Patterns of care and survival of cancer patients in Ireland 1994 to 2001:

time-trends and regional variation for breast, colorectal, lung and prostate cancer

Summary report

Paul M Walsh
Harry Comber

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Cork, Ireland

Telephone +353 21 4318014
Email info@ncri.ie
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A fuller version of this report, giving detailed results for each cancer site and a full description of the methods used, is available online at http://www.ncri.ie/pubs/pubs.shtml**.** The full report will not be published in printed form; however, we can provide duplicated laser-printed copies for individuals with no internet access

Patterns of care and survival of cancer patients in Ireland 1994 to 2001: time-trends and regional variation for breast, colorectal, lung and prostate cancer

SUMMARY

Main conclusions

Improvements in survival for breast, colorectal and prostate cancers, but not lung cancers, were seen at national scale between the earlier (1994-1997) and later (1998-2001) parts of the period examined. Improvements in treatment or in early diagnosis are presumably involved, but exaggeration of true survival improvements by lead-time bias cannot be ruled out, especially for prostate cancer.

Regional variation in survival is still apparent, as noted in our previous report (NicAmhlaoibh *et al*. 2004), with survival generally lowest for patients resident outside the Eastern region, except for lung cancer. This variation is partly but not wholly explained by variation in patient or tumour characteristics.

Trends in treatment appeared to be broadly in line with expectations of greater or better-targeted use of radiotherapy and chemotherapy, although no increase in radiotherapy use was seen for breast cancer. An apparent major fall in use of hormonal treatment for breast cancer may also be in line with expectations of improved targeting of appropriate treatment. This may also apply to increased use of hormone therapy and reduced use of surgery for prostate cancer.

At regional scales, there is still substantial variation in the use of particular treatment modalities. These variations are largely unexplained by patient and tumour characteristics, suggesting that geographic and institutional influences on treatment may be critical. Evidence of increased specialization or centralization of services is limited, although further analysis is required.

Introduction and methods

This is the second National Cancer Registry report focusing on treatment and survival of cancer patients in Ireland, for the four most important cancers in healthcare terms. The previous report covered the period 1994 to 1998 (NicAmhlaoibh *et al*. 2004). Coverage is provided here for the eight-year period 1994-2001, representing 49100 cancer patients with survival follow-up to December 2003.

Changes in scope or methodology from the previous report include: assessment of time-trends in survival and treatment; use of relative survival estimates and modelling (rather than crude and cause-specific equivalents); presentation of regional and other treatment comparisons as adjusted risk ratios (rather than odds ratios); and use of age-groups based on the EUROCARE-3 patient population (Capocaccia *et al*. 2003). Summary data on hospital and consultant caseloads are also presented for surgical patients. However, potential caseload, deprivation and co-morbidity influences on survival and treatment are not examined, pending further work on geo-coding and hospital-linkage of cancer registry data.

Time-trends

To allow for possible under-recording of treatments during 1994 and 1995, *trends in the proportions of patients treated are assessed for the period 1996 to 2001 only*. Patient follow-up data is complete for the period, and *survival comparisons are made between diagnosis periods 1994-97 and 1998-2001*.

Regional definitions

Results are presented for *eight regions of residence*, defined (partly for continuity with previous National Cancer Registry analyses) on the basis of the former Health Board areas plus the former Eastern Regional Health Authority area which applied during the period considered. The neutral term ‘region’ is deliberately used.

Survival

Survival is presented here as *estimates of relative survival*, i.e. the ratio of observed survival of patients to the expected survival among persons of the same age and sex in the general population. The regional estimates presented here are the first to be published for Ireland. Formal comparisons between regions, adjusted for relevant patient and tumour characteristics, are made using *relative survival modelling* (Dickman *et al*. 2004).

Treatment

Data analysed here are for treatments *administered within six months of the date of diagnosis*, if anti-tumour or tissue-destroying in effect, whether originally considered ‘curative’, ‘palliative’ or otherwise. Proportions of patients treated are summarized. Formal comparisons between years or regions are based on *logistic regression*, adjusted for relevant patient and tumour characteristics. Results (odds ratios) are *re-expressed as risk ratios* to avoid over-stating proportional differences (Zhang & Yu 1998).

Results

An overview of time-trends in relative survival and in treatment, nationally and regionally, is provided in *Table 1*. Other tables and figures summarize time-trends and regional variation in further detail.

Survival

General summary

National estimates of five-year relative survival for patients diagnosed during 1994-2001 as a whole were 75.4% for breast cancer, 49.2% for colorectal cancer, 8.6% for lung cancer and 69.5% for prostate cancer.

Time-trends in survival

Relative survival for breast, colorectal and prostate cancers showed obvious increases between the diagnosis period 1994-97 and 1998-2001 (*Table 2*), and showed a possible increase for lung cancer. Those for breast, colorectal and prostate cancers were confirmed by relative survival modelling (*Table 3*), which indicated age-adjusted reductions in excess mortality risk by 24%, 10% and 39%, respectively.

At regional scales, survival estimates showed some indication of improvement, in all regions for breast and prostate cancers and in most regions for colorectal and lung cancers (*Table 2*). Regional changes as assessed by modelling were significant for three regions for breast cancer (reduced excess risk i.e. improved relative survival in Eastern, North-Eastern and Southern regions), one region for colorectal cancer (improved survival in Western region), one region for lung cancer (reduced survival in North-Eastern region), but for seven of the eight regions for prostate cancer (improved survival) (*Table 3*).

Fuller adjustment for patient and tumour characteristics modified the national trends somewhat, but the reductions in excess risk remained significant for breast, colorectal and prostate cancer (*Table 3*). For breast cancer, the reduction in risk (improvement in survival) was less marked than in the basic model, but for colorectal cancer the reduction was more marked after fuller adjustment. For prostate cancer, the reduction in risk remained substantial.

Possible changes in patient or tumour characteristics over time thus appear to provide only a partial explanation of trends in survival. Improvements in treatment (see below) seem likely to account, in part, for the survival improvements seen. But changes in unmeasured or poorly measured factors could also be involved. For example, data on cancer stage were substantially incomplete, thus adjustment for possible improvements in early diagnosis may not have been adequate. This is particularly critical given the possibility of *lead-time bias*, whereby earlier detection of cancers through organized or unorganized screening can increase apparent survival times, even if there is no true survival benefit. Of the cancers considered here, the introduction of organized screening for breast cancer (2000/2001 onwards) should have had, at most, only a minor influence on survival trends presented here. For prostate cancer, however, major increases in both apparent survival and in numbers of diagnosed cases suggest that earlier detection through Prostate Specific Antigen (PSA) screening may already be influencing trends, although the true benefits of PSA screening are unclear.

Regional variation in survival

Apparent regional variations in relative survival estimates (*Table 2*) were confirmed for breast, colorectal and prostate cancers by relative survival modelling (*Figure 1*, *Table 4*). This indicated significantly poorer age-adjusted survival in most regions, compared with the Eastern region. Regional variation was less marked for lung cancer (and involved higher survival in several regions).

Fuller adjustment for stage and other tumour and patient variables modified and, in general, substantially reduced regional discrepancies (*Figure 2*, *Table 4*). In statistical terms, these variables appeared to 'explain' some of the differences.

This applied particularly to prostate cancer, for which little regional variation was apparent in the full model – significantly higher excess mortality (lower relative survival) among patients from the Southern region only. For breast cancer, full adjustment reduced the number of regions with significantly low survival from seven to four (Midland, Southern, South-Eastern and Western regions). For colorectal cancer, survival was significantly low among patients from the Mid-Western, Southern and South-Eastern regions. In contrast, survival of lung cancer patients was significantly high among patients from three regions (Mid-Western, North-Western and Western), although absolute differences were small for this high-fatality cancer.

No region had significantly poorer survival for all four cancers. Patients from the Southern region did have significantly poorer survival than the reference Eastern region for breast, colorectal and prostate cancers during 1994-2001 as a whole. In the most recent diagnosis period, 1998-2001, only colorectal and prostate cancers had significantly low survival in the Southern region (and also in the

Mid-Western and South-Eastern regions) (see full report).

It should be noted that prognostic and demographic variables were often substantially incomplete, and may have been correlated with the quality of diagnostic or prognostic investigations. Thus the full explanatory power of the models is difficult to assess.

Treatment

General summary of treatment

Treatments nationally and regionally are summarized in *Figure 3* (1998-2001) and treatment-combinations in *Figures 4-7* (1994-97 and 1998-2001).

For breast cancers diagnosed during 1998-2001, 96% of patients had some form of definitive or tumour-directed treatment within six months of diagnosis, 85% had surgical treatment, 45% chemotherapy, 44% radiotherapy and 43% hormonal therapy (*Figure 3*). In the same period, the most frequent treatments or combinations were surgery plus chemotherapy (18% of cases), surgery plus chemotherapy plus radiotherapy (14%), surgery plus hormonal therapy plus radiotherapy (13%), surgery plus hormone therapy (13%), and surgery only (10%) (*Figure 4*).

For colorectal cancer during 1998-2001, 84% of patients had any treatment, 77% had surgery, 33% chemotherapy and 14% radiotherapy (*Figure 3*). The main combinations were surgery only (46%), surgery plus chemotherapy (20%), and surgery plus chemotherapy plus radiotherapy (8%) (*Figure 5*).

For lung cancer during 1998-2001, 54% of patients had any treatment, 34% had radiotherapy, 16% chemotherapy and 13% surgery (*Figure 3*). Most patients had radiotherapy only (25%), surgery only (10%), or chemotherapy only (9%) (*Figure 6*).

For prostate cancer during 1998-2001, 78% of patients had any treatment, 43% had surgery, 41% hormonal therapy and 10% radiotherapy (*Figure 3*). Most had surgery only (30%), hormonal therapy only (26%), or surgery plus hormonal therapy (11%) (*Figure 7*).

Region of residence v. region of main surgical treatment

For colorectal and breast cancers, the majority of patients resident in a region received their main surgical treatment in the same region (see *Table 5* for the period 1998-2001). In contrast, most surgical cases of lung cancer from almost all regions (other than Southern region) had their main surgery in the Eastern region, albeit based on small numbers of surgical cases. For prostate cancer, regional patterns were intermediate between these extremes.

