Breast Cancer Incidence, Mortality, Treatment and Survival in Ireland: 1994-2009

National Cancer Registry Ireland

ABBREVIATIONS

Acronyms	
95% CI	95% confidence interval
APC	Annual percentage change
ASIR	Age standardised incidence rate (European standard population)
ASMR	Age standardised mortality rate (European standard population)
BC	Breast cancer
BCS	Breast conserving surgery
CSO	Central Statistics Office
DCO	Death certificate only (cases)
DNML	Dublin Mid Leinster
DNNE	Dublin North East
ECO	European Cancer Observatory
ENCR	European Network of Cancer Registries
GH	General hospital
HSE	Health Service Executive
ICD	International Statistical Classification of Diseases and Related Health Problems
NCR	National Cancer Registry
NOS	Not otherwise specified
RH	Regional hospital
RoI	Republic of Ireland
RR	Risk ratio
RS	Relative survival
SRR	Standardised rate ratio
UH	University hospital
WASIR	Age standardised incidence rate (World standard population)
XNOS	Unknown or not otherwise specified

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SUMMARY

This report examines patterns and trends of breast cancer incidence, mortality, treatment and survival in Ireland during the period 1994-2009.

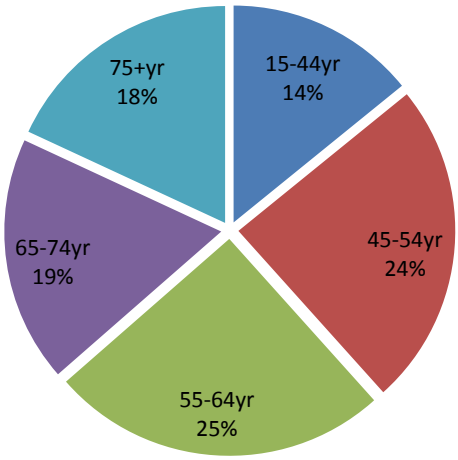
Incidence

One third of all invasive cancers (excluding non-melanoma skin cancer) in women were breast cancers, which makes this the most common tumour diagnosed in women (Table 1). Breast cancer was the second leading cause of cancer death in women (second only to lung cancer) during the period 2007-2009, and accounted for 16% of female cancer deaths. Approximately 2,670 women were diagnosed with breast cancer annually during 2007-2009. Irish females were reported to have a comparatively high incidence rate in the ECO estimates of cancer incidence for Europe in 2008.[29]

Table 1
Summary data for breast cancer in Ireland

	Females	Males
% of all new cancer cases, 2007-2009	17.3%	0.1%
% of all new cancer cases (excluding non melanoma skin cancer), 2007-2009	32.3%	0.2%
Average number of new cases per year, 2007-2009	2,673	20
Number of deaths during 2008	736	6
European age standardised incidence rate (per 100,000), 2007-2009	125.4	1.0
Annual percentage increase in incidence rate, 1994-2009	2.0%	2.2%
European age standardised mortality rate (per 100,000), 2008	31.8	0.3
APC in mortality rate, 1994-2009	-1.7%	-3.7%
15 year prevalence, 1994-2008[a]	20,827	123
10 year prevalence, 1999-2008[a]	17,041	107
5 year prevalence, 2004-2008[a]	10,403	72

Figure 1
Age distribution of incident female breast cancer cases diagnosis period: 1994-2009



Half of the women diagnosed with breast cancer were aged between 45 and 64 years (Figure 1). 14% of cases presented in those aged under 45 years, and 37% were aged 65 years and above.

The incidence rate for female breast cancer increased at 2% annually from 1994-2009, and the age-specific rate for the 50-64 age group increased at 8% annually during 2005-2009. This was probably due to the advent of organised screening in 2000. The proportion of patients diagnosed at stage I increased from 21% during 1994-1998 to 29% during 2004-2008, which was also probably due to the advent of organised screening.

[a] The number of persons still alive on 31/12/2008, who were diagnosed during the period shown

Mortality

736 women died from breast cancer in Ireland in 2008. This report presents evidence of a steady decline in mortality of almost 2% annually from 1990 to 2009. The ECO estimates of cancer deaths in 2008 showed Ireland to have the 4th highest breast cancer mortality rate of 30 European countries.[29]

Survival

Survival for women with breast cancer in Ireland was lower than the European average for the period 2000-2002; [36] this report highlights a trend towards significantly improved survival across the three diagnostic periods examined: 1994-1998, 1999-2003 and 2004-2008.

Treatment

Surgery is the first line treatment for breast cancer, both female and male. The proportion who received surgery (84%) did not change between 1999-2003 and 2004-2008. However, there was a significant increase in the proportion of women who received breast conserving surgery (38% during 1999-2003 *vs.* 45% during 2004-2008). The proportion of women who received radiotherapy increased from 49% during 1996-1998 to just over 60% for the period 1999-2008. The proportion of women who received chemotherapy increased from 36% during 1996-1998 to 50% during 1999-2008. The likelihood of a woman receiving surgery, radiotherapy or chemotherapy decreased with increasing age, especially in those aged greater than 65 years.

1. RISK FACTORS FOR BREAST CANCER

Table 2
Risk factors for female breast cancer, by strength of evidence

	Increases risk	Decreases risk
Convincing or probable	Family history; first degree relative(s) with breast cancer [1]	Breast feeding [15,16]
	Nulliparity and low parity [1,2]	Physical activity [15]
	Late age at first pregnancy [1,2]	Greater body fat (pre-menopausal breast cancer) [15]
	Late natural menopause [1,2]	Tamoxifen and raloxifene [17]
	Early menarche [1,2]	
	Oral contraceptives (oestrogen/progestogen combined pill) [3]	
	Hormone replacement therapy [3]	
	Exposure to diethylstilbestrol during pregnancy [3]	
	Greater body fatness, abdominal fatness and weight gain in adulthood (post-menopausal cancer) [4,5,6]	
	Alcohol [7,8]	
	Smoking [8]	
	Ionizing radiation [9, 10]	
	Benign breast disease [11]	
	High socio-economic status [12]	
Possible	Red meat (pre-menopausal cancer) [13]	Dairy foodstuffs [18]
	Higher (own) birth weight [14]	Isoflavones from soya foods [19]
		Vitamin D [20,21]
		Dietary fibre [22]
		Aspirin and other non steroidal anti-inflammatory drugs [23,24]

[1] Versonesi et al., 2005; [2] Key et al., 2001; [3] International Agency for Research on Cancer, 2011; [4] World Cancer Research Fund/ American Institute for Cancer Research, 2007; [5] Suzuki et al., 2009; [6] Vrieling et al., 2010; [7] Suzuki et al., 2008; [8] Secretan et al., 2009; [9] El Ghissassi et al., 2009; [10] Jansen-Van der Weide et al.,2010; [11] Zhou et al., 2011; [12] Faggiano et al., 1997; [13] Taylor et al., 2009; [14] Xu et al., 2009; [15] International Agency for Research on Cancer, 2002; [16] Collaborative Group on Hormonal factors in Breast Cancer, 2002; [17] Wickerham et al., 2009; [18] Dong et al., 2011a; [19] Dong & Qin, 2011; [20] Chen et al., 2010; [21] Yin et al., 2010; [22] Dong et al., 2011b; [23] Takkouche et al., 2008; [24] Zhao et al., 2009

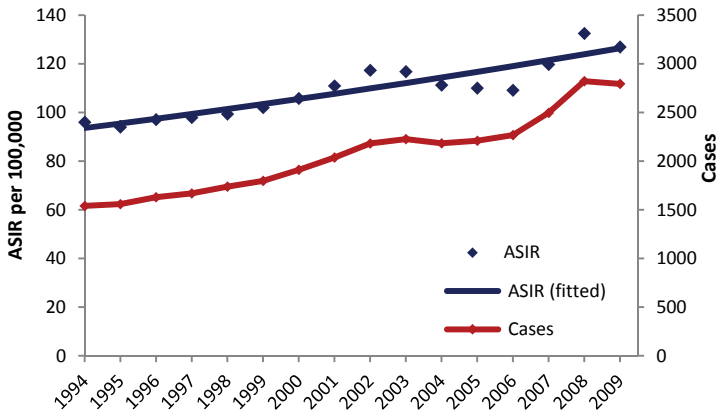
Breast cancer is a heterogeneous disease, comprising several distinct subgroups defined on the basis of hormonal receptor status and/or morphology. Recently interest has grown in distinguishing between risk factors for different subtypes. [5,6,8,25,26]

Up to 10% of breast cancer cases are hereditary and a woman's chance of developing breast cancer is increased if any of her first degree relatives had breast cancer, particularly if more than one relative was affected at a young age.[1] By age 70, women who carry BRCA1 gene mutations have a 65% chance of developing breast cancer, while those who carry BRCA2 mutations have a 45% risk.[27] Family history may interact with other factors to modify risk, for example, exposure to low doses of radiation such as x-rays [10] or history of benign breast disease.[11] Other than genetic factors, the major determinant of breast cancer risk is lifetime exposure to oestrogen.[1-3] Higher endogenous oestrogen exposure, as well as exogenous oestrogens, increases risk. In contrast, in pre-menopausal women at high risk of breast cancer, the anti-oestrogenic drugs tamoxifen and raloxifene reduce the chances of developing the disease by about half.[17]

2. INCIDENCE OF BREAST CANCER

2.1 Breast cancer incidence in Ireland

Figure 2
Number of cases and age standardised incidence rate (ASIR) of invasive female breast cancer: 1994-2009



Annual Percent Change (APC) in ASIR

from	to	APC	95%CI	trend*
1994	2009	2.0%	[1.5, 2.6%]	↑

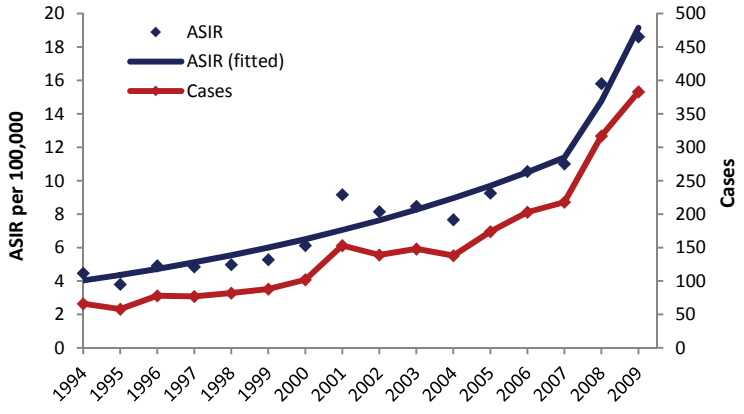
*↑ significant increase

Table 3
Incidence of invasive breast cancer: 1994-2009

	Females		Males	
YEAR	Cases	ASIR	Cases	ASIR
1994	1,539	96.0	14	0.8
1995	1,558	94.0	9	0.5
1996	1,629	97.1	17	1.0
1997	1,668	97.9	13	0.7
1998	1,738	99.3	8	0.5
1999	1,797	102.0	11	0.6
2000	1,911	105.7	15	0.8
2001	2,037	110.9	10	0.5
2002	2,181	117.3	15	0.8
2003	2,226	116.8	9	0.5
2004	2,183	111.2	15	0.7
2005	2,209	110.0	22	1.1
2006	2,267	109.1	23	1.1
2007	2,496	119.7	16	0.6
2008	2,822	132.5	18	0.8
2009	2,794	126.9	26	1.1
Total	**33,055**		**241**	

The total number of invasive female breast cancer cases recorded in the period 1994-2099 was 33,055 (Table 3). On average, 2,518 women were diagnosed with invasive breast cancer each year in the five years to 2009. The age standardised incidence rate of female breast cancer increased significantly, at 2.0% annually, between 1994 and 2009 (Figure 2).

Figure 3
Number of cases and age standardised incidence rates (ASIR) of female *in situ* breast cancer: 1994-2009



Annual percentage change (APC) in ASIR

from	to	APC	95%CI	trend*
1994	2007	8.3%	[6.0, 10.7%]	↑
2007	2009	29.7%	[3.8, 62.1%]	↑

*↑ significant increase

Table 4
Incidence of *in situ* female breast cancer: 1994-2009

year	Cases‡	ASIR
1994	66	4.5
1995	58	3.8
1996	78	4.9
1997	77	4.9
1998	82	5.0
1999	88	5.3
2000	102	6.1
2001	153	9.2
2002	139	8.2
2003	148	8.5
2004	138	7.7
2005	174	9.3
2006	203	10.6
2007	218	11.0
2008	317	15.8
2009	383	18.6
Total	**2,424**	

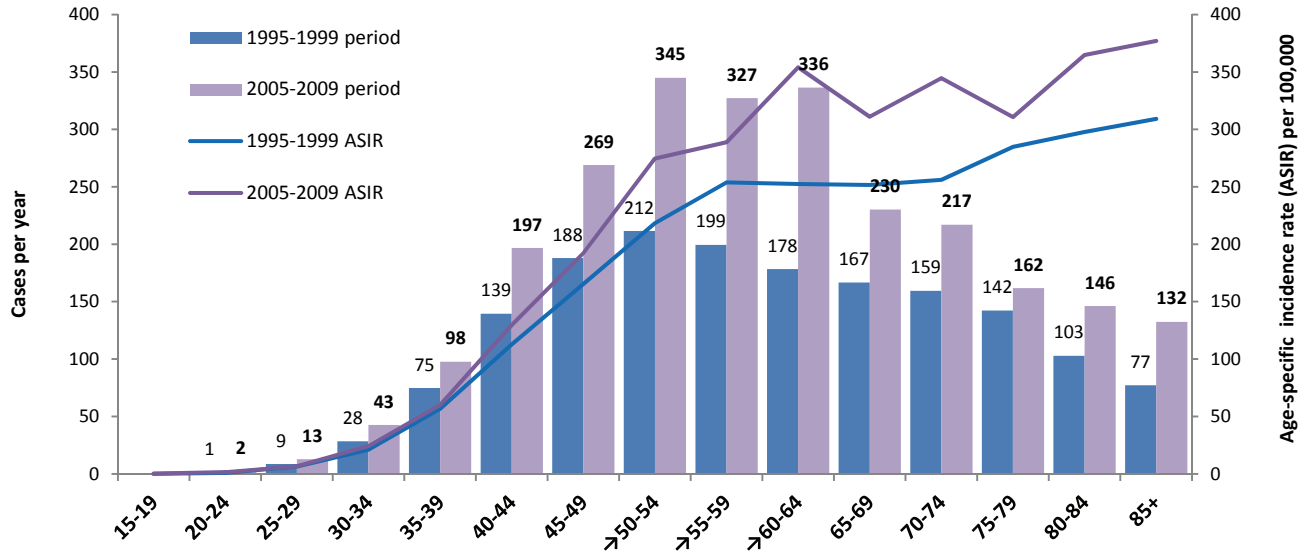
‡No prior or concomitant invasive breast tumours

On average, 260 women were diagnosed with an *in situ* breast neoplasm each year in the five years to 2009 (Table 4). The age standardised incidence rate of female *in situ* cancers increased significantly by 8% annually between 1994 and 2007 (Figure 3) and by 30% between 2007 and 2009. The latter increase was presumably due to the national roll-out of breast screening.

