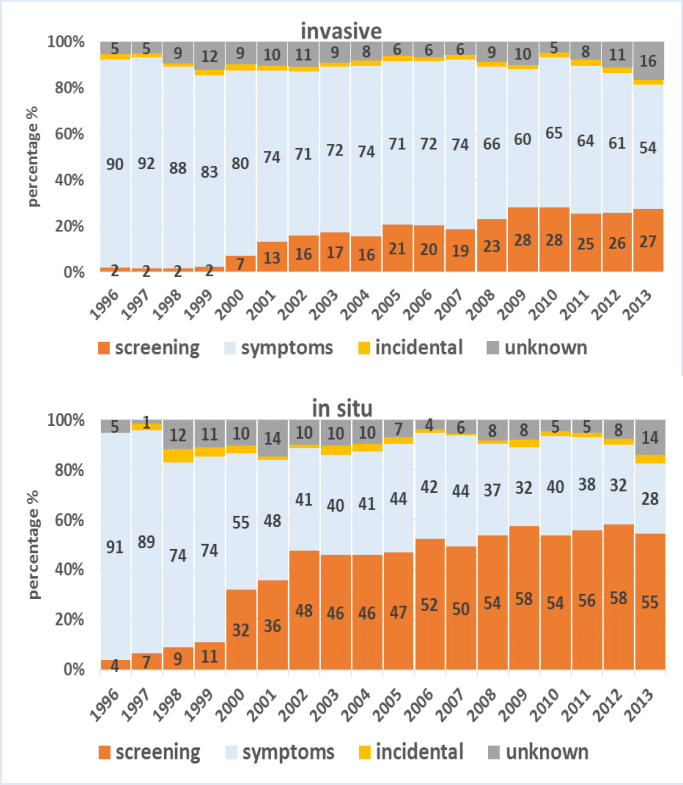


	age	to-from	APC	95%CI	trend
	<50	1994-2013	0.7%	[-0.2, 1.7]	↔
screened population	50-64	1994-1999	1.2%	[-0.7, 3.2]	↔
		1999-2002	9.9%	[2.0, 18.3]	↑
		2002-2005	-7.9%	[-14.1, -1.2]	↓
		2005-2008	10.0%	[2.8, 17.7]	↑
		2008-2013	- 1.6%	[-2.9, -0.3]	↓
	65-74	1994-2013	1.5%	[1.0, 2.0]	↑
	75+	1994-2013	1.5%	[1.0, 1.9]	↑

There were significant annual percentage increases in rates between 1994 and 2013 in all age categories apart from the <50 category, where rates were more static (Figure 7). There was a fairly consistent 1.5% annual increase in both the 65-74 and 75+ age categories. For the 50-64 age category, the trend was more complex, reflecting the roll-out of the national screening programme. In this group, an initial non-significant increase of 1.2% annually during 1994-1999 was followed by two periods of steeper increase (+9.9% per year 1999-2002 and +10.0% per year 2005-2008), each in turn followed by a significant decrease as rates stabilised.

ROUTE OF PRESENTATION

Figure 8. Route of presentation: 1996-2013



screening: includes organised (BreastCheck), opportunistic and unspecified screening

Before 2000 the national screening programme was not yet in place, and the proportions of breast cancer cases diagnosed through (mainly) opportunistic screening was <3% for invasive cancers, and ≤11% for in situ cases. After the initial implementation of BreastCheck, the proportion of cases presenting through screening began to increase, e.g. the proportion of invasive cases presenting through screening was 7% in 2000, 21% in 2005, and 28% in 2010 (Figure 8). For in situ cases, the proportion was 32%, 47% and 54% for the same years respectively.

In 2000, 80% of invasive cases and 55% of in situ cases presented with symptoms. By 2010 these proportions had decreased to 65% and 40% respectively, with further reductions subsequently. Proportions of cases presenting incidentally during other investigations or presenting through unknown routes have remained low (<4% and <11% respectively) for most years during 2003-2012.