Hospital and consultant caseloads

The general trend between 1994 and 2001 was for fewer surgical patients to be treated by hospitals or consultants having small average caseloads of breast, colorectal or prostate cancer patients (*Figure 8*). These trends were strongest for breast cancer, but were not evident (or the opposite trends were seen) for lung cancer. However, such trends in caseload do not, by themselves, necessarily indicate increased specialization or centralization of services. Further studies will examine the possible influence of caseload or specialization on survival or quality of treatment.

Time-trends in treatment

The proportions of patients receiving any tumour-directed treatment showed no significant trend for breast cancer during 1996-2001, increased for lung and to a lesser extent colorectal cancer, and fell slightly for prostate cancer (*Table 6*). The use of surgical treatment increased slightly for breast cancer, fell slightly for lung and to a lesser extent colorectal cancers, and fell more markedly for prostate cancer. Radiotherapy use increased markedly for prostate and colorectal (especially rectal) cancers, and to a lesser extent for lung cancer, but showed no trend for breast cancer. For breast cancer, the recorded use of hormonal treatment fell substantially, nationally and in all regions of residence, at the same time as a significant increase in the use of chemotherapy. Chemotherapy use also increased substantially for colorectal and lung cancers, and use of hormonal treatment increased moderately for prostate cancer. Trends for each region (generally but not always consistent with national trends) are presented in the full report.

Regional variation in treatment

There was clear regional variation in the proportions of patients receiving particular treatment modalities (*Figures 9-12* and *Tables 7-8*). Where significant differences were seen, colorectal and to a lesser extent lung cancer patients resident outside the Eastern region were less likely to receive particular treatments than those from the Eastern region. This also applied to radiotherapy for breast cancer and surgery for prostate cancer. However, there was significantly higher use of hormonal treatments for breast and prostate cancers in the other regions, and significant higher use of chemotherapy for breast cancer in up to four of those seven regions. Overall treatment varied less between regions, but was significantly low for lung cancer in most regions compared to the Eastern.

In broad terms, these findings hold both for basic models (adjusted for age, sex and lung cancer cell-type) and for more complex multivariate models. Thus regional variations in treatment appeared to be largely unrelated to the patient and tumour characteristics examined. This may indicate that geographic or institutional factors were critical influences on treatment. Notably, radiotherapy use for breast cancer was highest among patients from the two regions (Eastern and Southern) that had radiotherapy centres during the period examined, and from regions immediately adjacent to the Eastern. However, regional patterns of treatment were not necessarily consistent across cancers for a given treatment modality. The most consistent patterns were high use of hormonal therapy among patients from all regions other than the Eastern (for breast and prostate cancers), low use of radiotherapy in the Western region (for breast, colorectal and lung though not prostate cancers), and low use of chemotherapy in the Mid-Western region (for breast, colorectal and lung cancers).

The link between treatment and survival

Trends or regional variations in survival are likely to reflect, in part, the provision of appropriate treatments aimed at a cure or at prolonging life. Explicitly or convincingly demonstrating this link is difficult, however, especially against a background of increased earlier detection for some cancers (notably prostate). One possible approach is to include treatment status within statistical models of survival. This has not been attempted here, in part because patients receiving and not receiving particular treatments are likely to differ in unmeasured characteristics e.g. their general health. However, further analyses are planned, to take into account available information on co-morbidity (other health conditions in the same patients).

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Table 1 Summary of age-adjusted time-trends in survival and treatment, by region of residence: significant changes in relative survival (1994-97 to 1998-2001 change) or in proportions of patients receiving tumour-directed treatment within six months of diagnosis (1996 to 2001 trend). Trends for colorectal cancer are also adjusted for sex, and for lung cancer for sex and cell-type.

Cancer	Region	Relative survival	Overall treatment	Surgery	Radiotherapy	Chemotherapy	Hormone therapy
Breast	**Total**	+		+		+	-
(female)	East	+		+		+	-
n=13383	Midland						-
	Mid-West						
	North-East	+				+	-
	North-West				-	+	-
	South	+			+	+	-
	South-East				-	+	-
	West				+	+	-
Colorectal	**Total**	+	+	-	+	+	
n=13702	East		+		+	+	
	Midland			-	+		
	Mid-West				+		
	North-East			-	+	+	
	North-West						
	South				+	+	
	South-East		+		+	+	
	West	+			+	+	
Lung	**Total**		+		+	+	
n=11663	East		+			+	
	Midland						
	Mid-West				+		
	North-East				+		
	North-West	-					
	South						
	South-East						
	West						
Prostate	**Total**	+	-	-	+		+
n=10352	East	+	-	-			
	Midland	+		-			+
	Mid-West	+	-	-			
	North-East	+					
	North-West	+	-	-	+		
	South	+		-	+		+
	South-East		-	-	+		
	West	+	-	-			-

+ = significant increase, - = significant decrease.

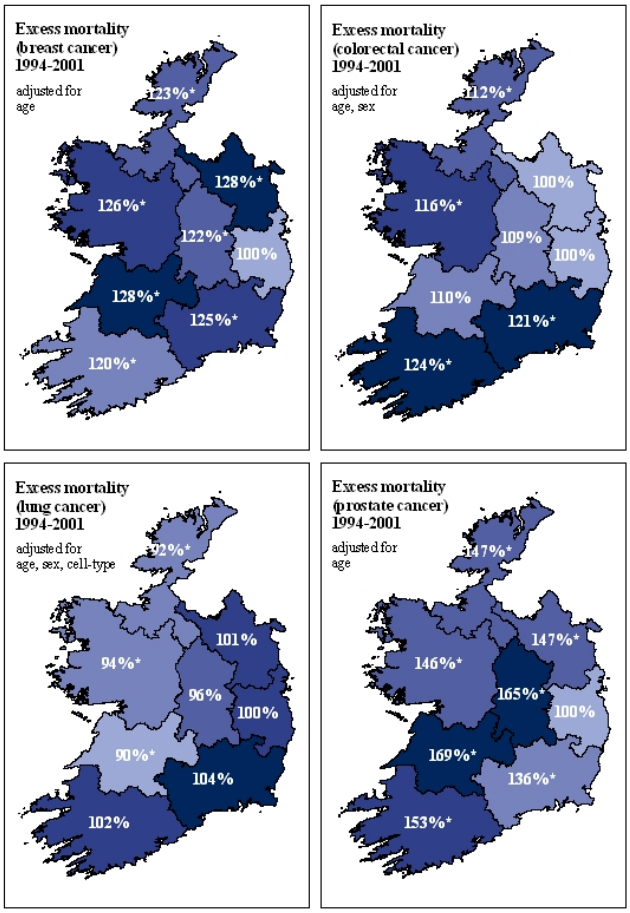
Table 2 Five-year relative survival for Irish cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population (from the same region for regional estimates).

Cancer	Region	1994-2001		1994-1997			1998-2001	
		survival	(95% CI)	survival	(95% CI)		survival	(95% CI)
Breast	**total**	**75.4%**	(74.4%-76.3%)	**72.9%**	(71.6%-74.2%)	+	**78.2%**	(76.8%-79.6%)
(female)	E	78.6%	(77.1%-80.0%)	76.1%	(73.9%-78.1%)	+	81.4%	(79.1%-83.5%)
	M	74.1%	(69.9%-77.9%)	73.2%	(67.5%-78.3%)		76.3%	(69.8%-81.8%)
	MW	73.0%	(69.4%-76.2%)	71.6%	(66.8%-76.0%)		75.1%	(69.5%-80.0%)
	NE	72.3%	(68.5%-75.7%)	68.6%	(63.3%-73.4%)	+	75.6%	(69.9%-80.7%)
	NW	74.1%	(69.8%-78.0%)	71.9%	(66.0%-77.1%)		76.3%	(69.6%-82.1%)
	S	74.7%	(72.2%-77.0%)	70.8%	(67.3%-74.0%)	+	79.3%	(75.6%-82.6%)
	SE	73.5%	(70.3%-76.4%)	72.0%	(67.6%-76.0%)		74.0%	(68.9%-78.5%)
	W	74.1%	(70.8%-77.0%)	71.4%	(67.0%-75.5%)		78.8%	(74.1%-82.8%)
Colorectal	**total**	**49.2%**	(48.1%-50.3%)	**47.7%**	(46.1%-49.1%)	+	**51.0%**	(49.3%-52.6%)
	E	51.9%	(50.0%-53.8%)	50.3%	(47.7%-52.8%)		54.3%	(51.4%-57.1%)
	M	48.8%	(44.2%-53.3%)	47.8%	(41.8%-53.7%)		50.2%	(42.9%-57.2%)
	MW	49.7%	(45.7%-53.6%)	51.0%	(45.4%-56.5%)		48.2%	(42.2%-54.0%)
	NE	52.4%	(48.6%-56.0%)	53.1%	(47.8%-58.3%)		51.5%	(45.9%-56.9%)
	NW	49.3%	(45.1%-53.4%)	45.7%	(40.2%-51.1%)		53.5%	(47.0%-59.9%)
	S	47.1%	(44.4%-49.7%)	46.0%	(42.3%-49.5%)		47.9%	(43.9%-51.8%)
	SE	46.4%	(43.2%-49.6%)	44.6%	(40.2%-48.8%)		48.4%	(43.3%-53.3%)
	W	46.3%	(43.0%-49.6%)	41.0%	(36.7%-45.4%)	+	51.8%	(46.7%-56.8%)
Lung	**total**	**8.6%**	(8.0%-9.2%)	**8.2%**	(7.4%-9.0%)		**9.0%**	(8.1%-9.9%)
	E	9.0%	(8.0%-9.9%)	8.3%	(7.1%-9.5%)		9.6%	(8.1%-11.2%)
	M	9.4%	(6.9%-12.4%)	8.9%	(5.5%-13.2%)		10.1%	(6.6%-14.4%)
	MW	8.2%	(6.2%-10.5%)	7.8%	(5.1%-11.1%)		8.5%	(5.6%-12.2%)
	NE	9.0%	(6.9%-11.2%)	8.6%	(5.8%-11.9%)		9.6%	(6.8%-12.8%)
	NW	9.9%	(7.5%-12.5%)	11.3%	(7.9%-15.3%)		7.9%	(4.7%-11.9%)
	S	7.3%	(5.9%-8.9%)	6.5%	(4.7%-8.5%)		8.7%	(6.4%-11.2%)
	SE	8.7%	(6.9%-10.6%)	9.3%	(6.8%-12.1%)		7.8%	(5.4%-10.7%)
	W	8.1%	(6.2%-10.2%)	7.4%	(5.0%-10.3%)		8.8%	(6.0%-12.1%)
Prostate	**total**	**69.5%**	(67.9%-70.9%)	**63.0%**	(60.8%-65.1%)	+	**75.9%**	(73.7%-77.9%)
	E	77.4%	(74.7%-79.9%)	70.8%	(66.9%-74.6%)	+	84.1%	(80.4%-87.5%)
	M	63.5%	(57.1%-69.7%)	53.1%	(44.5%-61.7%)	+	72.3%	(62.8%-81.2%)
	MW	62.3%	(56.9%-67.5%)	56.9%	(49.9%-63.8%)	+	70.2%	(61.6%-78.2%)
	NE	67.3%	(61.9%-72.5%)	61.0%	(53.6%-68.1%)	+	74.1%	(66.1%-81.4%)
	NW	64.5%	(58.8%-70.0%)	58.2%	(50.1%-66.2%)	+	68.1%	(59.4%-76.3%)
	S	67.8%	(63.9%-71.5%)	59.3%	(53.9%-64.6%)	+	75.7%	(70.1%-80.8%)
	SE	69.0%	(64.8%-73.1%)	65.2%	(59.1%-70.9%)		72.3%	(66.0%-78.2%)
	W	66.4%	(61.8%-70.8%)	60.3%	(54.1%-66.4%)	+	73.7%	(66.9%-80.0%)

+ Significant improvement in survival, based on modeling adjusted for age, or age and sex (*Table 3*).