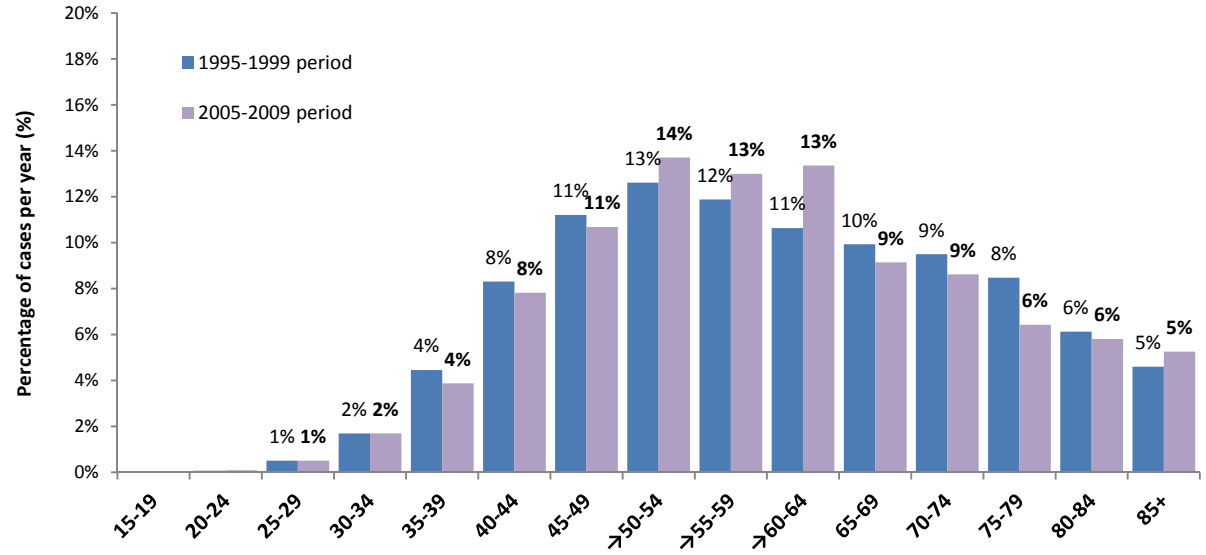
2.2 Incidence of breast cancer by age

Figure 4
Age-specific incidence of invasive female breast cancer: 1995-1999 & 2005-2009

(a) Number of cases by age group & age-specific incidence rate



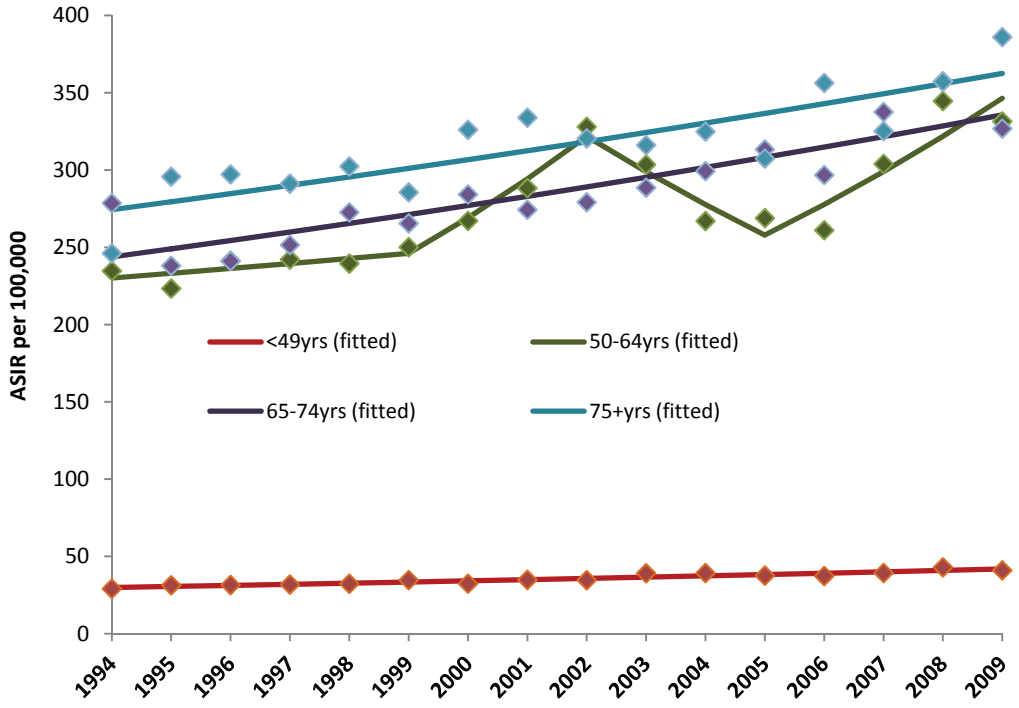
(b) Percentage (of the total) cases by age group



"→" identifies age groups covered by screening programme; initiated in February 2000 in the eastern half of the country and extended by 2007 to the rest of the country

The numbers of female cases presenting, and age-specific incidence rates in each 5-year age group are presented in Figure 4. The number of invasive breast cancers diagnosed during 1995-1999 was 8,390 (1,678/yr) and 12,588 (2,518/yr) during 2005-2009. The mean age of diagnosis in was 60.1 years during 1995-1999, and 59.6 years during 2005-2009. The number of cases was highest in the 50-54 age group. A higher percentage of cases was diagnosed within the 50-64 age group during 2005-2009 (40%) compared to 1995-1999 (36%), probably due to the start of the national breast screening programme in 2000.

Figure 5
Annual percentage change (APC) in age-specific incidence rate for female invasive breast cancer: 1994-2009



Points on graph indicate actual ASIR data
Lines indicate fitted trends (Joinpoint)[42]

Annual Percent Change (APC) in ASIR

age category	from	to	APC	95%CI	*trend
<49 yrs	1994	2009	2.3%	[1.8, 2.7%]	↑
50-64 yrs	1994	1999	1.4%	[-2.8, 5.7%]	↔
	1999	2002	9.4%	[-9.2, 31.7%]	↔
	2002	2005	-7.1%	[-22.9, 11.9%]	↔
	2005	2009	7.7%	[1.5, 14.2%]	↑
65-74yrs	1994	2009	2.2%	[1.5, 2.8%]	↑
75+yrs	1994	2009	1.9%	[1.2, 2.6%]	↑

*↑ =significant increase, ↓=significant decrease, ↔=no change

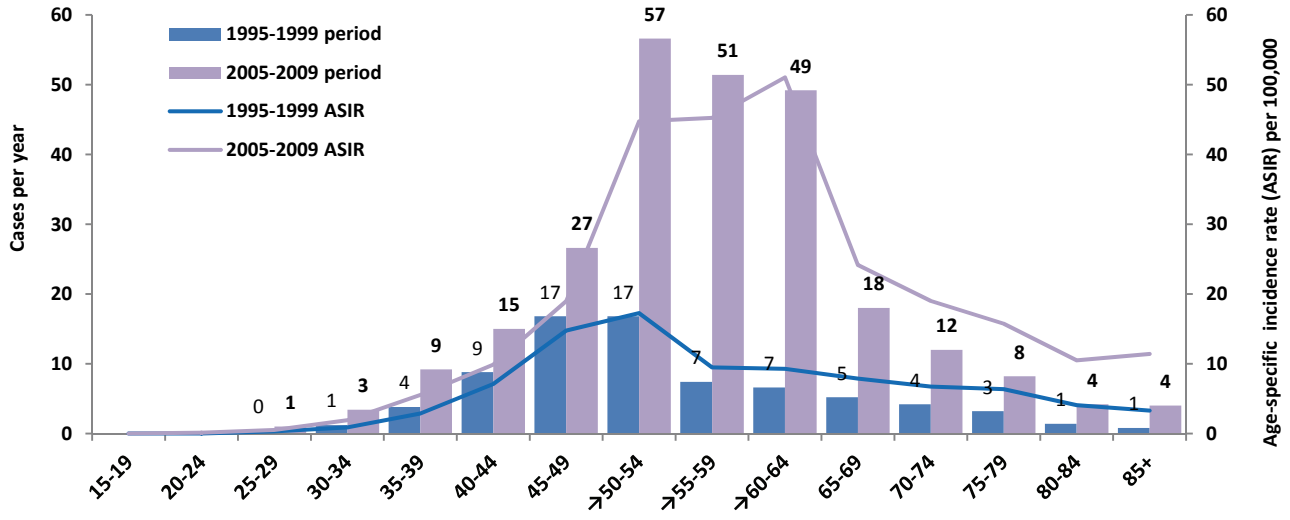
The annual percentage changes in age-specific incidence rates are presented in Figure 5. There were significant annual percentage increases between 1994 and 2009 in all age categories.

There was an annual 2.3% increase between 1994 and 2009 in the incidence rate for the youngest age group (<49 years) (27% of cases); of 2.2% in the 65-74 age group (18% of cases) and of 1.9% in the 75+ age group (18% of cases). The annual incidence rate varied significantly during 1994-2009 in the 50-64 age category (37% of cases). The annual percentage change in incidence from 1994 to 1999 was 1.4% and from 1999 to 2002, 9.4%. From 2002 to 2005 there was a 7.1% decrease, followed by a significant annual increase of 7.7% during 2005-2009.

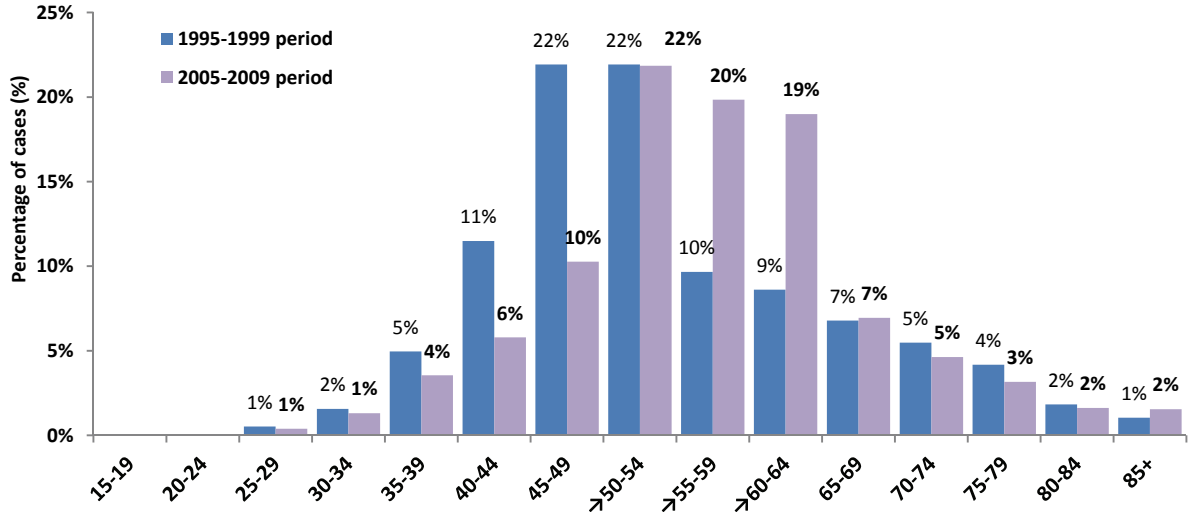
These changes in incidence rate in the 50-64 age category were probably due to the initiation of the national organised breast screening program in February 2000, and its extension nationwide by 2007.

Figure 6
Age-specific incidence of *in-situ* female breast cancer: 1995-1999 & 2005-2009‡

(a) Number of cases by age group & age-specific incidence rate



(b) Percentage (of the total) cases by age group



"→" identifies age groups covered by screening programme; initiated in February 2000 in the eastern half of the country and extended by 2007 to the rest of the country

‡Includes patients with *in-situ* tumours only; these women had no prior or concurrent invasive breast tumours

Age-specific case numbers and incidence rates for *in situ* breast cancers are presented in Figure 6.

The number of *in situ* breast cancers diagnosed during 1995-1999 was 77 annually and 259 annually in 2005-2009. The mean age of diagnosis for *in situ* cancer was 54.1 years during 1995-1999, and 56.6 years during 2005-2009. The number of cases was highest in the 50-54 age category (22% of cases).

A higher percentage of cases was diagnosed within the 50-64 age group during 2005-2009 (61%) compared to 1995-1999 (41%). This was probably due to the breast screening programme.

2.3 Summary of patient and tumour characteristics

Table 5
Summary of patient and tumour characteristics for incident breast cancer cases
Diagnostic periods 1994-1998, 1999-2003, 2004-2009

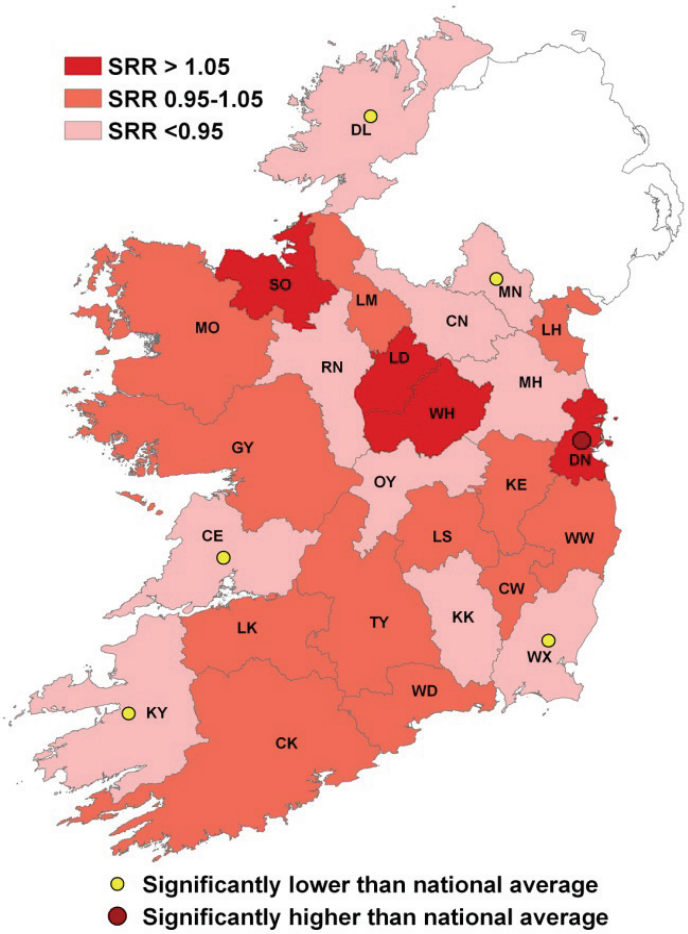
Variable	Category	1994-1998		1999-2003		2004-2009	
		cases	% of cases	cases	% of cases	cases	% of cases
	Total	**8,193**	**100%**	**10,212**	**100%**	**14,891**	**100%**
Age	15-44 yrs	1,220	15%	1,387	14%	2,084	14%
	45-54 yrs	1,924	23%	2,474	24%	3,626	24%
	55-64 yrs	1,816	22%	2,688	26%	3,880	26%
	65-74 yrs	1,678	20%	1,804	18%	2,663	18%
	75+ yrs	1,555	19%	1,859	18%	2,638	18%
Gender	Females	8,132	>99%	10,152	>99%	14,771	>99%
	Males	61	<1%	60	<1%	120	<1%
Marital status	Ever married	6,480	79%	8,242	81%	11,657	78%
	Never married	1,249	15%	1,568	15%	2,102	14%
	Unknown	464	6%	402	4%	1,132	8%
Smoking status	Never smoker	3,884	47%	4,735	46%	6,492	44%
	Ex smoker	646	8%	1,014	10%	1,796	12%
	Smoker	1,664	20%	1,963	19%	2,617	18%
	Unknown	1,999	24%	2,500	24%	3,986	27%
Deprivation quintiles	1 (Least deprived)	2,059	25%	2,569	25%	3,627	24%
	2	1,047	13%	1,486	15%	2,069	14%
	3	1,047	13%	1,343	13%	2,088	14%
	4	1,352	17%	1,721	17%	2,301	15%
	5 (Most deprived)	2,286	28%	2,795	27%	3,565	24%
	Unknown	402	5%	298	3%	1,241	8%
Site of tumour	Nipple	189	2%	293	3%	240	2%
	Central	1,128	14%	979	10%	1,019	7%
	Upper inner quadrant	774	9%	873	9%	1,256	8%
	Lower inner quadrant	355	4%	447	4%	644	4%
	Upper outer quadrant	2,843	35%	3,450	34%	4,731	32%
	Lower outer quadrant	571	7%	672	7%	850	6%
	Axillary tail	46	1%	57	1%	75	1%
	Overlapping	958	12%	1,535	15%	1,780	12%
	Breast, NOS	1,329	16%	1,906	19%	4,296	29%
Side	Left	4,014	49%	5,158	51%	7,426	50%
	Right	3,764	46%	4,684	46%	6,902	46%
	Both	97	1%	77	1%	51	<1%
	Unknown	318	4%	293	3%	512	3%
Tumour grade	Well differentiated	573	7%	1,010	10%	1,493	10%
	Moderately differentiated	1,698	21%	3,524	35%	7,024	47%
	Poorly differentiated	2,347	29%	3,124	31%	4,771	32%
	Unknown	3,575	44%	2,554	25%	1,603	11%

A summary of patient and tumour characteristics is presented above for patients diagnosed within the periods 1994-1998, 1999-2003 and 2004-2009 (Table 5). The variables are explored in more detail in the following sections. Some of the changes observed over time were:

- Increase in the proportion of cases presenting in the 55-64 year age group, with a decrease in the proportion presenting in the 65-74 and 75+ age groups.
- Increase in the proportion of cases microscopically verified at diagnosis.
- Increase in the proportion of ductal and lobular tumours, with a decrease in the proportion of tumours assigned to other, unspecified and unknown morphologies.
- Increase in the proportion of cases diagnosed at stage I, with a decrease in the proportion diagnosed at stage II.
- Decrease in the proportion of cases presenting symptomatically and an increase in cases presenting at screening.