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OTHER PATIENT AND TUMOUR CHARACTERISTICS

Table 2. Patient characteristics for invasive breast tumours

	1994-1998	1999-2003	2004-2008	2009-2013
TOTAL No.	8,132	10,144	11,979	14,157
AGE				
15-44	14.9%	13.6%	14.4%	13.2%
45-54	23.6%	24.3%	24.4%	25.5%
55-64	22.2%	26.4%	25.9%	26.9%
65-74	20.4%	17.6%	18.1%	17.2%
75+	19.0%	18.1%	17.3%	17.2%
MARITAL STATUS				
married	55.4%	58.3%	59.5%	59.7%
other	44.6%	41.7%	40.5%	40.3%
SMOKING STATUS				
never smoked	47.6%	46.6%	46.4%	44.2%
ex-smoker	7.9%	10.0%	13.0%	12.1%
current smoker	20.3%	19.3%	18.7%	14.8%
unknown	24.2%	24.2%	21.9%	28.9%
HSE AREA				
Dublin/Mid-Leinster	31.2%	31.3%	28.4%	28.6%
Dublin/North-East	19.3%	21.7%	20.3%	21.3%
South	25.8%	24.7%	26.9%	26.4%
West	23.8%	22.2%	24.4%	23.7%

Table 2 compares patient demographic variables and smoking status over four 5-year periods. The proportion presenting in the 45-64 age range increased over time due to screening. The highest proportion of patients were resident in the HSE Dublin/ Mid-Leinster area, the lowest in Dublin/North-East, and there were little change in the proportions resident in each HSE areas over the four periods.

Table 3. Tumour characteristics for incident breast tumours

	1994-1998	1999-2003	2004-2008	2009-2013
TOTAL No.	8,132	10,144	11,979	14,157
SITE OF TUMOUR				
nipple	2.3%	2.8%	1.6%	2.0%
central	13.6%	9.5%	7.5%	5.0%
upper inner quadrant	9.5%	8.6%	8.9%	10.5%
lower inner quadrant	4.4%	4.4%	4.6%	5.0%
upper outer quadrant	34.9%	34.0%	34.2%	32.8%
lower outer quadrant	7.0%	6.6%	6.1%	6.3%
axillary tail	0.6%	0.6%	0.5%	0.5%
overlapping	11.7%	15.0%	13.0%	12.8%
breast, NOS	16.1%	18.6%	23.5%	25.2%
SIDE OF TUMOUR				
left	49.0%	50.6%	51.0%	50.7%
right	46.0%	45.9%	47.4%	48.1%
bilateral	1.2%	0.8%	0.4%	0.4%
unknown	3.8%	2.8%	1.1%	0.9%
STAGE OF TUMOUR [6]				
stage I	21.0%	26.2%	30.7%	32.4%
stage II	48.8%	48.6%	44.4%	43.7%
stage III	13.5%	11.9%	12.7%	12.3%
stage IV	7.4%	6.7%	7.6%	6.4%
unknown	9.2%	6.6%	4.7%	5.2%
GRADE OF TUMOUR				
well differentiated	7.0%	9.9%	10.0%	10.7%
moderately differentiated	20.6%	34.5%	47.8%	51.6%
poorly/undifferentiated	28.6%	30.7%	33.0%	33.2%
unknown	43.7%	25.0%	9.2%	4.5%
MORPHOLOGY OF TUMOUR				
ductal adenocarcinoma	65.6%	67.6%	74.6%	76.4%
lobular carcinoma	12.1%	15.3%	15.5%	15.8%
other & NOS & unknown	22.3%	17.1%	9.9%	7.8%

Table 3 compares tumour characteristics over four 5-year periods. The greatest proportion of tumours occurred in the upper-outer quadrant of the breast (c.33%) or in the upper-inner quadrant (c.11%). There was a small preponderance of tumours of the left breast throughout (e.g. 51% left vs. 48% right during 2009-2013).

Grading of tumour was much more complete from 2004 onwards, coinciding with a major increase in the proportion of moderately differentiated tumours to 52% of cases in 2009-2013. For the period 2009-2013, >75% of tumours were ductal adenocarcinomas, c.16% were lobular tumours, and the proportion of other or unknown sub-types decreased over the four diagnostic periods.