Explanatory note

Relative survival: This is the *survival observed in a particular group of patients as a percentage or proportion of the survival expected among persons of the same age and sex in the general population*. For example, if the expected five-year survival of a group of persons of a given age is 80%, and the observed survival of a group of cancer patients of the same age is 60%, the five-year relative survival of the cancer patients is expressed as (60/80)% = 75%. Use of relative survival allows assessment of the influence of a given diagnosis (e.g. breast cancer) on survival, over and above other potential causes of death, without needing to know (or rely on) the actual cause of death for any patients who die.

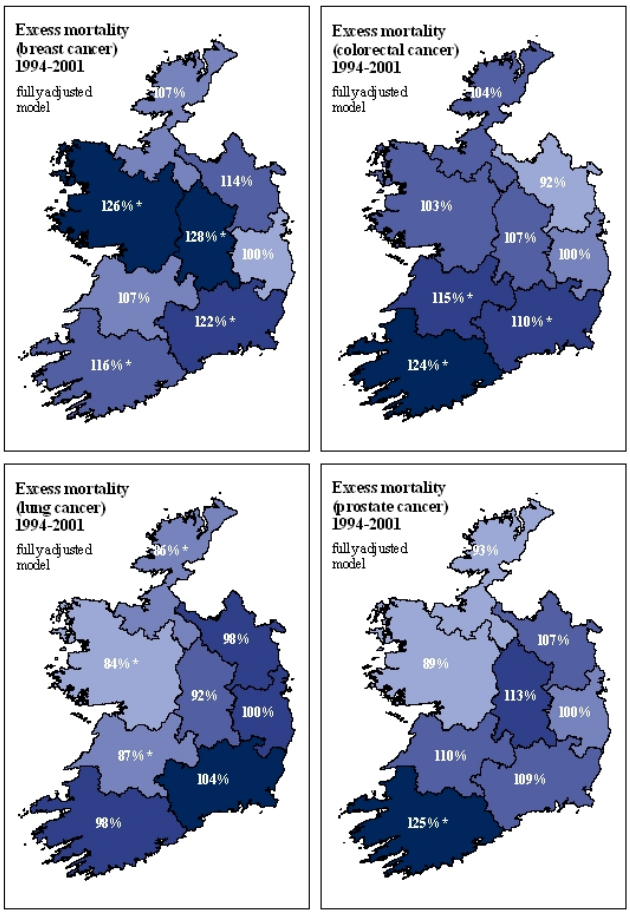


Explanatory note

Excess mortality hazard: This is the 'extra' mortality among a group of patients with a specific disease, having allowed for the expected mortality rate among persons of the same age and sex in the general population. It is the equivalent, for relative survival, of the hazard used in Cox regression modelling of crude or cause-specific survival.

Excess hazard ratio: When comparing two or more patient groups, the ratio of excess mortality hazards is calculated, generally by a statistical model which allows adjustment for age or other patient characteristics – see *Tables 3-4*. Excess hazard ratios thus involve two comparisons: between patients and general population in a given region (to estimate the excess mortality rate), then between patients in different regions (to compare the excess mortality rates, as an excess hazard ratio). Excess hazard ratios in this report are expressed in comparison with patients from the Eastern region. To simplify presentation in *Figures 1-2*, a ratio of 1.21 has been mapped as 121%, for example (compared with 100% for Eastern region).

Figure 1 Regional variation in excess mortality hazards (based on relative survival) adjusted for age, sex and lung cancer cell-type, expressed in comparison to patients from the Eastern region (100%). * = significantly high or low excess mortality (P<0.05). Low excess mortality = high relative survival, high excess mortality = low survival. Excess mortality = in relation to persons of same age and sex in general population. See also *Table 4*.



Explanatory note

Adjustment: In simple terms, adjusting two or more datasets being compared helps ensure that we are comparing like with like. For example, if two groups of patients differ substantially in their average age, survival will tend to be highest for the younger group, other factors being equal.

Figure 2 Regional variation in excess mortality hazards (based on relative survival), fully adjusted for patient and tumour characteristics, expressed in comparison to patients from the Eastern region (100%). * = significantly high or low excess mortality (P<0.05). See also *Table 4*.

Table 3 Changes in relative survival (expressed in terms of excess hazard ratios) between diagnosis periods 1994-97 and 1998-2001, nationally and by region of residence. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant change in excess hazard compared with 1994-97 (<1 = lower excess risk of death i.e. higher survival, >1 = higher excess risk i.e. lower survival). *For example, the excess age-adjusted mortality associated with a breast cancer diagnosis in 1998-2001 was 76.4% that in 1994-1997 (i.e. 23.6% lower).*

Region	Breast cancer [a]EHR (95% CI)	Colorectal cancer EHR (95% CI)	Lung cancer EHR (95% CI)	Prostate cancer EHR (95% CI)
basic model: age-, (lung celltype-), sex-adjusted				
total	**0.764** (0.703-0.831)	**0.903** (0.856-0.952)	0.996 (0.958-1.036)	**0.614** (0.552-0.683)
E	**0.722** (0.623-0.836)	0.923 (0.838-1.017)	0.982 (0.922-1.044)	**0.575** (0.454-0.728)
M	0.994 (0.710-1.391)	0.892 (0.711-1.119)	1.017 (0.853-1.214)	**0.486** (0.335-0.706)
MW	0.853 (0.645-1.128)	1.080 (0.891-1.309)	0.937 (0.812-1.081)	**0.690** (0.493-0.964)
NE	**0.738** (0.551-0.989)	1.063 (0.878-1.285)	**1.172** (1.014-1.353)	**0.697** (0.492-0.987)
NW	0.747 (0.532-1.050)	0.827 (0.675-1.012)	1.091 (0.930-1.280)	**0.588** (0.411-0.842)
S	**0.700** (0.568-0.862)	0.903 (0.797-1.023)	0.964 (0.869-1.069)	**0.639** (0.503-0.811)
SE	0.825 (0.641-1.061)	0.854 (0.730-1.000)	1.043 (0.921-1.181)	0.760 (0.566-1.019)
W	0.811 (0.625-1.051)	**0.710** (0.605-0.832)	0.954 (0.832-1.094)	**0.604** (0.445-0.819)
final multivariate model[b]				
total	**0.906** (0.834-0.985)	**0.781** (0.703-0.867)	0.999 (0.960-1.040)	**0.584** (0.475-0.718)

[a,b]See Table 4.

Table 4 Variation in relative survival, by region of residence (compared to Eastern region), for patients diagnosed with cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (<1 = lower excess hazard thus higher relative survival than in Eastern region, >1 = higher excess hazard thus lower relative survival). *For example, the excess age-adjusted mortality associated with a breast cancer diagnosis was 22.4% higher in patients from the Midland compared to the Eastern region.*

Region	Breast cancer [a]EHR (95% CI)	Colorectal cancer EHR (95% CI)	Lung cancer EHR (95% CI)	Prostate cancer EHR (95% CI)
basic model: age-, (lung celltype-), sex-adjusted				
E	1.000	1.000	1.000	1.000
M	**1.224** (1.022-1.466)	1.087 (0.963-1.227)	0.957 (0.872-1.050)	**1.646** (1.329-2.040)
MW	**1.281** (1.098-1.493)	1.102 (0.990-1.227)	**0.896** (0.828-0.970)	**1.690** (1.391-2.053)
NE	**1.281** (1.092-1.502)	0.995 (0.895-1.106)	1.008 (0.933-1.088)	**1.470** (1.196-1.807)
NW	**1.226** (1.025-1.467)	**1.124** (1.006-1.256)	**0.915** (0.841-0.995)	**1.470** (1.194-1.811)
S	**1.203** (1.062-1.362)	**1.236** (1.143-1.337)	1.017 (0.958-1.080)	**1.529** (1.301-1.798)
SE	**1.248** (1.081-1.440)	**1.205** (1.100-1.321)	1.038 (0.969-1.112)	**1.356** (1.130-1.627)
W	**1.263** (1.091-1.461)	**1.158** (1.055-1.271)	0.939 (0.871-1.011)	**1.455** (1.211-1.749)
final multivariate model[b]				
E	1.000	1.000	1.000	1.000
M	**1.277** (1.068-1.527)	1.066 (0.939-1.210)	0.924 (0.841-1.015)	1.128 (0.923-1.377)
MW	1.069 (0.914-1.250)	**1.152** (1.032-1.286)	**0.871** (0.804-0.943)	1.104 (0.913-1.335)
NE	1.139 (0.971-1.336)	0.917 (0.825-1.020)	0.976 (0.903-1.055)	1.072 (0.889-1.292)
NW	1.066 (0.894-1.271)	1.038 (0.929-1.160)	**0.855** (0.785-0.931)	0.934 (0.772-1.129)
S	**1.162** (1.025-1.317)	**1.240** (1.145-1.343)	0.978 (0.919-1.039)	**1.248** (1.073-1.450)
SE	**1.222** (1.061-1.407)	**1.100** (1.003-1.206)	1.035 (0.966-1.109)	1.086 (0.919-1.284)
W	**1.262** (1.093-1.457)	1.027 (0.935-1.129)	**0.839** (0.779-0.905)	0.894 (0.755-1.057)

[a]EHR = excess hazard ratio estimated by a generalized linear model (GLM).
[b]Final (full) multivariate models, including some or all of the following (if they contributed significantly to model-fit): *sex* (for colorectal and lung cancers); *age-group*; *T, N, M categories*; *tumour grade*; *lung cancer cell-type*; *breast tumour morphology*; *colorectal site*; *microscopic verification status*; *method of presentation*; *smoking status*; *marital status*; individual *year of diagnosis*.