2.4 Geographical variation in incidence

Figure 7
County-level variation in female breast cancer incidence
Standardised rate ratios (SRR) relative to incidence rate for Ireland: 2004-2009



Variation in breast cancer incidence at county level in 2004-2009 is presented in Figure 7.

Age standardised incidence rates (ASIR) were calculated for the period 2004-2009 for each county. The incidence rate in Ireland was 109 (95%CI: 107, 111) per 100,000 persons.[b] Standardised rate ratios (SRR) were calculated as the ratio between the ASIR in each country and the national ASIR.

The incidence rate in Dublin (118/100,000) was significantly higher than that for the country as a whole. Conversely, the rates in Donegal (89/100,000), Monaghan (93/100,000), Clare (94/100,000), Kerry (97/100,000) and Wexford (97/100,000) were significantly lower than the national average.

Counties are demarcated by largely arbitrary boundaries with great variation in population densities. Geographical variation in incidence rates may be better visualised by consulting the all-Ireland cancer atlas which describes incidence ratios at the level of approximately 3,500 electoral divisions in RoI, and 580 wards in Northern Ireland during 1995-2007.[28]

Table 6
Area of residence and number of breast cancer patients
Diagnostic periods 1994-1998, 1999-2003, 2004-2009

HSE area of residence	1994-1998		1999-2003		2004-2009	
	cases	% of cases	cases	% of cases	cases	% of cases
Dublin Mid Leinster	2,554	31%	3,204	31%	4,530	30%
Dublin North East	1,572	19%	2,215	22%	2,752	19%
South	2,108	26%	2,527	25%	3,968	27%
West	1,959	24%	2,266	22%	3,641	24%

The distribution of cases between HSE areas remained quite constant between 1994-1998 and 2004-2008, with about half living in the two eastern regions (Table 6).

[b] Appendix II statistical methods

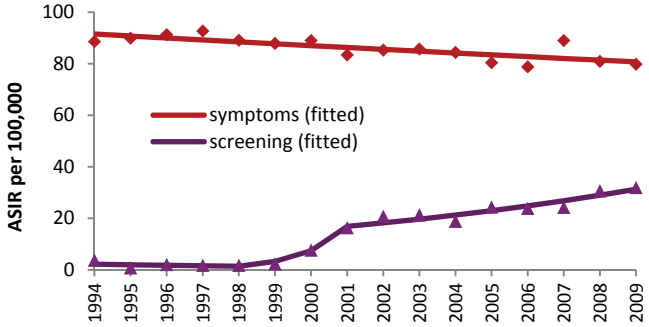
Table 7
Mode of presentation and number of breast cancer patients
Diagnostic periods 1994-1998, 1999-2003, 2004-2009

Presentation	1994-1998		1999-2003		2004-2009	
	cases	% of cases	cases	% of cases	cases	% of cases
Symptomatic	7,572	92%	8,033	79%	9,737	65%
Screen detected	149	2%	1,112	11%	2,801	19%
Unknown	472	6%	1,067	10%	2,353	16%

2.5 Mode of presentation

Most cases presented symptomatically (Table 7). However, there was a large increase between 1994-1998 (2%) and 2004-2009 (19%) in the percentage who were screen-detected.

Figure 8
Age standardised incidence rates (ASIR), observed and fitted, by mode of presentation in women with breast cancer: 1994-2009



Annual percentage change (APC)

Presentation	from	to	APC	95%CI	trend
symptoms	1994	2009	-0.8%	[-1.2, -0.5%]	↓
screening	1994	1998	-10.1%	[-39.8, 34.2%]	↔
	1998	2001	127.8%	[-35.8, 708.4%]	↔
	2001	2009	8.0%	[-5.9, 24.0%]	↔

Points indicate actual ASIR data.
Lines indicate fitted trends (Joinpoint)[42]

The age standardised incidence rates for cases diagnosed, by mode of presentation, are presented in Figure 8.

Presentation at screening increased and presentation with symptoms decreased during 1994-2009. The annual percentage change in the rate of presentation at screening was 128% during 1998-2001 and 8% during 2001-2009. The rate of presentation with symptoms decreased significantly, at 1% annually, during 1994-2009.

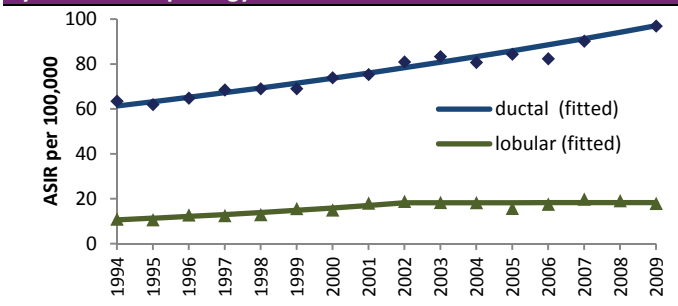
Table 8
Morphology and number of breast cancer patients
Diagnostic periods 1994-1998, 1999-2003, 2004-2009

Morphology	1994-1998		1999-2003		2004-2009	
	cases	% of cases	cases	% of cases	cases	% of cases
Ductal	5,379	65%	6,896	68%	11,111	75%
Lobular	982	12%	1,557	15%	2,249	15%
other adenocarcinoma	620	8%	661	6%	714	5%
other morphology	1,212	15%	1,098	11%	817	5%

2.6 Morphology

The number of cases assigned to each histological classification is shown in Table 8 and age standardised incidence rates in Figure 9.

Figure 9
Age standardised incidence rates (ASIR), observed and fitted, by tumour morphology: 1994-2009



Annual percentage change (APC)

Morphology	from	to	APC	95%CI	trend
ductal	1994	2009	3.1%	[2.7, 3.6%]	↑
lobular	1994	2002	7.0%	[4.5, 9.6%]	↑
	2002	2009	0.1%	[-2.8, 3.0%]	↔

Points on graph indicate actual ASIR data.
Lines indicate fitted trends (Joinpoint)[42]

The incidence rate of ductal tumours increased by 3% annually during 1994-2009 and that of lobular tumours by 7% annually during 1994-2002, with no increase thereafter (Figure 9).

The proportion of cases allocated to 'other morphologies' decreased from 15% to 5% in the periods 1994-1998 and 2005-2009 respectively (Table 8) which is probably reflective of more precise pathology laboratory reporting over the last 10 years.

2.7 Stage at diagnosis

Percentages of cases presenting at various stages of disease over the three diagnostic periods are presented in Table 9 and Figure 10.

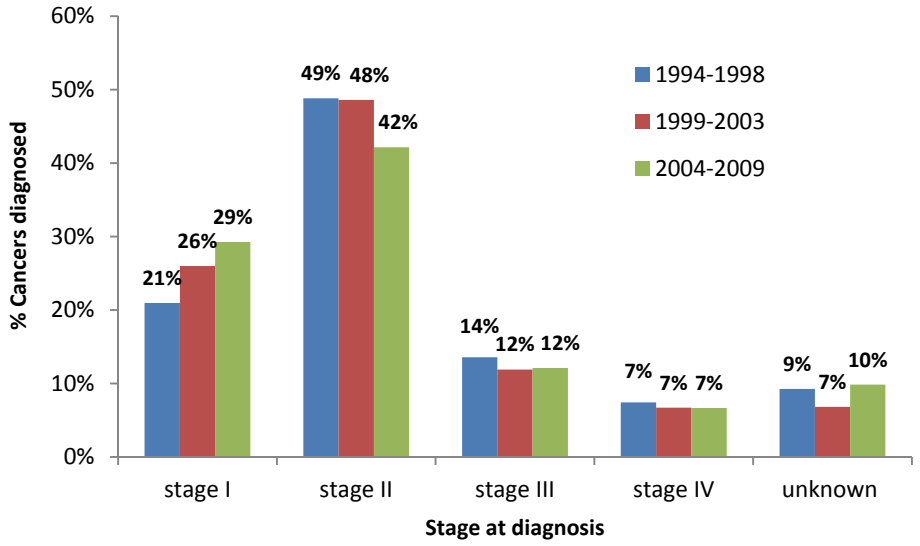
The proportions of cases presenting at stage I increased from 21% to 29% between 1994-1998 and 2004-2009. Conversely, the proportions presenting at stage II decreased from 49% to 42% for the periods 1994-1998 and 2004-2009 respectively. These changes may be accounted for by organised breast screening from 2000 onwards.

There was a marginal decrease in the proportion presenting at stage III (14% to 12% for periods 1994-1998 and 2004-2009 respectively) and no change for the proportion presenting at stage IV (7%).

Table 9
Stage at diagnosis and number of breast cancer patients
Diagnostic periods 1994-1998, 1999-2003, 2004-2009

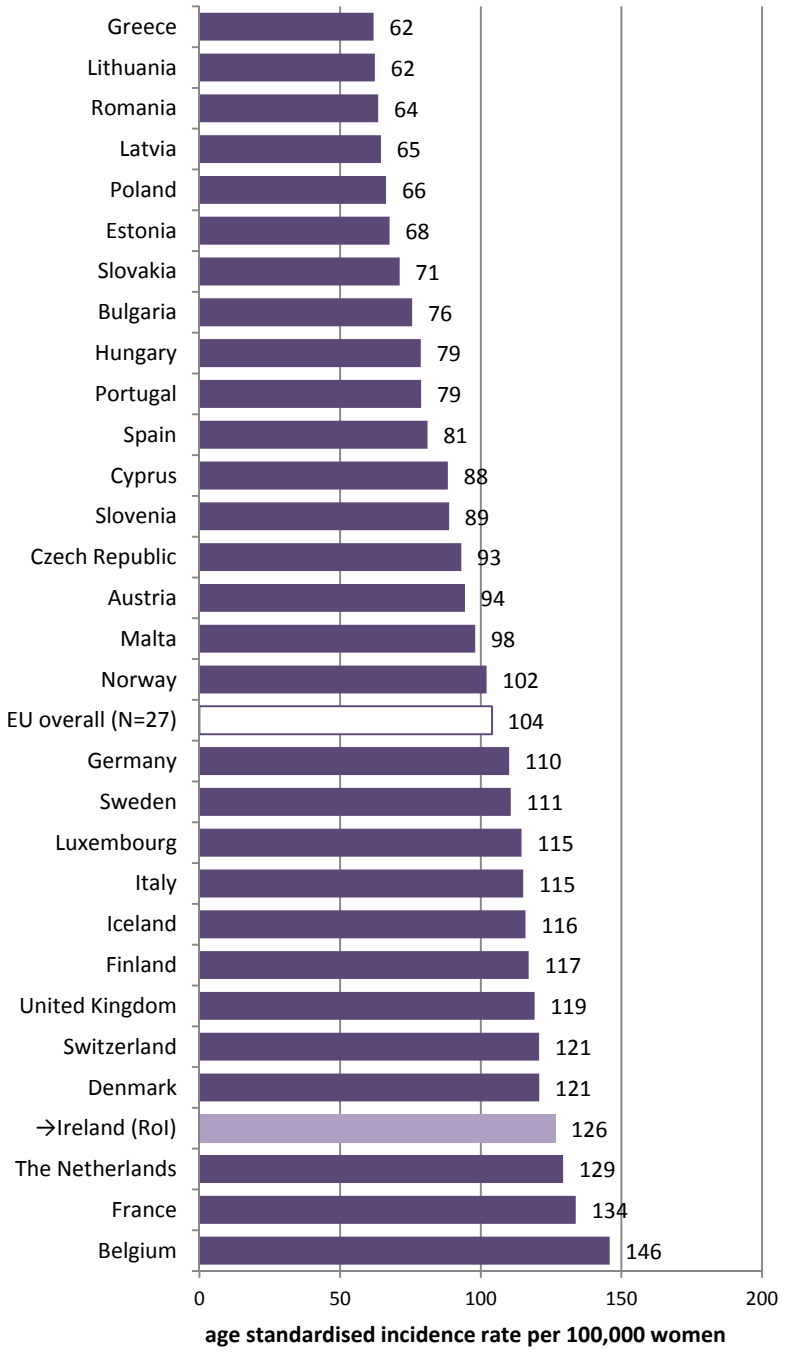
Variable	Category	1994-1998		1999-2003		2004-2009	
		cases	% of cases	cases	% of cases	cases	% of cases
Stage	Stage I	1,717	21%	2,654	26%	4,356	29%
	Stage II	3,999	49%	4,964	48%	6,278	42%
	Stage III	1,111	14%	1,215	12%	1,802	12%
	Stage IV	608	7%	684	7%	990	7%
	unknown	758	9%	695	7%	1,465	10%

Figure 10
Stage at diagnosis for female breast cancer patients
Diagnostic periods 1994-1998, 1999-2003, 2004-2009



2.8 International comparison of incidence

Figure 11
Estimated age standardised incidence rates (ASIR)‡ for invasive female breast cancer: 2008



Source: European Cancer Observatory (ECO) [29]
‡European standard population

Estimated age standardised incidence rates (ASIR) for 2008 are presented in Figure 11.[29]

Irish females had one of the highest incidence rates of the European countries shown, coming fourth highest (126/100,000 persons), and somewhat higher than our nearest neighbours in the United Kingdom (119/100,000). The overall mean incidence rate for the 27 member states of the EU was 104/100,000 which was significantly lower than that of Ireland.

In 2008 the ASIR for Ireland (126/100,000) was lower than that for Belgium (146/100,000), France (134/100,000) and the Netherlands (129/100,000). The five countries with the lowest incidence in 2008 were; Poland (66/100,000), Latvia (65/100,000), Romania (64/100,000), Lithuania (62/100,000) and Greece (62/100,000). However, it should be noted that these figures are estimates and many countries shown have either no, or very limited, registration of cancer.

2.9 The breast screening program and interval cancers

The aim of the *BreastCheck* screening programme is to reduce deaths from breast cancer by detecting breast cancers at an earlier stage. The screening program in Ireland is aimed at women in the age range 50-64 years and subscribes to European guidelines for quality assurance in breast cancer screening and diagnosis.[30] Invasive breast cancers detected in this population group in the interval between mammograms are referred to as *interval cancers*. In order for screening to be effective it is required that the detection of cancers occurring in the interval between screens (*interval cancers*) is relatively low. The effectiveness of a screening programme depends on both the sensitivity of the screening test and the frequency of screening. *Sensitivity* of the screening programme is estimated by dividing the number of screen detected cancers by the sum of screen detected and interval cancers.[30] The interval cancer rate almost doubled from 7.5/10,000 in the first year after screening to 13.7/10,000 in the second year after screening (Table 10).