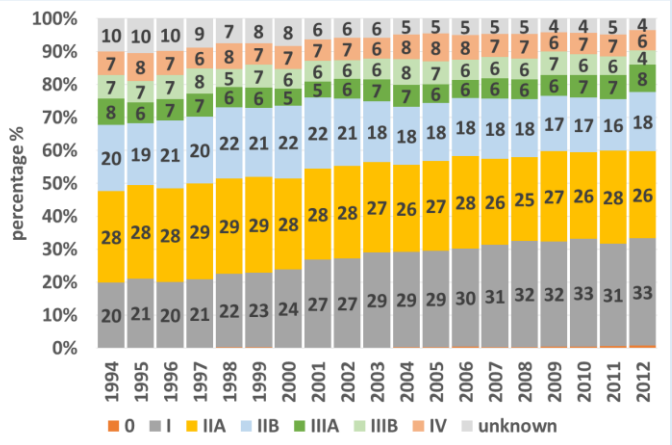
Table 4. Hormone receptor status for invasive breast tumours

	2004-2008	2009-2013
TOTAL No.	11,979	14,157
OESTROGEN RECEPTOR (ER)		
negative	18.3%	14.9%
positive	72.9%	80.6%
unknown	8.7%	4.5%
PROGESTERONE RECEPTOR (PR)		
negative	27.0%	28.0%
positive	51.2%	55.1%
unknown	21.9%	16.9%
OESTROGEN or PROGESTERONE (ER/PR)		
negative	16.4%	14.3%
positive	75.7%	81.8%
unknown	7.9%	3.8%

Hormone receptor status determines suitability for hormonal (endocrine) therapy. The information collected by the registry is presented in Table 4 for the period 2004 onwards as data were much less complete before this. During the period 2009-2013 81% of patients were known to be ER positive and 55% PR positive.

TUMOUR STAGE

Figure 9. Trend in stage of invasive breast cancer at diagnosis



TNM 5th edition [6]. Paget disease of the nipple with no underlying tumour is classed as stage 0 (in situ); other in situ breast cancers are not included

The most noticeable change during the period 1994 to 2013 was a consistent and gradual increase in the proportion of cases diagnosed at stage I, e.g. from 20% in 1994 to 29% in 2003 and to 33% in 2012 (Figure 9). The increase in stage I was accompanied by decreases in the proportions diagnosed at stage II (e.g. 48% in 1994 to 44% in 2013) and stage III (e.g. 15% in 1994 to 12% in 2013). There was little change in the proportions diagnosed at stage IV (7% in 1994 to 6% in 2013). The proportion of unstaged cases decreased from 10% in 1994 to 4% in 2013.

For a substantial number of cases, nodal status (N category) or distant metastatic status (M category) was coded 'unknown' – these were assumed to be 'N0' and 'M0' for stage-assignment purposes.

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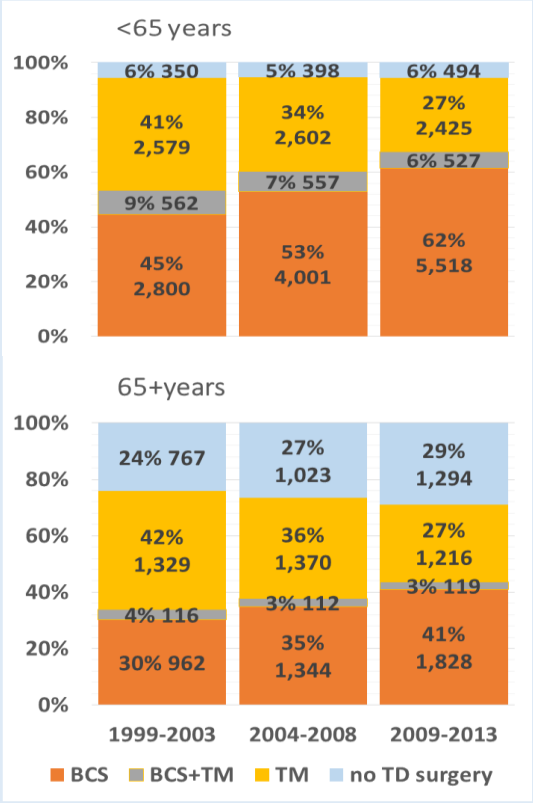
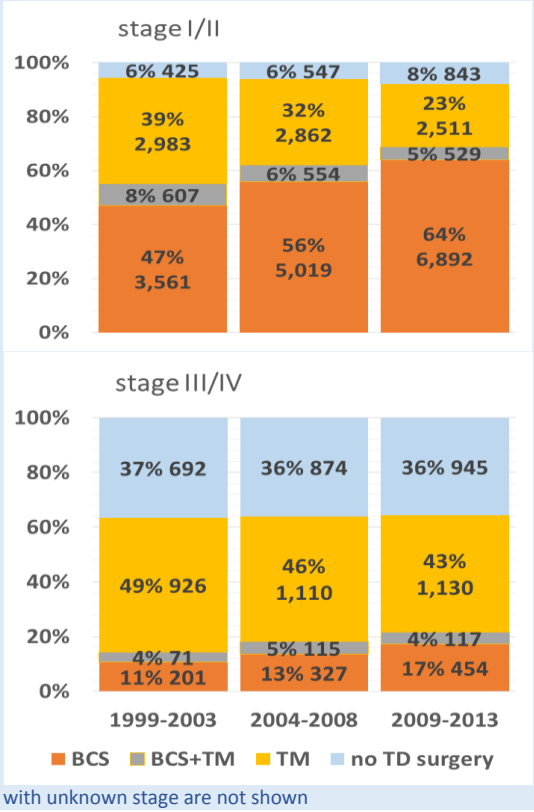
TREATMENT MODALITIES