Explanatory note **Why compare hazards, not survival proportions?** Hazards (mortality rates) have technical advantages for statistical modelling to quantify differences in survival, typically with adjustment for patient and tumour characteristics that might complicate comparisons. Model-based comparison of hazards also allows a fuller description of differences in survival between patient groups, throughout follow-up, rather than reflecting simply the percentages of patients who survive to fixed points, e.g. five years, after diagnosis.

Table 5 Breakdown of surgical treatment for cancers diagnosed during 1998-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases.

Region where surgically treated		Region of residence								
		E	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Breast cancer										
Eastern	%	**99.2**	31.2	6.8	35.1	13.6	1.1	17.5	4.6	**46.6**
Midland	%	0.7	**55.8**	1.3	2.3	0.3	0.0	0.2	0.2	3.8
Mid-Western	%	0.0	0.3	**69.3**	0.0	0.0	0.2	0.8	0.0	5.5
North-Eastern	%	0.1	0.6	0.0	**62.7**	1.5	0.0	0.0	0.0	5.1
North-Western	%	0.0	0.0	0.0	0.0	**77.1**	0.0	0.0	0.9	4.3
Southern	%	0.0	0.0	6.2	0.0	0.0	**98.7**	4.3	0.0	15.9
South-Eastern	%	0.0	1.7	4.7	0.0	0.0	0.0	**77.3**	0.0	8.2
Western	%	0.0	10.5	11.7	0.0	4.5	0.0	0.0	**94.3**	10.5
Northern Ireland	%	0.0	0.0	0.0	0.0	3.0	0.0	0.0	0.0	0.2
Colorectal cancer										
Eastern	%	**98.4**	13.0	5.7	21.7	10.7	0.8	8.2	3.7	**37.5**
Midland	%	0.4	**78.5**	0.9	0.4	0.8	0.0	0.7	0.2	4.3
Mid-Western	%	0.0	0.4	**79.3**	0.0	0.0	0.2	0.7	0.0	6.9
North-Eastern	%	0.6	1.1	0.0	**77.0**	4.0	0.0	0.0	0.0	7.6
North-Western	%	0.1	0.0	0.0	0.4	**83.5**	0.0	0.2	2.1	6.1
Southern	%	0.2	0.0	5.5	0.0	0.0	**98.7**	4.1	0.0	17.1
South-Eastern	%	0.3	0.4	4.6	0.2	0.0	0.2	**86.0**	0.0	9.5
Western	%	0.2	6.7	4.1	0.2	0.5	0.0	0.0	**94.1**	10.9
Northern Ireland	%	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0
Lung cancer										
Eastern	%	**100.0**	**100.0**	**54.3**	**95.6**	**92.3**	4.2	**76.5**	**58.1**	**80.2**
Midland	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mid-Western	%	0.0	0.0	6.5	0.0	0.0	0.0	0.0	0.0	0.4
North-Eastern	%	0.0	0.0	0.0	4.4	0.0	0.0	0.0	0.0	0.4
North-Western	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Southern	%	0.0	0.0	30.4	0.0	0.0	**95.8**	19.1	0.0	15.4
South-Eastern	%	0.0	0.0	0.0	0.0	0.0	0.0	4.4	0.0	0.4
Western	%	0.0	0.0	8.7	0.0	7.7	0.0	0.0	41.9	3.3
Prostate cancer										
Eastern	%	**99.3**	**63.2**	17.0	**75.6**	40.4	3.1	**49.2**	30.5	**62.0**
Midland	%	0.4	32.2	0.7	0.0	0.0	0.0	0.0	0.0	2.4
Mid-Western	%	0.1	1.2	**55.1**	0.0	0.0	0.3	0.8	0.0	3.4
North-Eastern	%	0.2	0.0	0.0	23.3	0.0	0.0	0.0	0.0	2.5
North-Western	%	0.0	0.0	0.0	0.8	**53.9**	0.0	0.0	3.7	2.2
Southern	%	0.0	0.0	17.0	0.0	0.0	**96.6**	3.9	0.0	15.0
South-Eastern	%	0.0	1.2	5.4	0.4	0.0	0.0	46.1	0.0	6.9
Western	%	0.0	2.3	4.8	0.0	1.1	0.0	0.0	**65.8**	5.3
Northern Ireland		0.0	0.0	0.0	0.0	4.5	0.0	0.0	0.0	0.2

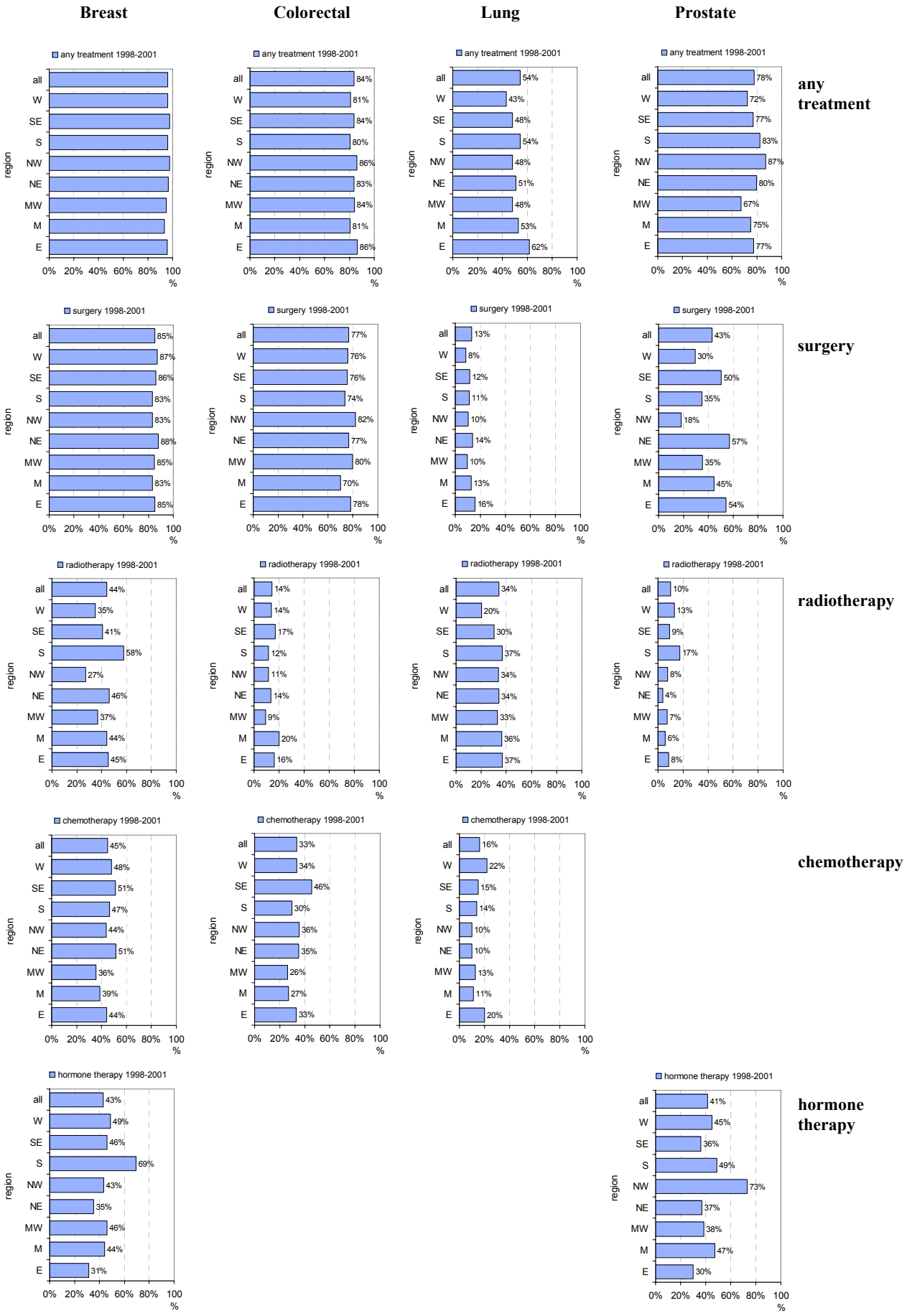


Figure 3 Proportions of cancer patients resident in each region who had tumour-directed treatment within six months of diagnosis, 1998-2001. Note: Results are shown only for standard treatment modalities for a given cancer.

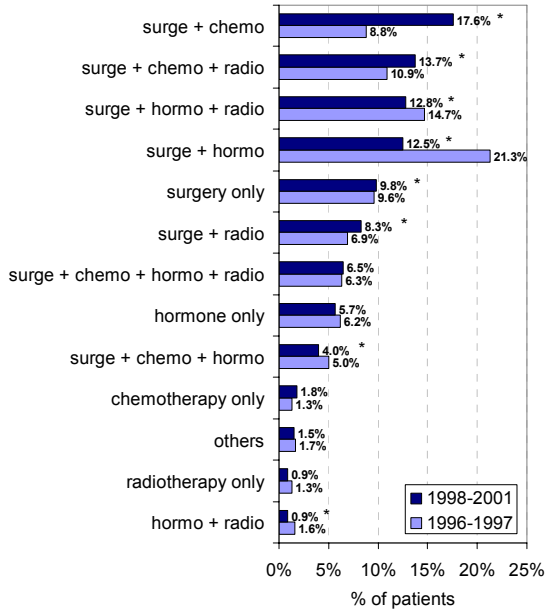


Figure 4 Treatment combinations for breast cancer.
*Significant changes between diagnosis periods.