Table 10
Number of screen detected and interval invasive cancers diagnosed in the period 2000-2009 for women aged 50-64 screened in the period 2000-2007

	Number of cases	Time since negative screen	
		0-11 months	12-23 months
Invasive cancers	3,223	2,187	506
Screen detected cancers	1,926	1,911	10
Interval cancers	772	276	496
Others (detected outside 2 year post screen period)	525		
Number of screens	372,633		
Woman years at risk	731,656	369,880	361,776
Background rate (per 10,000 woman years at risk)	27.9		
Interval cancer rate (per 10,000 woman years at risk)	10.6	7.5	13.7
Program sensitivity	0.71		
Proportionate incidence	38%	27%	48%

Proportionate incidence is another way of measuring interval cancers, where the incidence of interval cancer is expressed as a percentage of background incidence. The background incidence based on the years 1997-2002 was estimated to be 27.9/ 10,000 woman years. The *proportionate incidence* of interval cancer was 27% in the first year after screening, rising to 48% in the second year. Table 11 presents interval cancer detection rates from the Irish screening programme in comparison with those in neighbouring countries for which published estimates exist. In the first year after screening, the incidence of interval cancers in Ireland was highest (7.5/10,000 woman years) of the countries listed. This may be explained by the higher background incidence in Ireland compared to other countries.

Table 11
Interval cancer rate and proportionate incidence in Ireland and other regions

Region [31-35]	Time period	background incidence rate (prior to screening)	Time in since negative screen			
			Interval cancers: 0 - 11 months		Interval cancers: 12 - 23 months	
			rate	Proportionate incidence %*	rate	Proportionate incidence % *
East Anglia (England) [31]	1988-1993	22.0‡	5.2‡	24%	12.8‡	58%
Scotland [32]	1991-1995	22.0‡	4.8‡	22%	12.1‡	55%
Wales [33]	1989-1999	22.0‡	4.9‡	22%	9.0‡	41%
Netherlands [34]	1990-1993	23.2‡	6.2‡	27%	12.2‡	53%
Stockholm (Sweden) [35]	1989-1997	25.8^	7.3^	28%	13.8^	53%
Marseille (France) [35]	1993-1998	20.1^	5.4^	27%	12.1^	60%
Ireland (RoI)	2000-2007	27.9‡	7.5‡	27%	13.7‡	49%
	*interval cancer rate divided by the estimated background incidence ‡ cases per 10,000 woman years ^cases per 10,000 screens					

20% of interval cancers were less than 15mm in diameter, compared to 47% of screen detected cancers. A higher percentage (25%) of interval cancers had no information on size compared with screen detected cancers (15%). Only 9% of interval cancers were 'well differentiated' compared to 21% of screen detected cancers. This tendency to larger size and higher grade suggests that interval breast cancer was more aggressive than that detected through screening (Table 12).

Table 12
Characteristics of interval and screen detected invasive cancers for women screened in the period 2000-2007

		size of invasive cancer			Level of differentiation (Grade)			
	Number of cases	**≤15mm**	**>15mm**	**Unknown**	**well**	**moderate**	**poor**	**Unknown**
Interval	772	20%	55%	25%	9%	37%	44%	10%
Screen detected	1,926	47%	38%	15%	21%	53%	21%	5%
Total	**2,648**	**39%**	**43%**	**18%**	**18%**	**48%**	**28%**	**6%**

3. TREATMENT

3.1 Treatment received[c]

Primary course of treatment was defined as receipt of any: surgery, radiotherapy, chemotherapy or hormone therapy within one year of diagnosis date. Information on BCS, chemotherapy, radiotherapy and hormone therapy was not available for the years 1994 and 1995. In the following sections, 'treatment' refers to primary course of treatment only.

Table 13
Surgery received by breast cancer patients
Number and percentage of female patients in receipt of surgery: 1996-1998, 1999-2003, 2004-2008

	1996-1998		1999-2003		2004-2008		Change in case fraction: 1999-2008	
	patients/yr	%	patients/yr	%	patients/yr	%	APC	*trend
Breast conserving surgery	-	-	769	38%	1,074	45%	13.6	↑
Mastectomy	-	-	938	46%	938	39%	-5.4	↓
No surgery	294	18%	324	16%	384	16%	-0.8	↔
Total	**1,678**	**100%**	**2,031**	**100%**	**2,396**	**100%**		

*trend over 1996-2008: ↑=significant increase, ↓=significant decrease, ↔=no change
- BCS/Mastectomy figures were not available during 1996-1998

The proportions of patients who had different types of breast surgery are presented in Table 13. During 2004-2008, 84% of cases had a resection, 45% as breast conserving surgery (BCS). There was a significant annual percentage increase of 14% in the proportion who had BCS during 1999-2008. Conversely, the proportion who had mastectomy (39%) showed an annual decrease of 5% during the same period.

Table 14
Treatment received by female breast cancer patients†
Number and percentage of patients in receipt of treatment: 1996-1998, 1999-2003, 2004-2008

	1996-1998		1999-2003		2004-2008		Change in case fraction: 1996-2008	
	patients/yr	%	patients/yr	%	patients/yr	%	APC	*trend
Surgery	1,384	82%	1,707	84%	2,012	84%	0.1	↔
Radiotherapy	830	49%	1,238	61%	1,489	62%	2.1	↑
Chemotherapy	603	36%	995	49%	1,196	50%	3.1	↑
Hormone	909	54%	964	47%	1,188	50%	-0.6	↔
No treatment	104	6%	112	6%	123	5%	-1.6	↔
Total†	**1,678**		**2,031**		**2,396**			

†Treatments were not mutually exclusive
*trend over 1996-2008: ↑=significant increase, ↓=significant decrease, ↔=no change

The proportions of patients who had different types of treatment during 1996-2008 are presented in Table 14.

During the period 2004-2008, 62% of cases underwent radiotherapy, 50% underwent chemotherapy, 50% underwent hormone therapy, and 5% had no tumour directed therapy. The proportion who underwent radiotherapy increased significantly, at 2% annually, during the period 1996-2008, and the proportion who underwent chemotherapy increased by 3% annually over the same period.

[c] Appendix II: Treatment definitions

The most common treatment combinations during 2004-2008 were surgery, radiotherapy & chemotherapy (18%) and surgery, radiotherapy, chemotherapy and hormone treatment (17%) (Table 15). Use of the latter combination increased by 3.3% annually between 1999 and 2008. Combinations consisting of surgery & radiotherapy (with or without other modalities) made up 59% of treatments during 2004-2008, compared to 44% during 1996-1998. Combinations consisting of surgery & chemotherapy (as the main modalities) made up 46% of treatments during the years 2004-2008 compared to 33% during the years 1996-1998.

Table 15
Treatment received by female breast cancer patients†
Number and percentage of patients in receipt of treatment: 1996-1998, 1999-2003, 2004-2008

	1996-1998		1999-2003		2004-2008		10yr change in case fraction: 1999-2008		
All treatment options†	**patients/yr**	**%**	**patients/yr**	**%**	**patients/yr**	**%**	**APC**	**95%CI**	***trend**
Surgery/ radiotherapy/chemo	203	12%	430	21%	431	18%	-2.5	[-6.5, 1.7]	↔
Surgery/ radiotherapy/chemo/hormone	173	10%	279	14%	400	17%	**3.3**	[1.3, 5.3]	↑
Surgery/ radiotherapy/ hormone	231	13%	268	13%	324	14%	0.5	[-1.8, 2.9]	↔
Surgery/ radiotherapy	145	9%	178	9%	242	10%	2.4	[-0.6, 5.5]	↔
Surgery	162	10%	144	7%	177	7%	0.1	[-2.3, 2.4]	↔
Surgery/ hormone	295	17%	191	9%	166	7%	**-6.0**	[-7.8, -4.1]	↓
Surgery/ chemotherapy	97	6%	132	7%	150	6%	0.0	[-2.9, 2.9]	↔
Surgery/ chemotherapy/ hormone	79	5%	84	4%	122	5%	**3.7**	[0.2, 7.4]	↑
Hormone	88	5%	100	5%	117	5%	-0.5	[-2.9, 1.8]	↔
Chemotherapy	14	1%	22	1%	32	1%	**3.9**	[0.1, 7.7]	↑
Radiotherapy	27	2%	21	1%	27	1%	0.0	[-8.7, 9.5]	↔
Radiotherapy/ chemotherapy	17	1%	27	1%	26	1%	-4.5	[-10.8, 2.1]	↔
Radiotherapy/ hormone	24	1%	22	1%	23	1%	-3.1	[-7.7, 1.8]	↔
Chemotherapy/ hormone	10	1%	8	<1%	19	1%	**11.4**	[1.12, 2.7]	↑
Radiotherapy/ chemo/ hormone	9	1%	13	1%	17	1%	2.0	[-4.5, 9.0]	↔
No treatment	104	6%	112	6%	123	5%	-0.1	[-4.4, 4.5]	↔
Total	**1,678**	**100%**	**2,031**	**100%**	**2,396**	**100%**			

†Treatment options were mutually exclusive
*trend during 1999-2008: ↑=significant increase, ↓=significant decrease, ↔=no change

3.2 Region of surgery

Table 16
HSE-area of breast surgery relative to HSE area of residence
Diagnostic periods 1999-2003 & 2004-2008

HSE area of residence	HSE area of surgery			
	DNML	**DNNE**	**South**	**West**
	1999-2003			
DNML	91%	8%	-	1%
DNNE	26%	74%	-	-
South	15%	4%	78%	3%
West	30%	5%	4%	62%
	2004-2008			
DNML	89%	9%	-	1%
DNNE	23%	77%	-	-
South	12%	5%	80%	3%
West	11%	2%	3%	84%

The proportion of patients who underwent tumour resection, by HSE area of residence and HSE area of treatment, is presented in Table 16.

Almost all cases resident in the two eastern HSE areas had their surgery within one of these areas. 20% of cases resident in HSE South and 16% of those resident in HSE West travelled to other HSE areas for their surgery during 2004-2008.

3.3 Hospital caseload: surgery

Table 17
Female breast cancer surgical caseload by hospital
Diagnostic periods 1996-1998, 1999-2003, 2004-2008

	1996-1998		1999-2003		2004-2008	
	resections ‡/yr	%	resections ‡/yr	%	resections ‡/yr	%
Total	**1,575**	**100%**	**1,942**	**100%**	**2,273**	**100%**
St. Vincent's Private Hospital, DN	83	5%	188	10%	291	13%
South Infirmary Hospital, CK	65	4%	93	5%	221	10%
Mater Misericordiae UH, DN	82	5%	175	9%	221	10%
University College Hospital, GY	106	7%	106	5%	197	9%
Mater Private Hospital, DN	65	4%	114	6%	116	5%
St. James's Hospital, DN	58	4%	104	5%	103	5%
Tallaght Regional Hospital, DN	8	1%	96	5%	99	4%
Cork University Hospital, CK	23	1%	73	4%	93	4%
St. John's Hospital, LK	38	2%	64	3%	84	4%
Beaumont Hospital, DN	57	4%	62	3%	83	4%
St. Vincent's UH, DN	159	10%	114	6%	81	4%
Our Lady of Lourdes Hospital, LH	38	2%	49	3%	75	3%
Waterford Regional Hospital, WD	51	3%	63	3%	73	3%
Sligo General Hospital, SO	28	2%	44	2%	64	3%
Letterkenny General Hospital, DL	38	2%	35	2%	59	3%
Mayo General Hospital, MO	27	2%	40	2%	51	2%
Bon Secours Hospital, CK	53	3%	55	3%	48	2%
Mid-Western Regional Hospital, LK	29	2%	25	1%	44	2%
Tralee General Hospital, KY	37	2%	49	3%	41	2%
Other hospitals	530	35%	393	20%	229	10%

‡Counts of surgical resections performed within 1 year of diagnosis, by hospital. Figures include multiple resections performed on the same woman. Biopsies were not counted.

Surgical resections received within one year of diagnosis were deemed to be part of the primary course of treatment. The annual average number of breast cancer resections performed is presented for each diagnostic period, by hospital, in Table 17. The hospitals listed may have carried out further surgical procedures after the 1st anniversary of diagnosis, but these were not counted.

The bulk of breast surgery (90%) was carried out in 19 hospitals during 2004-2008. St Vincent's Private Hospital accounted for 13% of cases in 2004-2008. Other hospitals with more than 5% of cases in 2004-2008 were: South Infirmary Cork (10%), Mater Public Hospital (10%), UCH Galway (9%), Mater Private Hospital (5%) and St James's Hospital (5%).

Of the larger Dublin hospitals, only St Vincent's University Hospital showed a decrease in the number of surgical cases over time; down from 10% during 1996-1998 to 4% during 2004-2008. Tallaght Regional Hospital took some share of caseload, commencing breast surgery in the period 1999-2003 (5%).

3.4 Hospital caseload: radiotherapy

Table 18
Female breast cancer radiotherapy caseload by hospital
Diagnostic periods: 1996-1998, 1999-2003, 2004-2008

Diagnostic period	1996-98		1999-03		2004-08	
	sessions‡/yr	%	sessions‡/yr	%	sessions‡/yr	%
Total	**977**	**100%**	**1,331**	**100%**	**1,696**	**100%**
St. Luke's hospital, DN	469	48%	691	52%	560	33%
Cork University Hospital, CK	133	14%	250	19%	372	22%
Mater Private Hospital, DN	111	11%	217	16%	313	18%
University College Hospital, GY	13	1%	-	-	157	9%
St. Vincent's Private Hospital, DN	81	8%	166	12%	95	6%
Mid-Western Radiation Oncology Unit, LK	-	-	-	-	85	5%
Other private hospitals/clinics	11	1%	-	-	103	6%
Other hospitals	159	16%	7	1%	11	1%

‡Counts of radiotherapy sessions administered within 1 year of diagnosis, by hospital. Figures include multiple sessions administered to the same woman.

Radiotherapy sessions administered within one year of diagnosis were deemed to be part of the primary course of treatment. The annual average number of radiotherapy sessions performed is presented for each diagnostic period, by hospital, in Table 18. The hospitals shown may have administered further radiotherapy after the 1st anniversary of diagnosis, but these sessions were not counted. The bulk of radiotherapy services for breast cancer (93%) was provided by six hospitals over the period 2004-2008. St Luke's Hospital provided most radiotherapy sessions, albeit this share fell from 52% in 1999-2003 to 33% in 2004-2008. This fall may be accounted for by the introduction of radiotherapy at UCH Galway (9%) and the Mid-Western Radiation Oncology Unit, Limerick (5%).

3.5 Hospital caseload: chemotherapy

Table 19
Female breast cancer chemotherapy caseload by hospital
Diagnostic periods: 1996-1998,1999-2003, 2004-2008

Diagnostic period	1996-98		1999-03		2004-08	
	administrations‡/yr	%	administrations‡/yr	%	administrations‡/yr	%
Total	**705**	**100%**	**1,099**	**100%**	**1,430**	**100%**
St. Vincent's Private Hospital, DN	53	7%	105	10%	123	9%
South Infirmary Hospital, CK	33	5%	57	5%	98	7%
Waterford Regional Hospital, WD	24	3%	59	5%	94	7%
University College Hospital, GY	39	6%	73	7%	93	6%
St. Vincent's UH, DN	90	13%	103	9%	90	6%
Mater Misericordiae UH, DN	41	6%	62	6%	83	6%
Mid-Western RH, LK	8	1%	36	3%	77	5%
Tallaght Regional Hospital, DN	-	-	4	<1%	77	5%
Mater Private Hospital, DN	30	4%	65	6%	67	5%
St. James's Hospital, DN	28	4%	90	8%	64	4%
Cork University Hospital, CK	29	4%	59	5%	63	4%
Beaumont Hospital, DN	26	4%	64	6%	55	4%
Letterkenny General Hospital, DL	12	2%	18	2%	51	4%
General Hospital Tullamore, OY	1	<1%	19	2%	49	3%
Our Lady of Lourdes Hospital, LH	16	2%	32	3%	46	3%
Mayo General Hospital, MO	3	<1%	15	1%	41	3%
Sligo General Hospital, SO	5	1%	16	1%	41	3%
The Galway Clinic, GY	-	-	-	-	34	2%
Tralee General Hospital, KY	7	1%	25	2%	27	2%
Wexford General Hospital, WX	5	1%	13	1%	26	2%
Bon Secours Cork, CK	24	3%	28	3%	25	2%
Other hospitals	231	33%	156	14%	106	7%

‡Counts of chemotherapy administrations given within 1 year of diagnosis, by hospital. Figures include multiple administrations given to the same woman.