Figure 10. Trend in surgery by age and diagnosis period : percentage and numbers of invasive BC patients



BCS=breast conserving surgery (at least one BCS operation), TM= mastectomy (total breast-removal), no TD surgery=no tumour directed surgery. Figures refer to patients who had surgery between one month before and one year after date of diagnosis

Figure 11. Trend in surgery by stage and diagnosis period: percentage and numbers of invasive BC patients



Patients with unknown stage are not shown

The most common treatment modality for breast cancer is surgery. Breast-conserving surgery (BCS) in tandem with radiotherapy is as effective as mastectomy in early stage breast cancer [7][8]. BCS enables faster recovery and obviates the need for reconstruction after mastectomy. However, some patients who have BCS require further surgery if the margins are not clear. Trends over three consecutive 5-year periods show that use of BCS increased consistently, and during 2009-2013 approximately twice as many surgical patients had BCS as had mastectomy. BCS was more common in younger women; e.g. during 2009-2013, 62% of patients under 65 years had BCS only, compared with 41% of older patients (65+).

For the 65+ group, there was a noticeable increase in the proportion who did not have tumour directed surgery; e.g. it increased from 24% during 1994-2003 to 29% during 2009-2013, whereas only 5-6% of younger patients did not have surgery for the same periods (Figure 10). This was probably due an increase in the more elderly subset (80+) from 34% during 1994-2003 to 43% during 2009-2013.

BCS was much more common in patients with stage I/II disease, where 64% of patients had BCS as their main surgery during 2009-2013, compared with only 17% of stage II/IV patients in the same period (Figure 11).

Table 5. Percentage of patients who received treatment‡

	1999-2003	2004-2008	2009-2013
surgery	85.5%	85.4%	84.5%
radiotherapy	62.0%	65.6%	68.7%
hormone therapy	48.7%	52.2%	55.1%
chemotherapy	49.4%	49.4%	46.8%

‡between 1 month before and 1 year after date of diagnosis

Throughout three 5-year intervals, the proportion of breast cancer patients who received treatment regimens with a surgical component remained at c.85% (Table 5). The proportion who had radiotherapy (either before/after surgery or without surgery) increased from 62% in 1999-2003 to 69% in 2009-2013. Use of hormone therapy (as part of a regimen or as a single agent) increased from 49% in 1999-2003 to 55% in 2009-2013. The proportion who had chemotherapy, as part of a regimen or as a single agent decreased slightly from 49% in 1999-2003 to 47% in 2009-2013 - most likely reflecting an increase in elderly patients.

Table 6. Trend in tumour-directed treatment combinations: mutually exclusive regimens

	1999-2003	2004-2008	2009-2013
Total No.	10,008	11,910	14,116
surgery, chemo & radiotherapy	21.3%	18.8%	16.9%
surgery & chemo & radio & hormone	14.0%	17.2%	19.2%
surgery & radio & hormone	13.7%	15.8%	18.0%
surgery & radiotherapy	8.9%	10.4%	11.3%
surgery only	7.2%	6.4%	5.7%
surgery & hormone therapy	9.6%	7.1%	5.7%
surgery & chemotherapy	6.6%	5.4%	4.0%
surgery & chemo & hormone	4.2%	4.3%	3.7%
hormone therapy only	5.0%	5.3%	6.3%
other treatments or combinations	5.5%	5.4%	5.0%
no tumour directed treatment	4.0%	3.8%	4.1%