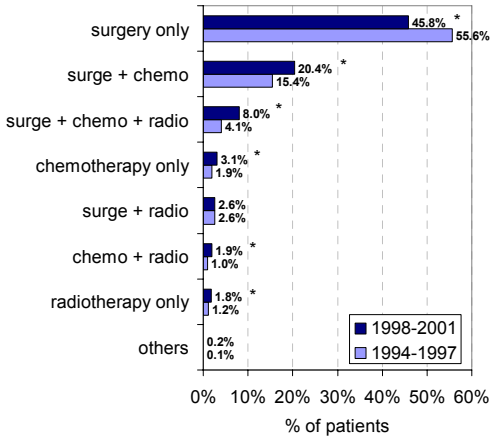


Figure 5 Treatment combinations for colorectal cancer.

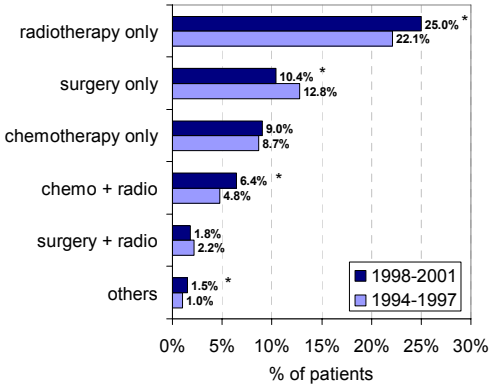


Figure 6 Treatment combinations for lung cancer.

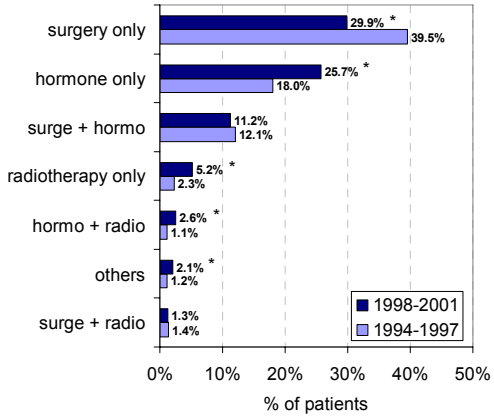


Figure 7 Treatment combinations for prostate cancer.

Table 6 Average annual percentage changes (1996-2001) in proportions of cancer patients having tumour-directed treatment within six months of diagnosis, adjusted for age and sex only (also cell-type for lung cancer). Statistically significant trends are highlighted in bold. In general, further adjustment for stage-related and other variables had only minor effects on the direction, magnitude and statistical significance of these trends.

Treatment modality	Diagnosis period	Breast cancer trend (95% CI)	Colorectal cancer trend (95% CI)	Lung cancer trend (95% CI)	Prostate cancer trend (95% CI)
Overall treatment	1996-2001	-0.1% p.a. (-0.4%, +0.2%)	**+0.6%** p.a. (+0.0%, +1.2%)	**+2.5%** p.a. (+1.1%, +3.9%)	**-1.4%** p.a. (-2.1%, -0.8%)
Surgery	1996-2001	**+0.5%** p.a. (+0.0%, +1.1%)	**-0.7%** p.a. (-1.4%, -0.1%)	**-3.4%** p.a. (-6.5%, -0.2%)	**-7.6%** p.a. (-8.7%, -6.5%)
Radiotherapy	1996-2001	-0.4% p.a. (-1.7%, +1.0%)	**+10.8%** p.a. (+7.4%, +14.2%)	**+2.2%** p.a. (+0.3%, +4.2%)	**+13.2%** p.a. (+8.3%, +18.3%)
Chemotherapy	1996-2001	**+12.6%** p.a. (+10.7%, +14.5%)	**+12.3%** p.a. (+10.1%, +14.6%)	**+6.4%** p.a. (+2.9%, +10.0%)	
Hormone therapy	1996-2001	**-8.9%** p.a. (-9.9%, -7.8%)			**+3.3%** p.a. (+1.5%, +5.0%)

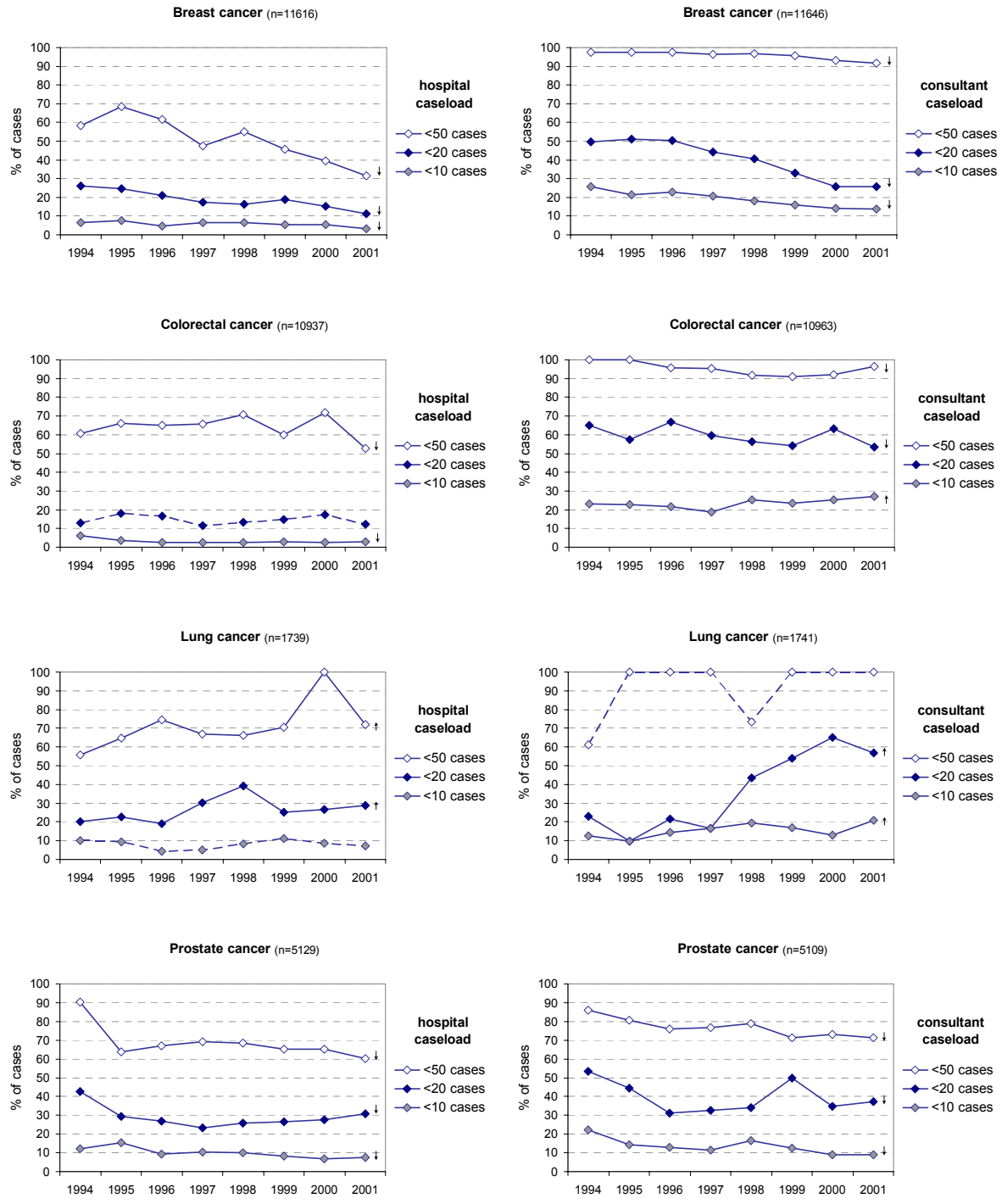
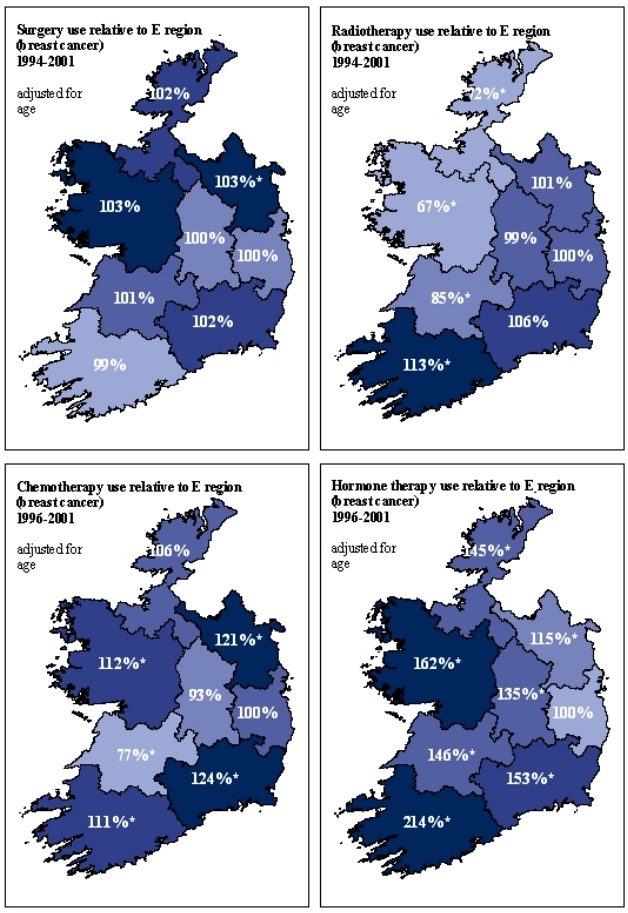


Figure 8 Proportions of surgical patients who had surgery in hospitals which treated, or under a consultant with responsibility for, <10, <20 or <50 surgical patients in a given year, for a given cancer. For this analysis, patients are counted once for each relevant hospital or consultant within six months of diagnosis, for surgical procedures only. Hospitals or consultants outside of the Republic of Ireland are excluded. Significant overall trends (based on Mantel's trend test for proportions) are indicated by solid lines.



Explanatory note

Relative risk (of treatment): In simple terms, if 50% of one group of cancer patients receive a particular treatment within a given time after diagnosis, compared with 40% of another group, the relative risk (RR) for treatment of the first group is (50/40) = 1.25, i.e. patients from the first group are 25% more likely to have been treated. This can be also expressed as a RR of 125% (as in *Figures 9-12*). If the age-composition or other characteristics of two groups of patients differ, those characteristics may also influence the proportion of patient treated. Thus, to examine the effect of, say, region of residence on treatment, it will generally be important to *adjust* for other factors that may complicate comparisons (or help 'explain' some of the apparent differences between regions).