Chemotherapy administrations received within one year of diagnosis were deemed to be part of the primary course of treatment. The annual average number of chemotherapy sessions administered is presented for each diagnostic period, by hospital, in Table 19. The hospitals shown may have administered further chemotherapy after the 1st anniversary of diagnosis, but these sessions were not counted.

During 2004-2008, St Vincent's Private Hospital provided the largest number of chemotherapy administrations (9%). Other hospitals with significant chemotherapy caseload were South Infirmary Cork (7%), Waterford RH (7%), UCH Galway (6%), St Vincent's UH (6%), Mater MUH (6%), MWRH Limerick (5%), Tallaght Regional Hospital (5%), and the Mater Private Hospital (5%).

Other hospitals with less than 5% of national caseloads in 2004-2008 included: St James's Hospital (4%), Cork University Hospital (4%), Beaumont Hospital (4%) and Letterkenny General Hospital (4%).

The bulk of chemotherapy services (93%) were provided by 21 hospitals during 2004-2008. MWRH Limerick (5%) and Tullamore GH (3%) were more recent significant providers of chemotherapy services.

3.6 Factors associated with receipt of treatment

The patient and tumour factors associated with tumour directed treatment were identified and are presented in Tables 20-27. *Treatment* was defined as receipt of any: surgery, radiotherapy, chemotherapy or hormone therapy within one year of diagnosis date. A *risk ratio (RR)* less than 1.0 indicates a lesser likelihood of treatment relative to the baseline level of a variable (1.0). Similarly, a risk ratio greater than 1.0 indicates a greater likelihood of treatment after adjusting for the other variables in the models.[d]

Table 20
Age group and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Age group	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
15-44	3,847	93%	1.00		72%	1.00		77%	1.00		42%	1.00	
45-54	6,555	94%	0.99	[0.95, 1.04]	69%	**0.95**	[0.90, 0.99]	66%	**0.92**	[0.88, 0.97]	46%	**1.07**	[1.01, 1.14]
55-64	6,923	92%	0.98	[0.94, 1.02]	68%	**0.93**	[0.89, 0.98]	51%	**0.75**	[0.71, 0.79]	49%	**1.13**	[1.07, 1.20]
65-74	4,927	84%	**0.94**	[0.90, 0.99]	57%	**0.82**	[0.78, 0.87]	32%	**0.45**	[0.42, 0.48]	54%	**1.24**	[1.17, 1.32]
75+	4,912	51%	**0.64**	[0.61, 0.67]	27%	**0.49**	[0.46, 0.53]	8%	**0.12**	[0.11, 0.14]	56%	**1.41**	[1.32, 1.51]

Risk ratios were adjusted for stage, grade, mode of presentation, deprivation, area of residence and period of diagnosis
Risk ratios in bold are significantly different from baseline (1.0)

Age had a strong influence on whether a patient received any of the four treatments listed. With each increment in age group the likelihood of receiving surgery, chemotherapy or radiotherapy diminished significantly (Table 20). For example, only 8% of patients >75 years received chemotherapy compared to 77% of patients aged 15-44, (RR=0.12, 95%CI: 0.11, 0.14). Conversely, for hormone therapy, the likelihood of treatment increased with each increment in age group. Only 27% of patients aged >75 years received radiotherapy compared to 72% of patients aged 15-44 years (RR=0.49 95%CI: 0.46, 0.53).

[d] Appendix II: Statistical methods

Table 21
Stage of disease and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Stage of disease	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
I	7,313	94%	1.00		62%	1.00		27%	1.00		42%	1.00	
II	12,649	94%	1.00	[0.97, 1.03]	63%	**1.06**	[1.02, 1.10]	59%	**2.08**	[1.98, 2.19]	52%	0.98	[0.94, 1.03]
III	3,384	81%	**0.90**	[0.86, 0.94]	67%	**1.25**	[1.19, 1.32]	62%	**2.36**	[2.21, 2.51]	50%	**0.93**	[0.88, 0.99]
IV	1,927	34%	**0.38**	[0.35, 0.41]	43%	**1.10**	[1.01, 1.19]	50%	**2.42**	[2.21, 2.64]	48%	**0.89**	[0.82, 0.96]
unknown	1,891	35%	**0.43**	[0.39, 0.47]	25%	**0.74**	[0.67, 0.82]	17%	**1.18**	[1.04, 1.33]	23%	**0.55**	[0.49, 0.61]

Risk ratios were adjusted for age, grade, mode of presentation, deprivation, area of residence and period of diagnosis

Stage of disease was strongly associated with treatment receipt (Table 21). The likelihood of receiving surgery decreased with more advanced stage. Only 34% of cases diagnosed at stage IV received surgery compared to 94% of cases diagnosed at stage I (RR=0.38, 95%CI: 0.35, 0.41). The likelihood of receiving radiotherapy increased with more advanced stage. 67% of cases with stage III received radiotherapy compared to 62% of cases at stage I (RR=1.25, 95%CI: 1.19, 1.32). Similarly, the likelihood of receiving chemotherapy increased with more advanced stage. 62% of cases at stage III received chemotherapy compared with only 27% of cases at stage I (RR=2.36, 95%CI: 2.21, 2.51).

Table 22
Tumour grade and treatment modalities in female breast cancer: 1996-2008

Tumour grade		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
(Differentiation)	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
Well	2,568	91%			65%			27%	1.00		56%	1.00	
Moderately	10,297	89%	-	- -	63%	-	- -	47%	**1.46**	[1.35, 1.59]	56%	0.96	[0.91, 1.02]
Poorly	8,436	90%	-	- -	65%	-	- -	64%	**1.77**	[1.63, 1.92]	42%	**0.73**	[0.69, 0.78]
Unknown	5,863	61%	-	- -	42%	-	- -	32%	**1.36**	[1.24, 1.49]	46%	**0.82**	[0.77, 0.88]

Risk ratios were adjusted for age, stage, mode of presentation, deprivation, area of residence and period of diagnosis

Cases with poorly differentiated tumours were more likely to receive chemotherapy compared with cases with well differentiated tumours (64% vs. 27% respectively, RR=1.77, 95%CI: 1.63, 1.92) (Table 22).

Table 23
Mode of presentation and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Presentation	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
Symptomatic	21,208	84%			59%	1.00		49%	1.00		54%	1.00	
screening	3,459	96%	-	- -	73%	**1.05**	[1.01, 1.11]	40%	**0.84**	[0.79, 0.89]	48%	**0.92**	[0.87, 0.98]
Unknown	2,497	68%	-	- -	47%	0.94	[0.88, 1.00]	35%	**0.85**	[0.79, 0.91]	16%	**0.37**	[0.33, 0.41]

Risk ratios were adjusted for age, stage, deprivation, area of residence and period of diagnosis

Cases who presented at screening were more likely to receive radiotherapy compared to cases presenting symptomatically (73% *vs.* 59% respectively, RR=1.05, 95%CI: 1.01, 1.11) and less likely to receive chemotherapy (40% *vs.* 49% respectively, RR=0.84, 95%CI: 0.79, 0.89) (Table 23).

Table 24
Deprivation and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Deprivation	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
1 Least	6,893	85%			61%			47%			46%	1.00	
2	3,866	85%	-	- -	61%	-	- -	49%	-	- -	49%	1.05	[0.99, 1.11]
3	3,725	84%	-	- -	59%	-	- -	49%	-	- -	49%	1.02	[0.96, 1.08]
4	4,482	84%	-	- -	59%	-	- -	47%	-	- -	53%	1.05	[0.99, 1.11]
5 Most	7,263	82%	-	- -	58%	-	- -	46%	-	- -	52%	**1.09**	[1.03, 1.14]
Unknown	935	80%	-	- -	53%	-	- -	42%	-	- -	45%	**0.99**	[0.90, 1.10]

Risk ratios were adjusted for age, stage, grade, mode of presentation, area of residence and period of diagnosis

Cases from the most deprived quintile of population were more likely to receive hormone therapy compared to the least deprived quintile (52% *vs.* 46% respectively, RR=1.09 95%CI: 1.03, 1.14) (Table 24). Deprivation was not influential on whether a patient received surgery, radiotherapy or chemotherapy.

Table 25
Area of residence and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Residence	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
DNML	8,217	83%	-	- -	57%	1.00		46%	-	- -	43%	1.00	
DNNE	5,596	85%	-	- -	65%	**1.15**	[1.10, 1.20]	45%	-	- -	39%	**0.90**	[0.85, 0.95]
South	7,015	83%	-	- -	62%	**1.10**	[1.06, 1.15]	48%	-	- -	60%	**1.29**	[1.23, 1.35]
West	6,336	83%	-	- -	55%	0.99	[0.95, 1.04]	48%	-	- -	56%	**1.21**	[1.16, 1.27]

Risk ratios were adjusted for age, stage, grade, mode of presentation, deprivation and period of diagnosis

Cases living in DNNE (RR=1.15 95%CI: 1.10, 1.20) and South (RR=1.10 95%CI: 1.06, 1.15) were more likely to receive radiotherapy (65% and 62% respectively) relative to DNML (57%) (Table 25). Hormone treatment was significantly more common in HSE South (RR=1.29 95%CI: 1.23, 1.35) and West (RR= 1.21 95%CI: 1.16, 1.27) compared to DNML.

Table 26
Period of diagnosis and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Period	Cases	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI	yes%	risk ratio	95% CI
1996-1998	5,035	82%	-	- -	49%	1.00		36%	1.00		54%	1.00	
1999-2003	10,152	84%	-	- -	61%	**1.18**	[1.13, 1.24]	49%	**1.38**	[1.30, 1.45]	47%	**0.88**	[0.84, 0.93]
2004-2008	11,977	84%	-	- -	62%	**1.18**	[1.13, 1.24]	50%	**1.42**	[1.35, 1.50]	50%	**0.89**	[0.85, 0.94]

Risk ratios were adjusted for age, stage, grade, mode of presentation, deprivation and area of residence

Cases diagnosed during 2004-2008 were more likely to receive radiotherapy compared to cases diagnosed during 1996-1998 (62% *vs.* 49% respectively, RR=1.18 95%CI: 1.13, 1.24) (Table 26). Similarly, cases diagnosed during 2004-2008 were more likely to receive chemotherapy relative to cases from 1996-1998 (50% *vs.* 36%, RR=1.42 95%CI: 1.35, 1.50). Conversely, cases from 2004-2008 were less likely to receive hormone therapy than cases diagnosed during 1996-1998 (50% *vs.* 54% respectively, HR 0.89 95%CI: 0.85, 0.94).

Table 27
Surgery and treatment modalities in female breast cancer: 1996-2008

		Surgery			Radiotherapy			Chemotherapy			Hormone therapy		
Surgery	**Cases**	**yes%**	**risk ratio**	**95% CI**	**yes%**	**risk ratio**	**95% CI**	**yes%**	**risk ratio**	**95% CI**	**yes%**	**risk ratio**	**95% CI**
no	4,418	0%			25%	1		22%	1.00		45%	-	- -
yes	22,746	100%			66%	**1.84**	[1.71, 1.98]	52%	**1.37**	[1.26, 1.49]	51%	-	- -

Risk ratios were adjusted for age, stage, grade, mode of presentation, deprivation, area of residence and period of diagnosis

Cases who received surgical resection were more likely to receive radiotherapy relative to cases who received no resection (66% *vs.* 25% respectively, RR=1.84 95%CI: 1.71, 1.98) (Table 27). Similarly, cases who received surgery were more likely to receive chemotherapy relative to cases who did not receive surgery (52% *vs.* 22% respectively, RR=1.37 95%CI: 1.26, 1.49).

4. SURVIVAL

4.1 Comparison of survival over three diagnostic periods

Observed survival is simply the proportion remaining alive after a given period of time. *Relative survival (RS)* is the ratio of the observed survival proportion for a given group of cancer cases to the expected survival proportion of a group of individuals with the same demographic attributes. In practice, relative survival is similar to *cause-specific survival*—it measures the excess mortality due specifically to the cancer, and so is always greater than observed survival. Relative survival is now used by most cancer registries in place of *cause-specific survival* because the actual cause of death in any given cancer case is not always known. Relative survival also facilitates international comparison, as it reduces problems related to international inconsistency in coding cause of death. Autopsy-only cases, DCO cases, *in-situ* cases, breast cancers concomitant with another invasive malignancy and breast cancers incident during 2009 were excluded for survival analysis (Table 41).

Table 28
Percentage survival for breast cancer
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
females	1994-98	90.7%	[90.0,91.3%]	66.1%	[65.1,67.2%]
n=29,286	1999-03	93.1%	[92.6,93.6%]	74.0%	[73.1,74.8%]
	2004-08	94.4%	[94.0,94.8%]	77.8%	[76.8,78.8%]
males	1994-98	79.3%	[66.5,87.7%]	46.6%	[33.4,58.7%]
n=202	1999-03	87.7%	[76.0,94.0%]	70.2%	[56.5,80.3%]
	2004-08	90.8%	[82.5,95.3%]	65.3%	[49.4,77.3%]
	RELATIVE SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
females	1994-98	90.6%	[89.7,91.5%]	71.8%	[70.2,73.3%]
n=29,286	1999-03	93.1%	[92.3,93.8%]	78.2%	[76.8,79.5%]
	2004-08	94.1%	[93.4,94.7%]	81.4%	[79.7,83.0%]
males	1994-98	85.0%	[69.8,92.9%]	59.3%	[38.8,74.9%]
n=202	1999-03	91.3%	[75.8,97.1%]	87.9%	[58.5,96.9%]
	2004-08	95.4%	[84.5,98.7%]	84.5%	[56.7,95.1%]

Observed and relative survival estimates at 1 year and 5 years post-diagnosis are presented for breast cancer cases in Ireland across three periods: 1994-1998, 1999-2003 and 2004-2008 in (Table 28, Figure 12).

There was a steady improvement in female relative survival at one (91%, 93% and 94%) and five years (72%, 78% and 81%) across the three diagnostic periods 1994-1998, 1999-2003, 2004-2008 respectively (Table 28). Similar, but not statistically significant, trends were seen for male breast cancer.