Surgery (tumour-directed) = BCS or mastectomy or both; chemo = chemotherapy; radio = radiotherapy; hormone= hormone therapy. Order of treatments or whether treatment was given as neo-adjuvant is not specified. Window of analysis was from -1 month to 12 months after diagnosis date

Most cancer treatments are not administered in isolation but are given as part of a regimen with the aim of achieving therapeutic synergy. The most commonly administered treatment combinations

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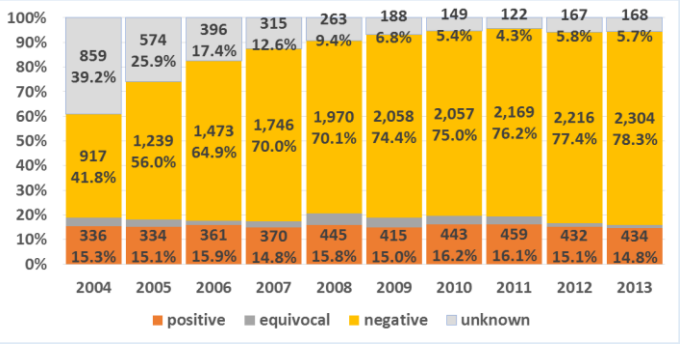
for breast cancer in 2009-2013 were surgery + chemotherapy + radiotherapy (SCR, 17%), and combined with hormone therapy (SCRH, 19%), the same combination bar chemotherapy (SRH, 18%), and surgery + radiotherapy (11%) (Table 6). Radiotherapy as sole modality was used for only c.1% of patients. Less than 7% of patients received hormone therapy as sole agent, but treatment combinations including hormonal therapy increased is use: SCRH from 14% of patients in 1999-2003 to 19% in 2009-2013, and SRH from 14% in 1999-2003 to 18% in 2009-2013. Figures for hormonal therapy here are minima, as outpatient prescriptions may be missed unless mentioned in hospital notes. The proportion of breast cancer patients who had no tumour-directed treatment was about 4% in all three periods examined, although these patients did receive other supportive and palliative treatments.

TREATMENT: HER2 status and trastuzumab

Figure 12. Trend in HER2 status: 2004-2013: cases and percentage diagnosed each year



Information on HER2 status (c-erbB-2 over-expression, associated with poorer prognosis) was first collected by the National Cancer Registry from about 2002. The proportion of cases with 'unknown' HER2 status decreased over time (Figure 12). During 2009-2013, c.15% of patients were HER2+ at diagnosis – a similar proportion as observed in south-east Wales, UK [9]. For <7% of cases there was insufficient information to assign a code. A small proportion of patients (<5%) were coded as equivocal, mostly cases with an immunochemistry score of 2+ (unless positivity was confirmed by a gene-amplification test).

Table 7. Trastuzumab (TZB) administration in patients diagnosed during 2011-2013, by HER2 status

HER2 status	patients	received TZB‡	TZB %
positive	1,325	865	65.3%
equivocal	178	9	5.1%
negative	6,687	69	1.0%
unknown	430	8	1.9%
Total	8,620	951	11.0%

‡ received at least one dose of TZB within 1 year after diagnosis

From 2011, the NCR has collected detailed information on all specific medical oncology drugs and regimens for newly diagnosed cancers. Trastuzumab (a monoclonal antibody) is indicated as treatment for early and metastatic breast cancer with HER2+ tumours, following surgery, chemotherapy and radiotherapy.

Of the breast cancer patients diagnosed in the 3-year period 2011-2013, approximately 11% received TZB overall (within a year after diagnosis), or 65% of the HER2+ subset, similar to the percentages observed in the south-east Wales (70.7%) and Trent cancer networks (69.7%) in the UK [10][11] (Table 7). Only small proportions of patients with negative, equivocal or unknown HER2 status received the drug, and in some of these cases HER2 status may have been misclassified if full details of HER2 testing were not available to NCR.

Table 8. Trastuzumab (TZB) administration in patients diagnosed during 2011-2013, by HER2 status and age

	AGE <65			AGE 65+		
HER2 status	patients	TZB	TZB %	patients	TZB	TZB %
positive	950	682	71.8%	375	183	48.8%
equivocal	101	6	5.9%	77	3	3.9%
negative	4,333	58	1.3%	2,354	11	0.5%
unknown	202	8	4.0%	228	0	-
Total	5,586	754	13.5%	3,034	197	6.5%

Younger patients (<65) were more likely to receive TZB; of the HER2+ group, 72% received TZB vs. 49% of the older subset (65+) (Table 8).