Figure 9 Regional variation in breast cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age.
* = significantly high or low values (P<0.05).

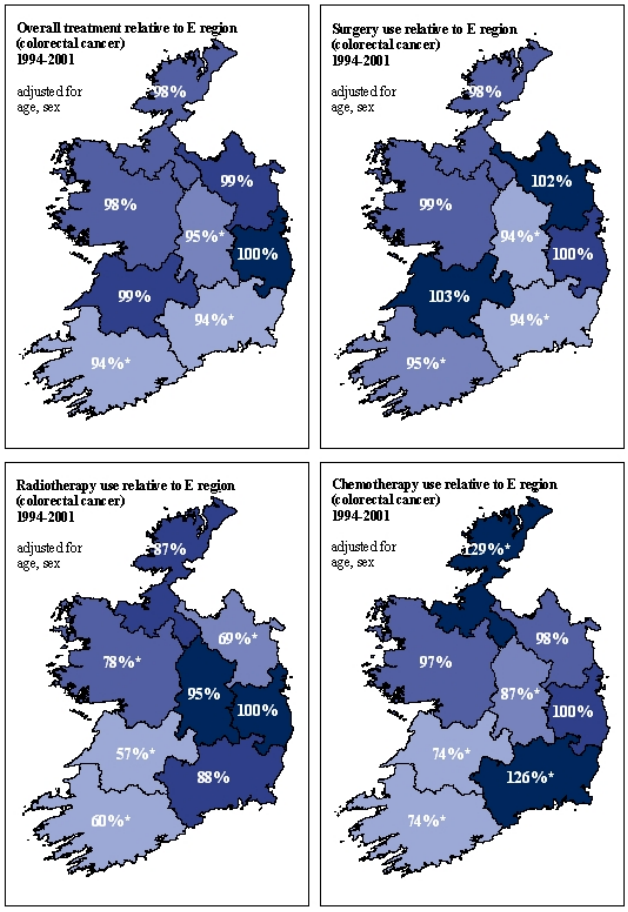


Figure 10 Regional variation in colorectal cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age and sex.
* = significantly high or low values (P<0.05).

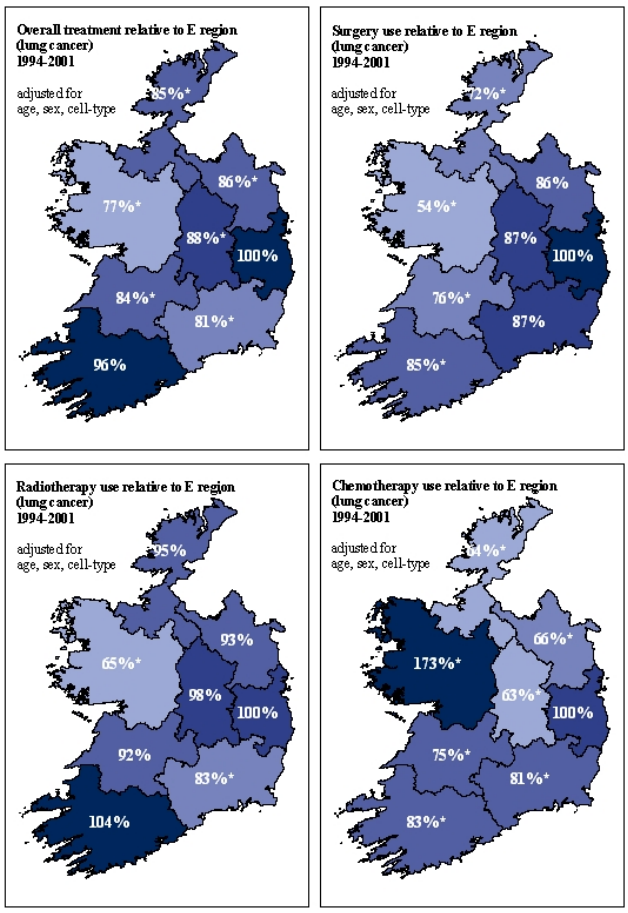


Figure 11 Regional variation in lung cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age, sex and cell-type. * = significantly high or low values (P<0.05).

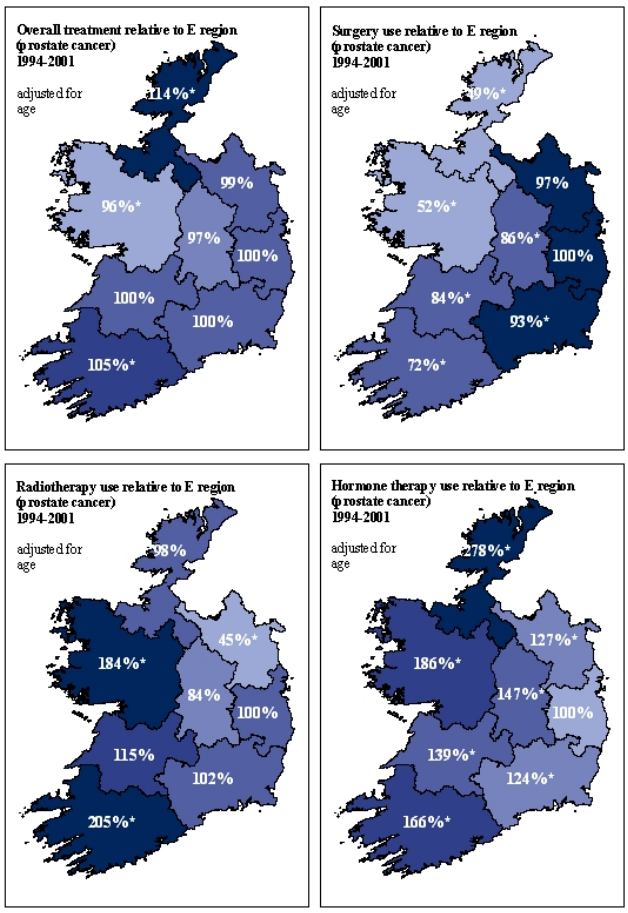


Figure 12 Regional variation in prostate cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age.
* = significantly high or low values (P<0.05).

Table 7 Variation in treatment, by region of residence (compared to Eastern region), for patients diagnosed with invasive cancer during 1994-2001, adjusted for age and sex only (also cell-type for lung cancer). Analysis is based on tumour-directed treatments received within six months of diagnosis. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

Treatment modality	Region	Breast cancer [a]RR (95% CI)	Colorectal cancer RR (95% CI)	Lung cancer RR (95% CI)	Prostate cancer RR (95% CI)
Overall treatment	E	1.000	1.000	1.000	1.000
	M	0.989 (0.967-1.006)	**0.950** (0.911-0.984)	**0.878** (0.798-0.958)	0.974 (0.923-1.020)
	MW	1.003 (0.986-1.015)	0.989 (0.957-1.017)	**0.837** (0.767-0.908)	0.999 (0.954-1.040)
	NE	1.007 (0.991-1.019)	0.991 (0.961-1.018)	**0.861** (0.793-0.928)	0.989 (0.944-1.030)
	NW	**1.023** (1.010-1.032)	0.982 (0.949-1.011)	**0.854** (0.780-0.928)	**1.140** (1.105-1.169)
	S	1.009 (0.998-1.018)	**0.936** (0.910-0.961)	0.959 (0.906-1.010)	**1.052** (1.021-1.081)
	SE	**1.022** (1.011-1.030)	**0.937** (0.906-0.965)	**0.805** (0.744-0.866)	0.998 (0.960-1.033)
	W	1.005 (0.990-1.016)	0.977 (0.949-1.002)	**0.773** (0.708-0.839)	**0.960** (0.919-0.998)
Surgery	E	1.000	1.000	1.000	1.000
	M	0.995 (0.957-1.029)	**0.943** (0.898-0.984)	0.868 (0.694-1.077)	**0.862** (0.789-0.936)
	MW	1.009 (0.977-1.036)	1.029 (0.993-1.060)	**0.760** (0.613-0.935)	**0.839** (0.772-0.907)
	NE	**1.034** (1.004-1.059)	1.016 (0.981-1.047)	0.864 (0.716-1.037)	0.974 (0.908-1.039)
	NW	1.016 (0.982-1.045)	0.979 (0.940-1.015)	**0.720** (0.573-0.899)	**0.491** (0.433-0.554)
	S	0.988 (0.963-1.011)	**0.948** (0.919-0.976)	**0.846** (0.733-0.974)	**0.715** (0.665-0.766)
	SE	1.020 (0.992-1.044)	**0.942** (0.907-0.974)	0.865 (0.729-1.021)	**0.929** (0.872-0.985)
	W	1.027 (0.999-1.051)	0.992 (0.960-1.022)	**0.544** (0.433-0.680)	**0.520** (0.469-0.574)
Radiotherapy	E	1.000	1.000	1.000	1.000
	M	0.986 (0.901-1.074)	0.952 (0.778-1.157)	0.975 (0.857-1.099)	0.839 (0.584-1.196)
	MW	**0.853** (0.781-0.928)	**0.565** (0.454-0.700)	0.920 (0.821-1.026)	1.149 (0.869-1.508)
	NE	1.007 (0.930-1.085)	**0.692** (0.570-0.836)	0.928 (0.831-1.030)	**0.452** (0.299-0.680)
	NW	**0.724** (0.645-0.808)	0.865 (0.710-1.048)	0.949 (0.843-1.062)	0.983 (0.716-1.339)
	S	**1.127** (1.068-1.186)	**0.600** (0.512-0.702)	1.036 (0.958-1.117)	**2.049** (1.720-2.428)
	SE	1.057 (0.987-1.127)	0.882 (0.753-1.029)	**0.832** (0.749-0.921)	1.021 (0.798-1.300)
	W	**0.667** (0.605-0.733)	**0.783** (0.661-0.923)	**0.649** (0.568-0.737)	**1.836** (1.491-2.246)
Chemotherapy[b]	E	1.000	1.000	1.000	-
	M	0.932 (0.820-1.049)	**0.867** (0.751-0.994)	**0.626** (0.472-0.822)	-
	MW	**0.769** (0.679-0.866)	**0.738** (0.646-0.839)	**0.750** (0.598-0.934)	-
	NE	**1.205** (1.099-1.312)	0.982 (0.878-1.092)	**0.664** (0.530-0.826)	-
	NW	1.060 (0.939-1.184)	**1.285** (1.154-1.420)	**0.641** (0.497-0.820)	-
	S	**1.105** (1.024-1.187)	**0.735** (0.665-0.811)	**0.834** (0.713-0.971)	-
	SE	**1.241** (1.143-1.338)	**1.255** (1.148-1.365)	**0.808** (0.669-0.971)	-
	W	**1.120** (1.022-1.220)	0.972 (0.876-1.075)	**1.725** (1.493-1.976)	-
Hormone therapy[b]	E	1.000	-	-	1.000
	M	**1.346** (1.215-1.478)	-	-	**1.474** (1.314-1.642)
	MW	**1.463** (1.348-1.577)	-	-	**1.385** (1.241-1.537)
	NE	**1.148** (1.038-1.262)	-	-	**1.268** (1.130-1.415)
	NW	**1.453** (1.321-1.585)	-	-	**2.777** (2.630-2.913)
	S	**2.139** (2.063-2.212)	-	-	**1.662** (1.543-1.783)
	SE	**1.534** (1.430-1.638)	-	-	**1.236** (1.118-1.361)
	W	**1.617** (1.509-1.723)	-	-	**1.859** (1.722-1.997)