Figure 12
Percentage survival for female breast cancer: Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

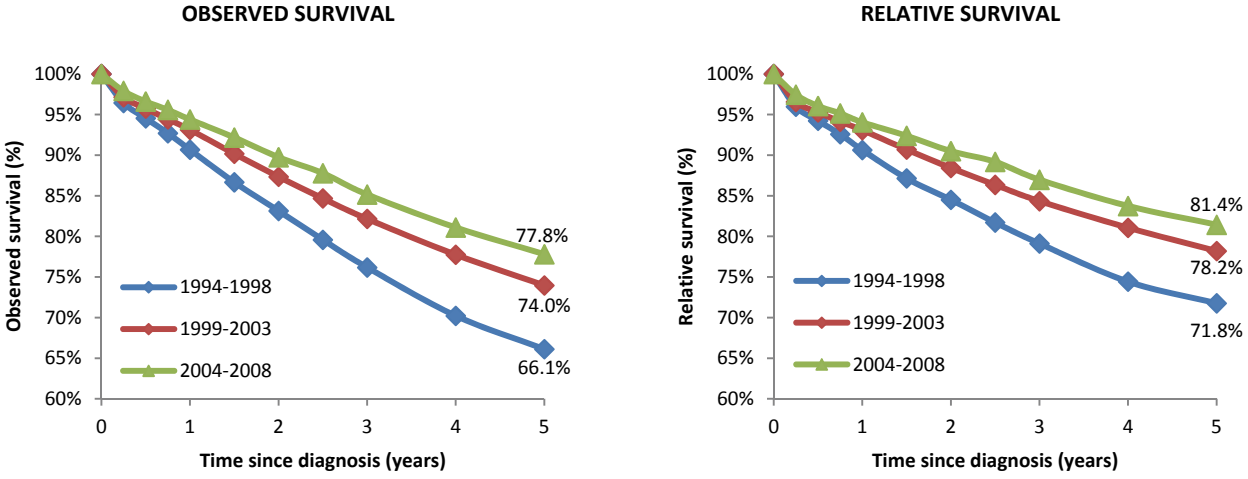


Table 29
Percentage survival for female breast cancer
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
age at diagnosis	**Period**	**1-year**	**95% CI**	**5-year**	**95% CI**
15-44 yr	1994-98	96.5%	[95.3,97.4%]	76.0%	[73.5,78.3%]
	1999-03	98.0%	[97.1,98.6%]	82.9%	[80.7,84.7%]
	2004-08	98.8%	[98.1,99.2%]	85.1%	[82.6,87.3%]
45-54 yr	1994-98	96.3%	[95.3,97.0%]	77.9%	[76.0,79.7%]
	1999-03	97.2%	[96.4,97.8%]	84.5%	[83.0,85.9%]
	2004-08	98.5%	[97.9,98.8%]	88.2%	[86.5,89.7%]
55-64 yr	1994-98	93.5%	[92.3,94.6%]	69.7%	[67.5,71.8%]
	1999-03	95.9%	[95.1,96.6%]	80.7%	[79.1,82.1%]
	2004-08	96.9%	[96.2,97.4%]	84.8%	[82.9,86.6%]
65-74 yr	1994-98	88.9%	[87.3,90.4%]	63.0%	[60.6,65.3%]
	1999-03	91.6%	[90.2,92.8%]	69.6%	[67.3,71.7%]
	2004-08	92.8%	[91.6,93.8%]	74.5%	[71.8,76.9%]
75+yr	1994-98	76.8%	[74.5,78.9%]	41.2%	[38.7,43.8%]
	1999-03	80.5%	[78.5,82.3%]	45.2%	[42.8,47.5%]
	2004-08	82.2%	[80.4,83.8%]	48.7%	[45.5,51.8%]
	RELATIVE SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
15-44 yr	1994-98	96.6%	[95.4,97.5%]	76.4%	[73.9,78.8%]
	1999-03	98.1%	[97.1,98.7%]	83.3%	[81.2,85.2%]
	2004-08	98.8%	[98.2,99.3%]	85.6%	[83.0,87.8%]
45-54 yr	1994-98	96.5%	[95.6,97.3%]	79.2%	[77.2,81.0%]
	1999-03	97.4%	[96.7,98.0%]	85.7%	[84.2,87.1%]
	2004-08	98.7%	[98.2,99.1%]	89.4%	[87.7,90.9%]
55-64 yr	1994-98	94.2%	[92.9,95.3%]	72.8%	[70.5,74.9%]
	1999-03	96.5%	[95.7,97.2%]	83.6%	[82.0,85.1%]
	2004-08	97.4%	[96.7,98.0%]	87.6%	[85.6,89.4%]
65-74 yr	1994-98	90.9%	[89.2,92.4%]	71.6%	[68.9,74.2%]
	1999-03	93.2%	[91.8,94.5%]	77.2%	[74.7,79.5%]
	2004-08	94.1%	[92.9,95.2%]	81.1%	[78.2,83.7%]
75+yr	1994-98	83.7%	[81.2,86.0%]	67.0%	[62.8,71.1%]
	1999-03	87.2%	[85.1,89.2%]	70.6%	[66.8,74.3%]
	2004-08	88.2%	[86.3,90.0%]	72.6%	[67.9,77.3%]

Observed and relative survival (RS) were calculated at one year and five years post-diagnosis by age group (Table 29).

For cases diagnosed in the most recent period, 2004-2008, 1 year relative survival remained in excess of 95% up to age 64. Thereafter, RS fell to 94% and 88% for the 65-74 and 75+ age groups respectively. Similarly, 5 year survival remained in excess of 85% up to age 64. Thereafter, it fell to 81% and 73% for the 65-74 and 75+ age groups respectively.

There was a steady improvement in survival over time for all age groups. Taking the age group with the highest incidence (55-64 years), 1 year relative survival increased from 94% during 1994-1998 to 97% for cases diagnosed during 2004-2008, and 5 year survival increased from 73% to 88% for the same periods.

In the youngest age group (15-44 years), 1 year relative survival increased from 97% to 99% from 1994-1999 to 2004-2008 respectively, and 5 year relative survival increased from 76% to 86% respectively for the same periods.

Table 30
Percentage survival for female breast cancer
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
Stage I	1994-98	98.0%	[97.2,98.6%]	84.5%	[82.7,86.1%]
	1999-03	98.5%	[97.9,98.9%]	90.0%	[88.8,91.1%]
	2004-08	99.0%	[98.6,99.3%]	92.1%	[90.7,93.3%]
Stage II	1994-98	95.4%	[94.7,96.0%]	71.2%	[69.8,72.6%]
	1999-03	96.9%	[96.4,97.4%]	80.1%	[78.9,81.2%]
	2004-08	97.8%	[97.4,98.2%]	84.1%	[82.6,85.4%]
Stage III	1994-98	85.3%	[83.0,87.3%]	47.9%	[44.9,50.8%]
	1999-03	89.1%	[87.2,90.8%]	52.2%	[49.3,55.0%]
	2004-08	91.8%	[90.2,93.1%]	61.8%	[58.2,65.2%]
Stage IV	1994-98	55.0%	[50.9,58.9%]	18.0%	[15.0,21.2%]
	1999-03	59.8%	[56.0,63.4%]	21.4%	[18.4,24.6%]
	2004-08	66.3%	[63.0,69.4%]	25.8%	[21.9,29.9%]
	RELATIVE SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
Stage I	1994-98	99.6%	[92.3,100%]	93.6%	[89.5,96.2%]
	1999-03	99.8%	[42.6,100%]	96.2%	[92.5,98.1%]
	2004-08	100.0%	[-]	96.1%	[91.2,98.3%]
Stage II	1994-98	96.2%	[95.0,97.1%]	77.6%	[75.3,79.8%]
	1999-03	97.6%	[96.5,98.3%]	85.0%	[82.9,86.8%]
	2004-08	98.7%	[97.7,99.2%]	89.5%	[86.7,91.7%]
Stage III	1994-98	84.6%	[81.8,87.0%]	51.2%	[47.2,55.1%]
	1999-03	90.2%	[87.9,92.2%]	58.7%	[54.8,62.4%]
	2004-08	91.4%	[89.3,93.2%]	66.4%	[61.4,71.0%]
Stage IV	1994-98	54.2%	[49.9,58.3%]	19.4%	[15.9,23.2%]
	1999-03	58.6%	[54.4,62.4%]	22.0%	[18.5,25.7%]
	2004-08	65.7%	[62.2,68.9%]	28.1%	[23.7,32.8%]

Observed and relative survival was calculated at one year and five years post diagnosis by stage of disease (Table 30).

The proportion alive at 1 and 5 years decreased with each increment in stage. In the most recent period, 2004-2008, relative survival at 1 year was almost 100% for stage I tumours and 99% for stage II tumours compared to 91% and 66% for stage III and IV tumours respectively.

In the same period, relative survival at 5 years was 96% for stage I tumours and 90% for stage II tumours compared to 66% and 28% for stage III and IV tumours respectively.

There was an increase in 5 year relative survival over time for all stages; RS increased from 78% to 90% for stage II cases, 51% to 66% for stage III cases and 19% to 28% for stage IV cases during the periods 1994-1998 and 2004-2008 respectively.

Table 31
Percentage survival for female breast cancer
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
No surgery	1994-98	65.3%	[62.6,67.9%]	30.4%	[27.9,32.9%]
	1999-03	66.8%	[64.3,69.3%]	30.2%	[27.8,32.7%]
	2004-08	70.9%	[68.6,73.0%]	30.7%	[27.5,33.9%]
surgery	1994-98	95.6%	[95.0,96.0%]	73.0%	[71.9,74.1%]
	1999-03	97.3%	[97.0,97.7%]	81.0%	[80.1,81.8%]
	2004-08	98.3%	[98.1,98.6%]	85.5%	[84.4,86.4%]
	RELATIVE SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
No surgery	1994-98	68.0%	[64.9,70.8%]	38.8%	[35.5,42.1%]
	1999-03	69.2%	[66.2,72.0%]	38.5%	[35.3,41.7%]
	2004-08	73.5%	[70.9,75.9%]	38.6%	[34.5,42.6%]
surgery	1994-98	96.2%	[95.3,97.0%]	79.8%	[77.9,81.6%]
	1999-03	98.3%	[97.5,98.8%]	86.5%	[84.9,88.0%]
	2004-08	99.2%	[98.5,99.6%]	90.7%	[88.6,92.4%]

Observed and relative survival was calculated at one year and five years post diagnosis for cases in receipt of surgery (Table 31).

Not all patients were suitable candidates for surgery. Cases who did not receive surgery (16%) are not comparable to those who did, being older, diagnosed at a more advanced stage and probably with greater co-morbidity, all of which would lead to poorer survival. In the most recent period, 2004-2008, cases who received surgery had better 5 year relative survival (91%) compared to cases who did not receive surgery (39%).

Table 32
Percentage survival for female breast cancer by deprivation quintile
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
	Period	**1-year**	**95% CI**	**5-year**	**95% CI**
1 Least	1994-98	91.7%	[90.4,92.9%]	70.5%	[68.4,72.4%]
	1999-03	94.3%	[93.3,95.1%]	78.2%	[76.5,79.8%]
	2004-08	95.5%	[94.7,96.2%]	79.1%	[77.0,81.1%]
2	1994-98	91.7%	[89.9,93.3%]	69.9%	[66.9,72.6%]
	1999-03	93.7%	[92.4,94.9%]	75.9%	[73.6,78.1%]
	2004-08	94.8%	[93.7,95.8%]	80.4%	[77.7,82.8%]
3	1994-98	90.6%	[88.7,92.3%]	67.8%	[64.8,70.5%]
	1999-03	93.5%	[92.0,94.7%]	72.5%	[70.0,74.9%]
	2004-08	94.9%	[93.8,95.9%]	79.5%	[76.8,81.9%]
4	1994-98	89.9%	[88.2,91.5%]	62.8%	[60.1,65.4%]
	1999-03	93.6%	[92.3,94.6%]	74.0%	[71.9,76.1%]
	2004-08	93.9%	[92.8,94.9%]	77.8%	[75.2,80.2%]
5 Most	1994-98	89.4%	[88.0,90.6%]	61.4%	[59.3,63.4%]
	1999-03	91.3%	[90.1,92.3%]	70.2%	[68.4,71.9%]
	2004-08	93.0%	[92.0,93.8%]	73.6%	[71.4,75.7%]

As life tables for Ireland do not take into account deprivation score, *observed survival* only is presented for one year and five years post-diagnosis by quintiles of deprivation score (Table 32).

1 year and 5 year survival was lower in the most deprived quintile relative to the least deprived quintile. However, the gap in five-year survival between the most and least deprived quintiles narrowed; from 9% in 1994-1998 to 5.5% in 2004-2008.

Table 33
Percentage 5-year survival for female breast cancer by deprivation quintile and by age (less than and greater than 70 years)
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

	OBSERVED SURVIVAL				
		Less than 70 years		**70 years and over**	
	Period	**5-year**	**95%CI**	**5-year**	**95%CI**
1 Least	1994-98	77%	[74, 79%]	53%	[48, 57%]
	1999-03	85%	[84, 87%]	54%	[50, 58%]
	2004-08	86%	[84, 88%]	58%	[53, 63%]
5 Most	1994-98	69%	[67, 71%]	43%	[39, 47%]
	1999-03	79%	[77, 81%]	47%	[43, 50%]
	2004-08	80%	[78, 83%]	56%	[51, 60%]

5 year observed survival was calculated by deprivation quintile ('least' and 'most' only) and diagnostic period according to whether the patient was aged less than or greater than 70 years at diagnosis (Table 33).

In the most recent period (2004-2008), in women *under* 70 years, 5 year survival was notably lower (80%) in the most deprived quintile compared to least deprived quintile (86%). The difference in survival between these quintiles has fallen only slightly, from 8% in 1994-1998 to 6% in 2004-2008. By contrast, although survival for women 70 years and over in the most deprived areas was much poorer in 1994-1998 (43% *vs.* 53%), by 2004-2008 the difference in survival was small (56% *vs.* 58% for the most and least deprived quintiles respectively). Survival for this age group, however, remains much poorer than for women under 70.

4.2 Factors associated with cause-specific survival

Survival analysis was performed on cases accrued over three diagnostic periods 1994-1998, 1999-2003 and 2004-2008. Cases were followed up until date of death (due to cancer) or censoring date (31/12/09), whichever occurred first.[e]

Table 34
Diagnostic period & cause-specific survival in patients with breast cancer: females (n=29,286) & males (n=202) combined

			Univariate model		Adjusted model^	
Diagnostic period	**Cases**	**‡surv %**	**Hazard ratio**	**95%CI**	**Hazard ratio**	**95%CI**
1994-1998	7,987	61%	1.00		1.00	
1999-2003	9,867	74%	**0.74**	[0.70, 0.78]	**0.89**	[0.84, 0.94]
2004-2008	11,634	88%	**0.59**	[0.56, 0.64]	**0.73**	[0.68, 0.78]
Total	**29,488**					

‡ Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for age, sex, stage, morphology, grade, mode of presentation, diagnostic method, smoking, deprivation and area of residence
Hazard ratios in bold are significantly different from baseline (1.0)

Univariate and adjusted (multivariate) models of the effect of period of diagnosis on cause-specific survival are presented in Table 34. A hazard ratio less than 1.0 indicates relatively improved survival.

The proportion who were alive at the end of follow-up from the latest period of 2004-2008 (88%) was significantly greater than the proportion who were alive from the earliest period of 1994-1998 (61%, HR= 0.73 95%CI: 0.68, 0.78). The incremental increase in cause-specific survival times observed over the three diagnostic periods was probably due to greater uptake of treatment and earlier diagnosis.

Table 35
Age group & gender
Cause-specific survival in patients with breast cancer
Diagnostic period: 1994-1998, 1999-2003, 2004-2008

Age	**Cases**	**‡surv %**	**Hazard ratio^**	**95%CI**
15-44 yrs	4,279	78%	1.00	
45-54 yrs	7,252	82%	**0.81**	[0.74, 0.88]
55-64 yrs	7,466	80%	0.98	[0.90, 1.06]
65-74 yrs	5,444	73%	**1.39**	[1.28, 1.51]
75+ yrs	5,047	65%	**2.33**	[2.15, 2.52]

Gender	**Cases**	**^surv %**	**Hazard ratio^**	**95%CI**
Females	29,286	76%	1.00	
Males	202	78%	0.91	[0.68,1.22]

‡ Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for stage, morphology, grade, mode of presentation, diagnostic method, smoking, deprivation and area of residence
Hazard ratios in bold are significantly different from baseline (1.0)

The proportion of cases alive decreased with increasing age (Table 35).

At the end of follow-up, 65% of cases in >75 years were alive compared to 78% in the 15-44 year age category (HR=2.33 95%CI: 2.15, 2.52).

There was no significant survival difference between males and females.

[e] Appendix II: Statistical methods

Table 36
Stage & cause-specific survival in patients with breast cancer
Diagnostic period: 1994-1998, 1999-2003, 2004-2008

Stage	Cases	‡surv %	Hazard ratio^	95%CI
I	7,823	93%	1.00	
II	13,976	80%	**2.34**	[2.14, 2.56]
III	3,778	59%	**5.64**	[5.12, 6.21]
IV	2,132	29%	**16.70**	[15.1, 18.4]
Unstaged	1,779	70%	**3.18**	[2.82, 3.60]

‡ Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for age, sex, morphology, grade, mode of presentation, diagnostic method, smoking, deprivation and area of residence
Hazard ratios in bold are significantly different from baseline (1.0)

Each increment in stage of disease at diagnosis was associated with incrementally shorter survival times (Table 36). For example, by the end of follow-up, only 29% of cases with stage IV disease were alive compared to 93% of stage I cases (HR=16.7 95%CI: 15.1, 18.4).