Table 9. Trastuzumab (TZB) administration in patients newly diagnosed during 2011-2013, by HER2 status and stage of disease

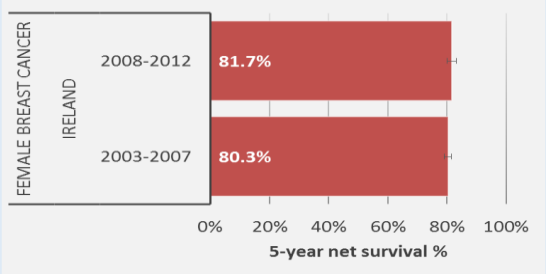
HER2 status	STAGE I			STAGE II		
	patients	TZB	TZB %	patients	TZB	TZB %
positive	318	186	58.5%	595	415	69.7%
equivocal	67	1	1.5%	71	2	2.8%
negative	2,223	7	0.3%	3,019	40	1.3%
unknown	173	2	1.2%	105	4	3.8%
Total	2,781	196	7.0%	3,790	461	12.2%
	STAGE III			STAGE IV		
	patients	TZB	TZB%	patients	TZB	TZB%
positive	213	152	71.4%	116	80	69.0%
equivocal	21	3	14.3%	12	3	25.0%
negative	748	16	2.1%	390	6	1.5%
unknown	26	0	-	51	2	3.9%
Total	1,008	171	17.0%	569	91	16.0%
	STAGE UNKNOWN					
	patients	TZB	TZB%			
positive	83	32	38.6%			
equivocal	7	0	-			
negative	307	0	-			
unknown	75	0	-			
Total	472	32	6.8%			

While 65% of the HER2+ subset received TZB overall, this proportion varied by stage: 59% for stage I, 70% for stage II, 71% for stage III, 69% for stage IV and 39% for the unstaged group (Table 9).

SURVIVAL

Net survival estimates to five years, including an assessment of recent survival changes and a breakdown by HSE area of residence, are presented in Figures 13-14. Net survival is calculated by comparing the observed survival of patients with the expected survival of persons of the same age and sex in the general population. It represents the cumulative probability of a patient surviving a given time in the hypothetical situation in which the cancer is the only possible cause of death.

Figure 13. Five-year net survival (age-standardised) and 95% confidence intervals for female breast cancer: 2003-2007 vs. 2008-2012



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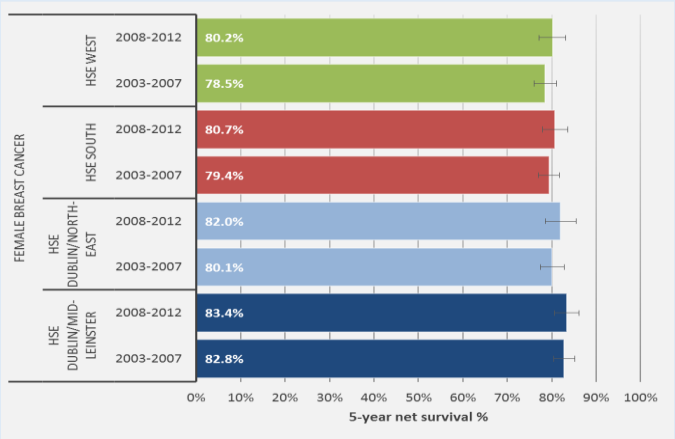
Only minor improvements in breast cancer survival were seen between 2003-2007 and 2008-2012, from 80% to 82% net survival at five years (Figure 13), with similar patterns at regional scale (Figure 14). This follows more substantial improvements in survival between the mid/late 1990s and early 2000s noted in a previous annual report of the NCR [12]. Regional variation was also quite small, although survival appeared to be higher among patients living in the Dublin/Mid-Leinster and Dublin/North-East regions. While the survival estimates were adjusted for age, they were not adjusted for stage distribution which could account for the minor differences between regions.

Figure 14. Percentage five-year net survival‡ and 95% confidence intervals by HSE area: breast cancer: 2003-2007 vs. 2008-2012



‡age-standardised

Further summaries of breast cancer survival in Ireland, including international comparisons, longer-term trends and stage-specific survival, are available from the EUROCARE-5 study [13], the NCR website for further details of stage by site, sex, age, stage and area of residence [14], and the NCR report for 1994-2012 [12].

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