[a]Risk ratios, compared with Eastern region, were derived using the method of Zhang & Yu (1998) from adjusted odds ratios calculated by logistic regression adjusted for the following patient and tumour variables: *sex* (for colorectal and lung cancers); *age-group* 15-44, 45-54, 55-64, 65-74, or 75+ (ages 15-54 to 85+ for prostate cancer); *lung tumour morphology* - non-small-cell (NSCLC), small- cell (SCLC), or other/unspecified.
[b]For breast cancer, data on use of chemotherapy and hormone therapy are for 1996-2001 only.

Table 8 Variation in treatment, by region of residence (compared to Eastern region), for patients diagnosed with invasive cancer during 1994-2001, adjusted for detailed patient and tumour characteristics. Analysis is based on tumour-directed treatments received within six months of diagnosis. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

Treatment modality	Region	Breast cancer [a]RR (95% CI)	Colorectal cancer RR (95% CI)	Lung cancer RR (95% CI)	Prostate cancer RR (95% CI)
Overall treatment	E	1.000	1.000	1.000	1.000
	M	**0.971** (0.937-0.995)	**0.916** (0.852-0.971)	**0.867** (0.783-0.950)	0.972 (0.918-1.021)
	MW	**1.015** (1.000-1.026)	1.013 (0.971-1.047)	**0.835** (0.762-0.908)	**1.073** (1.032-1.110)
	NE	1.005 (0.985-1.019)	0.992 (0.951-1.027)	**0.882** (0.811-0.952)	0.992 (0.944-1.036)
	NW	**1.025** (1.010-1.035)	0.992 (0.946-1.030)	**0.856** (0.778-0.934)	**1.161** (1.127-1.189)
	S	1.006 (0.991-1.017)	0.989 (0.955-1.018)	0.965 (0.910-1.020)	**1.061** (1.027-1.092)
	SE	**1.021** (1.007-1.031)	**0.944** (0.900-0.982)	**0.762** (0.699-0.826)	0.994 (0.952-1.032)
	W	1.002 (0.983-1.016)	1.030 (0.999-1.057)	**0.788** (0.720-0.857)	0.996 (0.955-1.034)
Surgery	E	1.000	1.000	1.000	1.000
	M	0.965 (0.907-1.013)	**0.880** (0.801-0.951)	0.774 (0.577-1.024)	**0.916** (0.833-0.999)
	MW	**1.059** (1.025-1.087)	**1.091** (1.047-1.127)	**0.715** (0.543-0.931)	1.052 (0.972-1.129)
	NE	1.037 (0.996-1.070)	1.032 (0.983-1.075)	0.863 (0.676-1.090)	1.054 (0.979-1.126)
	NW	1.031 (0.982-1.069)	0.950 (0.885-1.006)	**0.641** (0.477-0.851)	**0.509** (0.443-0.582)
	S	**0.954** (0.913-0.991)	0.988 (0.944-1.028)	0.840 (0.699-1.005)	**0.754** (0.695-0.815)
	SE	1.006 (0.965-1.040)	**0.952** (0.900-0.999)	**0.778** (0.625-0.962)	0.955 (0.890-1.020)
	W	**1.057** (1.024-1.084)	**1.069** (1.029-1.104)	**0.549** (0.415-0.719)	**0.523** (0.466-0.584)
Radiotherapy	E	1.000	1.000	1.000	1.000
	M	0.982 (0.895-1.071)	1.046 (0.826-1.313)	0.969 (0.850-1.096)	0.821 (0.567-1.179)
	MW	**0.890** (0.815-0.967)	**0.508** (0.395-0.651)	0.936 (0.833-1.044)	1.229 (0.918-1.631)
	NE	1.003 (0.923-1.083)	**0.729** (0.587-0.899)	0.950 (0.850-1.055)	**0.491** (0.323-0.742)
	NW	**0.727** (0.647-0.813)	0.997 (0.801-1.231)	0.934 (0.826-1.049)	0.953 (0.684-1.319)
	S	**1.136** (1.075-1.198)	**0.552** (0.461-0.660)	1.055 (0.972-1.140)	**2.093** (1.730-2.516)
	SE	1.063 (0.991-1.135)	0.852 (0.712-1.017)	**0.834** (0.749-0.926)	1.117 (0.868-1.430)
	W	**0.684** (0.619-0.751)	**0.681** (0.561-0.822)	**0.636** (0.555-0.725)	**1.831** (1.472-2.262)
Chemotherapy[b]	E	1.000	1.000	1.000	-
	M	0.871 (0.750-1.000)	0.883 (0.751-1.030)	**0.606** (0.451-0.805)	-
	MW	**0.751** (0.651-0.858)	**0.714** (0.612-0.827)	**0.767** (0.609-0.959)	-
	NE	**1.153** (1.031-1.275)	1.014 (0.897-1.140)	**0.706** (0.561-0.882)	-
	NW	0.941 (0.811-1.078)	**1.315** (1.169-1.467)	**0.640** (0.493-0.824)	-
	S	1.041 (0.947-1.136)	**0.762** (0.682-0.849)	0.854 (0.725-1.001)	-
	SE	**1.143** (1.033-1.255)	**1.257** (1.139-1.380)	**0.800** (0.658-0.967)	-
	W	1.089 (0.978-1.203)	0.920 (0.816-1.032)	**1.743** (1.503-2.003)	-
Hormone therapy[b]	E	1.000	-	-	1.000
	M	**1.305** (1.167-1.446)	-	-	**1.407** (1.235-1.589)
	MW	**1.482** (1.357-1.606)	-	-	**1.488** (1.321-1.664)
	NE	**1.184** (1.063-1.308)	-	-	**1.209** (1.061-1.367)
	NW	**1.344** (1.206-1.485)	-	-	**2.814** (2.654-2.960)
	S	**2.120** (2.034-2.200)	-	-	**1.658** (1.523-1.797)
	SE	**1.491** (1.378-1.604)	-	-	**1.279** (1.146-1.420)
	W	**1.581** (1.464-1.697)	-	-	**2.015** (1.860-2.169)

[a]Risk ratios, compared with Eastern region, were derived using the method of Zhang & Yu (1998) from adjusted odds ratios calculated by logistic regression adjusted for the following patient and tumour variables (if they contributed significantly to model-fit): *sex* (for colorectal and lung cancers); *age-group*; *T, N and M categories of stage*; *tumour grade*; *tumour morphology* (for lung and breast cancers); *colorectal site*; *microscopic verification status; method of presentation*; *smoking status*; *marital status*; individual *year of diagnosis*.
[b]For breast cancer, data on use of chemotherapy and hormone therapy are for 1996-2001 only.

Patterns of care and survival of cancer patients in Ireland 1994 to 2001:

time-trends and regional variation for breast, colorectal, lung and prostate cancer

Paul M Walsh
Harry Comber

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Published by the National Cancer Registry 2006

Cork, Ireland

Telephone 021-4318014

Email info@ncri.ie

Web site www.ncri.ie

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Contents

Patterns of care and survival of cancer patients in Ireland 1994 to 2001: time-trends and regional variation for breast, colorectal, lung and prostate cancer

SUMMARY

Main conclusions

Improvements in survival for breast, colorectal and prostate cancers, but not lung cancers, were seen at national scale between the earlier (1994-1997) and later (1998-2001) parts of the period examined. Improvements in treatment or in early diagnosis are presumably involved, but exaggeration of true survival improvements by lead-time bias cannot be ruled out, especially for prostate cancer.

Regional variation in survival is still apparent, as noted in our previous report (NicAmhlaoibh *et al*. 2004), with survival generally lowest for patients resident outside the Eastern region, except for lung cancer. This variation is partly but not wholly explained by variation in patient or tumour characteristics.

Trends in treatment appeared to be broadly in line with expectations of greater or better-targeted use of radiotherapy and chemotherapy, although no increase in radiotherapy use was seen for breast cancer. An apparent major fall in use of hormonal treatment for breast cancer may also be in line with expectations of improved targeting of appropriate treatment. This may also apply to increased use of hormone therapy and reduced use of surgery for prostate cancer.

At regional scales, there is still substantial variation in the use of particular treatment modalities. These variations are largely unexplained by patient and tumour characteristics, suggesting that geographic and institutional influences on treatment may be critical. Evidence of increased specialization or centralization of services is limited, although further analysis is required.

Introduction and methods

This is the second National Cancer Registry report focusing on treatment and survival of cancer patients in Ireland, for the four most important cancers in healthcare terms. The previous report covered the period 1994 to 1998 (NicAmhlaoibh *et al*. 2004). Coverage is provided here for the eight-year period 1994-2001, representing 49100 cancer patients with survival follow-up to December 2003.

Changes in scope or methodology from the previous report include: assessment of time-trends in survival and treatment; use of relative survival estimates and modelling (rather than crude and cause-specific equivalents); presentation of regional and other treatment comparisons as adjusted risk ratios (rather than odds ratios); and use of age-groups based on the EUROCARE-3 patient population (Capocaccia *et al*. 2003). Summary data on hospital and consultant caseloads are also presented for surgical patients. However, potential caseload, deprivation and co-morbidity influences on survival and treatment are not examined, pending further work on geo-coding and hospital-linkage of cancer registry data.