Table 37
Histological type & tumour grade
Cause-specific survival in patients with breast cancer
Diagnostic period: 1994-1998, 1999-2003, 2004-2008

Morphology	Cases	‡surv %	Hazard ratio^	95%CI
Ductal carcinoma	20,866	78%	1.00	
Lobular carcinoma	4,304	78%	**0.90**	[0.84, 0.97]
Other adenocarcinoma	1,824	76%	0.96	[0.87, 1.06]
Other/unknown	2,494	57%	**1.12**	[1.03, 1.21]

Grade (Differentiation)	Cases	‡surv %	Hazard ratio^	95%CI
Well	2,719	92%	1.00	
Moderately	10,728	84%	**1.71**	[1.48, 1.97]
Poorly	9,251	71%	**2.70**	[2.34, 3.11]
Unknown	6,790	64%	**2.20**	[1.91, 2.54]

‡Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for age, sex, stage, mode of presentation, diagnostic method, smoking, deprivation and area of residence

Cases with lobular tumours survived marginally longer than cases with ductal tumours (HR=0.90 95%CI: 0.84, 0.97) (Table 37).

Cases with poorly differentiated tumours had shorter survival times relative to cases with well differentiated tumours (HR=2.70 95%CI: 2.34, 3.11).

Table 38
Mode of presentation & histological verification
Cause-specific survival in patients with breast cancer
Diagnostic period: 1994-1998, 1999-2003, 2004-2008

Presentation	Cases	‡surv %	Hazard ratio^	95%CI
Symptomatic	23,826	73%	1.00	
Screening	3,454	95%	**0.46**	[0.39, 0.53]
Unknown	2,208	82%	**0.78**	[0.70, 0.87]

Verification	Cases	^surv %	Hazard ratio^	95%CI
Histological	28,873	77%	1.00	
Clinical only	542	33%	**2.14**	[1.87, 2.45]
Unknown	73	43%	**1.91**	[1.38, 2.65]

‡ Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for age, sex, stage, grade, smoking, deprivation & area of residence

Cases who presented at screening had significantly better survival than those who presented symptomatically (HR=0.46 95%CI: 0.39, 0.53) (Table 38).

Patients with no histological verification of their cancer, or where this was not recorded, had significantly poorer survival (HR=2.14 95%CI: 1.87, 2.45).

Table 39
Smoking status, deprivation & area of residence
Cause-specific survival in patients with breast cancer
Diagnostic periods: 1994-1998, 1999-2003, 2004-2008

Smoking status	Cases	‡surv %	Hazard ratio^	95%CI
Non smoker	13,867	77%	1.00	
Ex-smoker	3,113	79%	1.06	[0.97, 1.15]
Current smoker	5,754	76%	**1.17**	[1.10, 1.25]
Unknown	6,754	74%	**1.22**	[1.15, 1.30]

Deprivation	Cases	‡surv %	Hazard ratio^	95%CI
1 Least	7,477	79%	1.00	
2	4,153	78%	0.99	[0.91, 1.07]
3	4,001	76%	1.06	[0.98, 1.15]
4	4,894	75%	**1.09**	[1.01, 1.18]
5 Most	7,918	74%	**1.16**	[1.08, 1.24]
Unknown	1,045	74%	1.07	[0.94, 1.22]

HSE area	Cases	‡surv %	Hazard ratio^	95%CI
DNML	8,922	79%	1.00	
DNNE	6,013	76%	**1.18**	[1.10, 1.27]
South	7,622	75%	**1.15**	[1.08, 1.23]
West	6,931	74%	**1.18**	[1.10, 1.26]

‡ Survived cancer related death up to censoring date: 31/12/2009
^ Adjusted for age, sex, stage, morphology, grade, mode of presentation & diagnostic method

The relationship between survival and some patient characteristics is shown in Table 39.

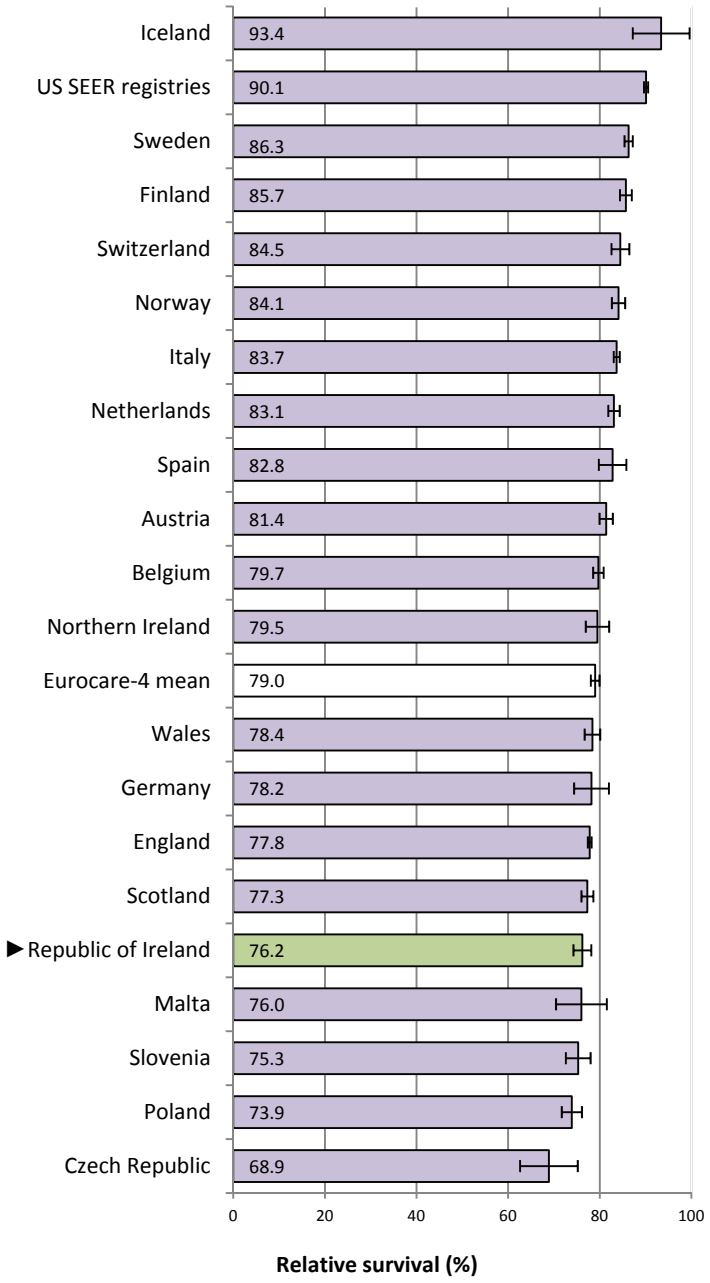
The proportion of current smokers who were alive at the end of follow-up (76%) was marginally lower than that of non-smokers (77%, HR=1.17 95%CI: 1.10, 1.25).

There was a decrease in the proportion who survived with each increment in deprivation quintile. For example, fewer cases in the most deprived quintile were alive (74%) compared to the least deprived quintile (79%, HR 1.16 95%CI 1.08, 1.24).

The proportion of cases who were alive at the end of follow-up in HSE West (74%, HR=1.18 95%CI: 1.10, 1.26), HSE South (75%, HR=1.15 95%CI: 1.08, 1.23) and DNNE (76%, HR=1.18 95%CI: 1.10, 1.27) were significantly lower than the proportion alive in DNML (79%).

4.3 International comparison of relative survival

Figure 13
Age adjusted 5-year relative survival of female breast cancer
Diagnosis period: 2000-2002



(Eurocare-4. Verdecchia A, et al., 2007) [36]

A comparison of 5-year period relative survival for breast cancer cases accrued during the years 2000-2002 is presented in Figure 13.[36]

5–year relative survival for cases in Ireland (76.2%) was lower than that of the Eurocare average (79.0%).

Pooled 5-year relative survival estimates derived from 13 SEER registries in the United States was 90.1%, which was significantly higher than 5-year survival for cases in Ireland during the same period (76.2%).

Relative survival in Ireland was lower than our nearest neighbours Scotland (77.3%), England (77.8%), Wales (78.4%) and Northern Ireland (79.5%).

Considering only the countries with national cancer registries, Iceland (93.4%), Sweden (86.3%), Finland (85.7%), Norway (84.1%) and the Netherlands (83.1%) all had significantly higher relative survival than Ireland while Malta (76.0%), Slovenia (75.3%), Poland (73.9%) and the Czech Republic (68.9%) all had marginally lower relative survival than Ireland.

5. MORTALITY

Breast cancer was the leading cause of cancer death in women in 2007-2009, after lung cancer, and accounted for 16% of female cancer deaths during that period. [37]

Table 40
Breast cancer deaths and age standardised mortality rate (ASMR) 1994-2009

	FEMALES		MALES	
YEAR	Cases	ASMR	Cases	ASMR
1994	648	37.6	4	0.25
1995	655	37.5	7	0.46
1996	635	35.7	6	0.49
1997	634	35.4	3	0.16
1998	599	32.2	6	0.38
1999	644	34.7	4	0.24
2000	668	35.2	1	0.06
2001	671	34.3	6	0.33
2002	604	29.8	4	0.24
2003	646	31.8	1	0.04
2004	663	31.6	3	0.16
2005	696	31.7	3	0.16
2006	678	30.4	9	0.50
2007	611	27.2	3	0.16
2008	736	31.8	6	0.31
2009	676	28.3	3	0.14
Total	**10,464**		**69**	
APC	0.5%	-1.7%	-1.6%	-3.7%
95%CI(APC)	(-0.1, 1.1%)	(-2.3, -1.2%)	(-8.6, 6.0%)	(-11.4, 4.7%)

5.1 Mortality trends

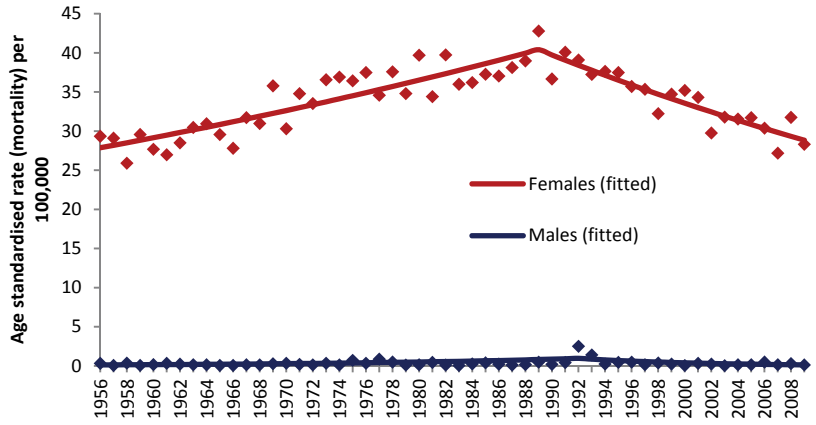
Mortality data obtained from the CSO for the period 1994-2009 is presented in Table 40. [48]

There were on average 679 female deaths per year and 5 male deaths per year from breast cancer between 2005 and 2009.

For females, the age standardised mortality rate (ASMR) fell from 38/100,000 in 1994 to 28/100,000 in 2009, an annual decrease of 1.7% during that period.

5.2 Long term mortality trend

Figure 14
Trends in breast cancer mortality rates in the Republic of Ireland: 1956-2009
Observed and fitted ASMR and annual percentage change (APC)



Gender	Period	APC	[95%CI]	*trend
Females	1956-1989	1.1%	[1.0, 1.4%]	↑
	1990-2009	-1.7%	[-2.1, -1.3%]	↓
Males	1956-1992	5.5%	[3.0, 8.1%]	↑
	1993-2009	-10.3%	[-14.8, 15.6%]	↓

* ↑=significant increase, ↓=significant decrease

Points on graph indicate actual ASMR data. Lines indicate fitted trends (Joinpoint)[42]

Age standardised mortality rates (ASMRs) for the period 1956-2009 are presented in Figure 14. [38]

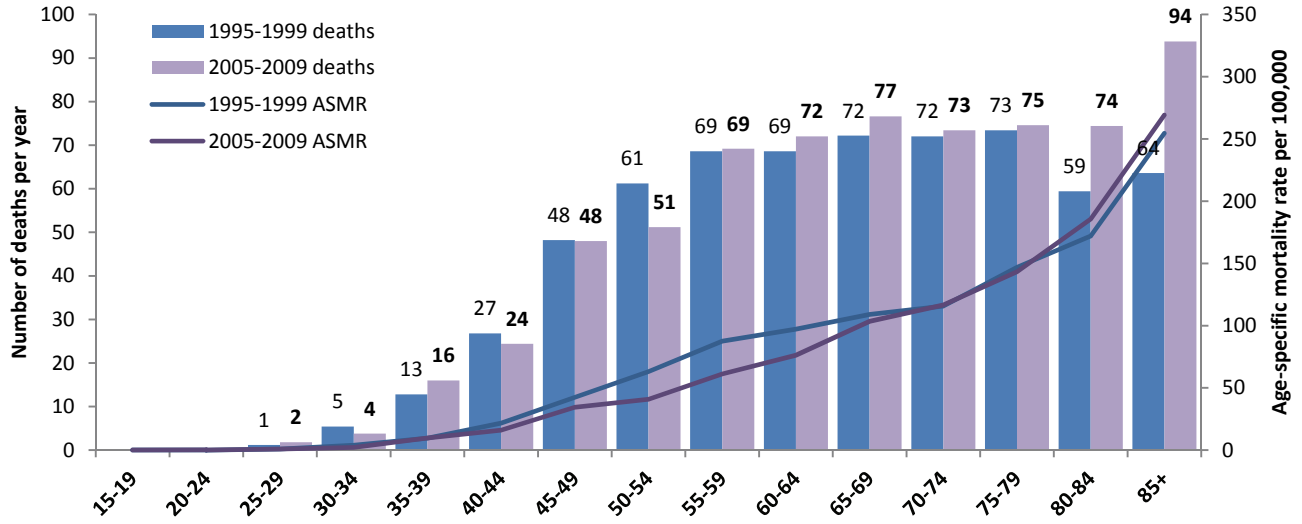
A significant 1.1% annual percentage increase in the female mortality rate was observed from 1956 to 1989. Thereafter, there was a significant 1.7% annual decrease in mortality, from 1990 to 2009.

The mortality rate in males decreased by 10% annually during the period 1993 to 2009.

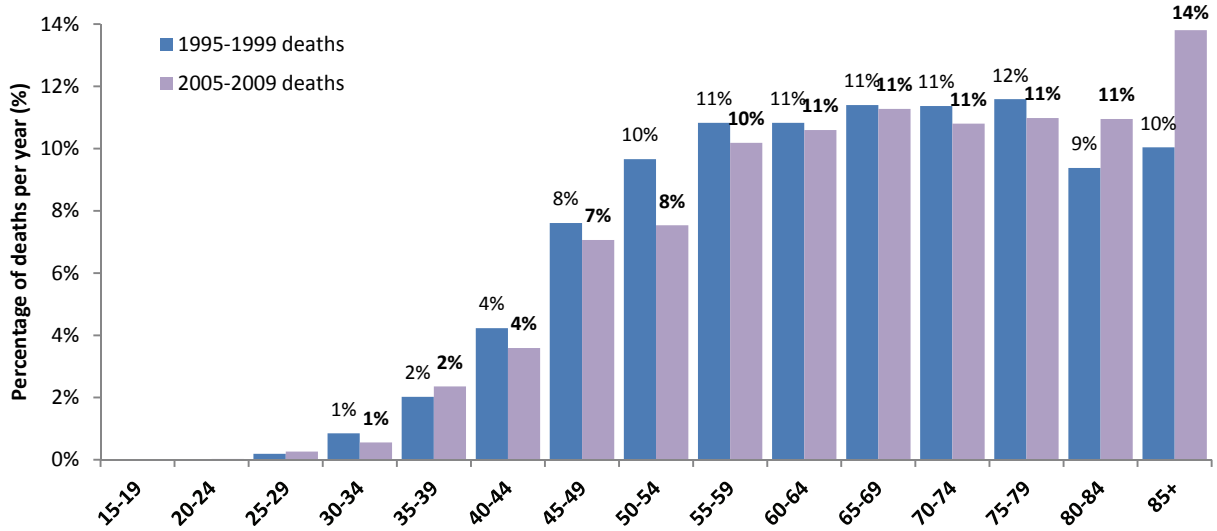
5.3 Age distribution of mortality

Figure 15
Mortality for female breast cancer : Diagnostic periods: 1995-1999 and 2005-2009

(a) Number of deaths by age group & age-specific mortality rate



(b) Percentage (of the total) deaths by age group

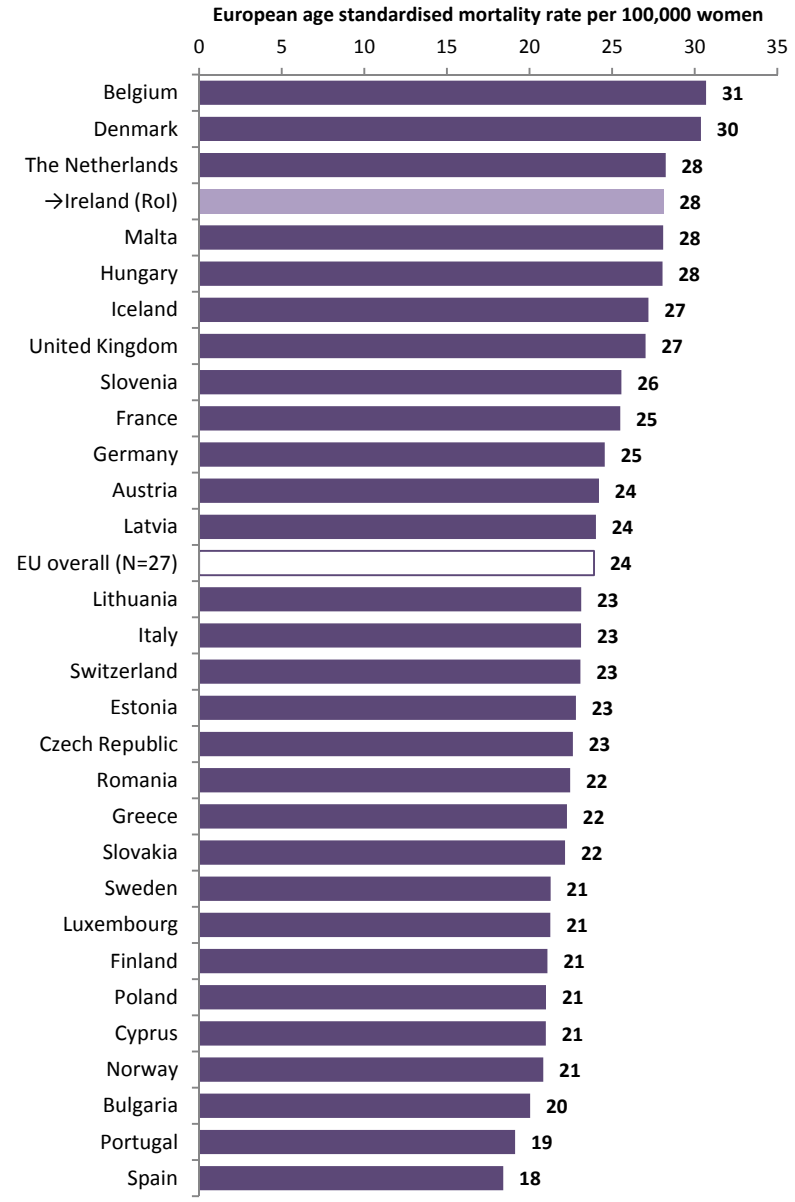


The number of female breast cancer deaths per year by age group over the periods 1995-1999 and 2005-2009 is presented in Figure 15.[48]

The number of deaths per year (73 per year) was highest in the 75-79 age group during 1995-1999 and in the 85+ age group (94 per year) during 2005-2009. The peak age-specific mortality rate, which occurred in the 85+ age group in both periods, was 255/100,000 women during 1995-1999, and 269/100,000 women during 2005-2009. There was a shift in the age distribution of deaths, from younger to older women, between the periods 1995-1999 and 2005-2009. This shift was most evident in the two oldest age groups (80-84 & 85+). There was no corresponding change in the age distribution of incident cases, so the relative increase in deaths in this age group may be due to random variation.

5.4 International comparisons of mortality

Figure 16
Comparisons of age standardised mortality rates (ASMR) for female breast cancer: 2008



European Cancer Observatory (ECO), 2008.[29]

An international comparison of estimated mortality rates for European countries in 2008 is presented for female breast cancer in Figure 16.[29]

Ireland ranked 4th highest of the 30 countries shown here, with an age standardised mortality rate of 28/100,000, behind Belgium (31/100,000), Denmark (30/100,000) and the Netherlands (28/100,000). Ireland's mortality rate was similar to that of the UK (27/100,000) but higher than the European average (24/100,000). The three countries with the lowest recorded mortality rates in 2008 were: Bulgaria (20/100,000), Portugal (19/100,000) and Spain (18/100,000).

In general, eastern and southern European countries had lower mortality rates than western Europe. The Scandinavian countries (except Denmark) also had relatively lower mortality rates: Norway (21/100,000), Sweden (21/100,000) and Finland (21/100,000)

APPENDIX I

Breast cancer: Data sources and dataset

Since 1st January 1994, all newly diagnosed cancers in Ireland have been registered by the National Cancer Registry. The process is highly effective. Currently the completeness of cancer registration for all invasive cancers diagnosed to end of 2007 is estimated to be over 96%.[28] Prior to 1994, there was no national cancer registration and therefore no reliable information on cancer incidence.

The dataset used in this report consisted of all primary invasive breast cancers (ICD-10 code C50) registered by the National Cancer Registry (NCR) with a date of diagnosis from 1 January 1994 to 31 December 2009. Inclusions and exclusions are shown in Table 41.

For analysis of incidence and treatment patterns, the dataset was divided into three diagnostic periods: 1994-1998, 1999-2003 and 2004-2008.

For survival analysis, the dataset was divided into three separate diagnostic periods; 1994-1998, 1999-2003, 2004-2008. Survival time was censored at 31 December 2009 to ensure that all cases had follow-up for at least one year. Only the first primary invasive tumours of the breast were included in the survival dataset.

Breast cancers were excluded from survival analyses if they were preceded by another cancer (other than non-melanoma skin cancer). Following convention, cases where the sole evidence of cancer was diagnosed from a death certificate or at autopsy were excluded from survival analysis. *In situ* breast neoplasms were counted from 1994 to 2009 if the case did not have a prior or concurrent invasive breast tumour.

Table 41
Cases of breast cancer diagnosed between 1994-2009 in females and males

All registered breast tumours (1994-2009)	35,737
Exclusions before incidence analysis‡	2,441
Final incidence dataset of invasive breast tumours (diagnosed during 1994-2009)	33,296
Further exclusions before survival analysis*	3,808
Final survival dataset (diagnosed during 1994-2008 and all followed up until death or 31/12/09, whichever occurred first)	29,488

‡In-situ tumours (i.e., cases where the patient had an *in-situ* tumour and no preceding or concurrent invasive breast tumour)
* Autopsy-only cases , DCO cases , breast cancers concomitant with another invasive malignancy and breast cancers incident during 2009

APPENDIX II

Variable definitions and methods of analysis
Demographic variables

Age

This was the age at diagnosis; the difference between date of birth and date of diagnosis. This variable was available for all patients. The EUROCARE convention for age categories in breast cancer was used: 15-44 years, 45-54 years, 55-64 years, 65-74 years and 75+ years. [39]

Smoking status

Breast cancer cases were classified as 'non smokers' if they had never smoked, 'ex-smokers' if they had ever smoked but had not smoked for a year prior to diagnosis. Current smokers were classified as 'smokers'.

Marital status

Breast cancer cases were classified as 'ever married' if they were married, widowed, divorced or separated and 'never married' if they had never been married.

Date of incidence

The NCR subscribes to the European network of cancer registries (ENCR) guidance for this data item.[40] Date of incidence was taken to be the date of histological confirmation (or date of clinical diagnosis if there was no histological confirmation).

Date of death

For survival calculations, the last day of follow-up was taken to be 31 December 2009 (censoring date). The date of death was taken to be that recorded on the death certificate if available, otherwise the date of death was that observed in the case hospital notes.

HSE area of residence

All patients in the dataset were allocated to a HSE administrative area according to their main address at the time of diagnosis: Dublin Mid Leinster (DNML), Dublin North East (DNNE), West (W) and South (S).

Deprivation

Quintiles of deprivation were derived from data in the 2002 census at electoral division (ED) level, and applied to individual patients by linkage of address.[47] The score consisted of 1 (least deprived) through to 5 (most deprived).

Tumour characteristics

TNM

TNM category of tumour was described in the medical record. Where a pathological T (primary tumour), N (regional nodes) or M (distant metastasis) category was given, this was used; otherwise the clinical diagnosis was used. Version 5 of the TNM AJCC manual was used for cases after 2000.[41] Cases in the earlier period (1994-1999) were staged using version 4 of the manual. However, there were no changes in the guidelines for breast cancer between version 4 and version 5. Cases where the metastasis was coded as 'MX' (unknown) were re-coded to 'M0' (i.e. assumed that metastasis had not occurred).

Table 42
Stage grouping: breast cancer

Stage 0	Tis	N0	M0
Stage I	T1	N0	M0
Stage IIA	T0	N1	M0
	T1	N1	M0
	T2	N0	M0
Stage IIB	T2	N1	M0
	T3	N0	M0
Stage IIIA	T0	N2	M0
	T1	N2	M0
	T2	N2	M0
	T3	N1, N2	M0
Stage IIIB	T4	Any N	M0
	Any T	N3	M0
Stage IV	Any T	Any N	M1

Summary stage

Summary stage was derived by algorithm from TNM categories and collapsed from the finer categories of stage IA, IB, IIA, IIB, IIIA, IIIB, IV to the simpler breakdown of stage I, II, III and IV.[41] (Table 42)

Grade

Tumour grade was transcribed from pathology reports and listed as 1 (well differentiated), 2 (moderately differentiated), 3 (poorly differentiated or undifferentiated) and 4 (unknown).

Morphology

Four broad categories of tumour histology were derived as follows: Ductal adenocarcinoma, lobular adenocarcinoma, other adenocarcinoma. Morphologies other than these three types were pooled as a single category for: 'other specified, other unspecified and unknown morphologies'.

Basis of diagnosis

Cases were classified as *microscopically verified* if the tumour had been confirmed by histological or cytological methods. Cases were classified as *clinically verified* if diagnosed by radiology, ultrasound or by autopsy.

Treatment definitions

The focus was on *tumour-directed treatment* administered within one year of the diagnosis date. This was interpreted as the primary course of treatment aimed at removing, reducing, destroying or preventing further growth of tumour. No distinction was made between 'curative' and 'palliative' treatment. For the purposes of this report, five treatment scenarios (a-e) were defined as follows:

a) *Surgery*

A case was considered to have undergone *surgery* if at least one tumour resection was recorded. Patients who underwent surgery were sub-classified according to whether they received breast conserving surgery or mastectomy.

b) *Chemotherapy*

A case was considered to have undergone *chemotherapy* if at least one chemotherapeutic agent was administered.

c) *Hormone therapy*

A case was considered to have undergone *hormone therapy* if at least one hormonally active agent (i.e. tamoxifen, raloxifene, etc.) was administered.

d) *Radiotherapy*

A case was considered to have undergone *radiotherapy* if least one radiotherapy session was recorded.

e) *Treated*

A case was considered to have been *treated* if at least one treatment was recorded for that case (i.e. treatment as defined in a-d above).

f) *Not treated*

A case was considered as *not treated* if there was no treatment recorded for that case as defined in a-d above. However, many cases had other types of medical and surgical interventions not covered in a-d above.

Information on chemotherapy, radiotherapy, hormone therapy and BCS was not available for the years 1994 and 1995. Proportions of treated patients were tabulated for three diagnostic periods; 1996-1998, 1999-2003, 2004-2008.

Statistical methods

Patient, tumour and treatment variables were tabulated across three diagnostic periods: 1994-1998, 1999-2003, and 2004-2009. Age standardised rates (ASR) for incidence and mortality were weighted against the European standard population. Annual percentage change (APC) of incidence and mortality over time were calculated using the Joinpoint regression program.[42] Joinpoint regression was also used to test for *linear trend* over time for selected variables in sections 2 (incidence) and 3 (treatment).

Standardised rate ratios (SRR) were calculated for the period 2004-2008. The age standardised incidence rate (ASIR) is the index of cases in a given population weighted by the European age structure. Rather than consider the most recent year (2008), the numbers of cases occurring during 2004-2008 in Ireland were summed and divided by the sum of persons at risk in the RoI (summed for 2004-2008) using intercensal population estimates. The ASIR for 2004-2008 was calculated for each county in a similar fashion. The ratio of county ASIR over country ASIR gives the standardised rate ratio (SRR). The 95% CI of the SRR ratio was also calculated.[43] A county was considered to have a significantly higher (or lower) incidence of cases than the national average if the 95% confidence interval of the SRR did not include unity.

Variables affecting treatment receipt were identified using logistic regression. An explanatory variable was included in a final model if the likelihood ratio test for exclusion of that variable from the multivariate model had a p-value less than 0.10. As treatment was common, the odds ratio overestimated the risk of treatment when it was more than 1 or underestimated the risk when it was less than 1. To overcome this problem, odds ratios were converted to risk ratios (RR) according to the formula $RR = [OR]/[(1 - P_0) + (OR * P_0)]$ where OR is the odds ratio for a group of patients who received treatment relative to the baseline group, and the proportion of patients treated in the baseline group is give by P_0.[44] Looking at tables of adjusted RR's leads to the same conclusions as adjusted OR's; except that the RR can be conveniently interpreted as the proportion who received treatment relative to the baseline level of a variable. Four models were derived (factors associated with surgery, radiotherapy, chemotherapy and hormone therapy). The latter three models were adjusted for surgery. All four models were adjusted for age, stage, grade, mode of presentation, method of diagnosis, area of residence and period of diagnosis.

Survival data is presented as *relative survival* (RS); the ratio of observed survival among a group of cases to the expected survival among the general population of the same age, sex and country. Relative survival was calculated using the '*strs*' command in STATA 11.0.[45] Age standardised RS was derived for each level of the variables: i.e., stage, diagnostic period, etc. As the life tables (for RoI) used to calculate relative survival did not take account of deprivation quintiles, *observed survival* for each quintile of the deprivation score was calculated using the Kaplan-Meier method. Variables affecting cause-specific survival were determined using a Cox proportional hazards regression model. An explanatory variable was included in the final Cox model if the likelihood ratio test for exclusion of that variable from the multivariate model had a p-value less than 0.10.

CONTRIBUTORS

The information in this report is based on the data held by the National Cancer Registry, and has been collected, processed and analysed since 1994 by dedicated and skilled Registry staff. The registry, in turn, is dependent on the help and support of hospital staff throughout the country. The CSO and General Register Office provided the death certificate data. Most of the data analysis was carried out by the writing group; Paul M Walsh extracted the breast cancer survival dataset and provided the *relative survival* figures. Neil McCluskey provided map graphics in section 3. The writing group for this report was: Joe McDevitt, Katie O'Brien, Linda Sharp and Harry Comber.

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