Time-trends

To allow for possible under-recording of treatments during 1994 and 1995, *trends in the proportions of patients treated are assessed for the period 1996 to 2001 only*. Patient follow-up data is complete for the period, and *survival comparisons are made between diagnosis periods 1994-97 and 1998-2001*.

Regional definitions

Results are presented for *eight regions of residence*, defined (partly for continuity with previous National Cancer Registry analyses) on the basis of the former Health Board areas plus the former Eastern Regional Health Authority area which applied during the period considered. The neutral term ‘region’ is deliberately used.

Survival

Survival is presented here as *estimates of relative survival*, i.e. the ratio of observed survival of patients to the expected survival among persons of the same age and sex in the general population. The regional estimates presented here are the first to be published for Ireland. Formal comparisons between regions, adjusted for relevant patient and tumour characteristics, are made using *relative survival modelling* (Dickman *et al*. 2004).

Treatment

Data analysed here are for treatments *administered within six months of the date of diagnosis*, if anti-tumour or tissue-destroying in effect, whether originally considered ‘curative’, ‘palliative’ or otherwise. Proportions of patients treated are summarized. Formal comparisons between years or regions are based on *logistic regression*, adjusted for relevant patient and tumour characteristics. Results (odds ratios) are *re-expressed as risk ratios* to avoid over-stating proportional differences (Zhang & Yu 1998).

Results

An overview of time-trends in relative survival and in treatment, nationally and regionally, is provided in *Table 1*. Other tables and figures summarize time-trends and regional variation in further detail.

Survival

General summary

National estimates of five-year relative survival for patients diagnosed during 1994-2001 as a whole were 75.4% for breast cancer, 49.2% for colorectal cancer, 8.6% for lung cancer and 69.5% for prostate cancer.

Time-trends in survival

Relative survival for breast, colorectal and prostate cancers showed obvious increases between the diagnosis period 1994-97 and 1998-2001 (*Table 2*), and showed a possible increase for lung cancer. Those for breast, colorectal and prostate cancers were confirmed by relative survival modelling (*Table 3*), which indicated age-adjusted reductions in excess mortality risk by 24%, 10% and 39%, respectively.

At regional scales, survival estimates showed some indication of improvement, in all regions for breast and prostate cancers and in most regions for colorectal and lung cancers (*Table 2*). Regional changes as assessed by modelling were significant for three regions for breast cancer (reduced excess risk i.e. improved relative survival in Eastern, North-Eastern and Southern regions), one region for colorectal cancer (improved survival in Western region), one region for lung cancer (reduced survival in North-Eastern region), but for seven of the eight regions for prostate cancer (improved survival) (*Table 3*).

Fuller adjustment for patient and tumour characteristics modified the national trends somewhat, but the reductions in excess risk remained significant for breast, colorectal and prostate cancer (*Table 3*). For breast cancer, the reduction in risk (improvement in survival) was less marked than in the basic model, but for colorectal cancer the reduction was more marked after fuller adjustment. For prostate cancer, the reduction in risk remained substantial.

Possible changes in patient or tumour characteristics over time thus appear to provide only a partial explanation of trends in survival. Improvements in treatment (see below) seem likely to account, in part, for the survival improvements seen. But changes in unmeasured or poorly measured factors could also be involved. For example, data on cancer stage were substantially incomplete, thus adjustment for possible improvements in early diagnosis may not have been adequate. This is particularly critical given the possibility of *lead-time bias*, whereby earlier detection of cancers through organized or unorganized screening can increase apparent survival times, even if there is no true survival benefit. Of the cancers considered here, the introduction of organized screening for breast cancer (2000/2001 onwards) should have had, at most, only a minor influence on survival trends presented here. For prostate cancer, however, major increases in both apparent survival and in numbers of diagnosed cases suggest that earlier detection through Prostate Specific Antigen (PSA) screening may already be influencing trends, although the true benefits of PSA screening are unclear.

Regional variation in survival

Apparent regional variations in relative survival estimates (*Table 2*) were confirmed for breast, colorectal and prostate cancers by relative survival modelling (*Figure 1*, *Table 4*). This indicated significantly poorer age-adjusted survival in most regions, compared with the Eastern region. Regional variation was less marked for lung cancer (and involved higher survival in several regions).

Fuller adjustment for stage and other tumour and patient variables modified and, in general, substantially reduced regional discrepancies (*Figure 2*, *Table 4*). In statistical terms, these variables appeared to 'explain' some of the differences.

This applied particularly to prostate cancer, for which little regional variation was apparent in the full model – significantly higher excess mortality (lower relative survival) among patients from the Southern region only. For breast cancer, full adjustment reduced the number of regions with significantly low survival from seven to four (Midland, Southern, South-Eastern and Western regions). For colorectal cancer, survival was significantly low among patients from the Mid-Western, Southern and South-Eastern regions. In contrast, survival of lung cancer patients was significantly high among patients from three regions (Mid-Western, North-Western and Western), although absolute differences were small for this high-fatality cancer.

No region had significantly poorer survival for all four cancers. Patients from the Southern region did have significantly poorer survival than the reference Eastern region for breast, colorectal and prostate cancers during 1994-2001 as a whole. In the most recent diagnosis period, 1998-2001, only colorectal and prostate cancers had significantly low survival in the Southern region (and also in the

Mid-Western and South-Eastern regions) (see full report).

It should be noted that prognostic and demographic variables were often substantially incomplete, and may have been correlated with the quality of diagnostic or prognostic investigations. Thus the full explanatory power of the models is difficult to assess.

Treatment

General summary of treatment

Treatments nationally and regionally are summarized in *Figure 3* (1998-2001) and treatment-combinations in *Figures 4-7* (1994-97 and 1998-2001).

For breast cancers diagnosed during 1998-2001, 96% of patients had some form of definitive or tumour-directed treatment within six months of diagnosis, 85% had surgical treatment, 45% chemotherapy, 44% radiotherapy and 43% hormonal therapy (*Figure 3*). In the same period, the most frequent treatments or combinations were surgery plus chemotherapy (18% of cases), surgery plus chemotherapy plus radiotherapy (14%), surgery plus hormonal therapy plus radiotherapy (13%), surgery plus hormone therapy (13%), and surgery only (10%) (*Figure 4*).

For colorectal cancer during 1998-2001, 84% of patients had any treatment, 77% had surgery, 33% chemotherapy and 14% radiotherapy (*Figure 3*). The main combinations were surgery only (46%), surgery plus chemotherapy (20%), and surgery plus chemotherapy plus radiotherapy (8%) (*Figure 5*).

For lung cancer during 1998-2001, 54% of patients had any treatment, 34% had radiotherapy, 16% chemotherapy and 13% surgery (*Figure 3*). Most patients had radiotherapy only (25%), surgery only (10%), or chemotherapy only (9%) (*Figure 6*).

For prostate cancer during 1998-2001, 78% of patients had any treatment, 43% had surgery, 41% hormonal therapy and 10% radiotherapy (*Figure 3*). Most had surgery only (30%), hormonal therapy only (26%), or surgery plus hormonal therapy (11%) (*Figure 7*).

Region of residence v. region of main surgical treatment

For colorectal and breast cancers, the majority of patients resident in a region received their main surgical treatment in the same region (see *Table 5* for the period 1998-2001). In contrast, most surgical cases of lung cancer from almost all regions (other than Southern region) had their main surgery in the Eastern region, albeit based on small numbers of surgical cases. For prostate cancer, regional patterns were intermediate between these extremes.

Hospital and consultant caseloads

The general trend between 1994 and 2001 was for fewer surgical patients to be treated by hospitals or consultants having small average caseloads of breast, colorectal or prostate cancer patients (*Figure 8*). These trends were strongest for breast cancer, but were not evident (or the opposite trends were seen) for lung cancer. However, such trends in caseload do not, by themselves, necessarily indicate increased specialization or centralization of services. Further studies will examine the possible influence of caseload or specialization on survival or quality of treatment.

Time-trends in treatment

The proportions of patients receiving any tumour-directed treatment showed no significant trend for breast cancer during 1996-2001, increased for lung and to a lesser extent colorectal cancer, and fell slightly for prostate cancer (*Table 6*). The use of surgical treatment increased slightly for breast cancer, fell slightly for lung and to a lesser extent colorectal cancers, and fell more markedly for prostate cancer. Radiotherapy use increased markedly for prostate and colorectal (especially rectal) cancers, and to a lesser extent for lung cancer, but showed no trend for breast cancer. For breast cancer, the recorded use of hormonal treatment fell substantially, nationally and in all regions of residence, at the same time as a significant increase in the use of chemotherapy. Chemotherapy use also increased substantially for colorectal and lung cancers, and use of hormonal treatment increased moderately for prostate cancer. Trends for each region (generally but not always consistent with national trends) are presented in the full report.

Regional variation in treatment

There was clear regional variation in the proportions of patients receiving particular treatment modalities (*Figures 9-12* and *Tables 7-8*). Where significant differences were seen, colorectal and to a lesser extent lung cancer patients resident outside the Eastern region were less likely to receive particular treatments than those from the Eastern region. This also applied to radiotherapy for breast cancer and surgery for prostate cancer. However, there was significantly higher use of hormonal treatments for breast and prostate cancers in the other regions, and significant higher use of chemotherapy for breast cancer in up to four of those seven regions. Overall treatment varied less between regions, but was significantly low for lung cancer in most regions compared to the Eastern.

In broad terms, these findings hold both for basic models (adjusted for age, sex and lung cancer cell-type) and for more complex multivariate models. Thus regional variations in treatment appeared to be largely unrelated to the patient and tumour characteristics examined. This may indicate that geographic or institutional factors were critical influences on treatment. Notably, radiotherapy use for breast cancer was highest among patients from the two regions (Eastern and Southern) that had radiotherapy centres during the period examined, and from regions immediately adjacent to the Eastern. However, regional patterns of treatment were not necessarily consistent across cancers for a given treatment modality. The most consistent patterns were high use of hormonal therapy among patients from all regions other than the Eastern (for breast and prostate cancers), low use of radiotherapy in the Western region (for breast, colorectal and lung though not prostate cancers), and low use of chemotherapy in the Mid-Western region (for breast, colorectal and lung cancers).

The link between treatment and survival

Trends or regional variations in survival are likely to reflect, in part, the provision of appropriate treatments aimed at a cure or at prolonging life. Explicitly or convincingly demonstrating this link is difficult, however, especially against a background of increased earlier detection for some cancers (notably prostate). One possible approach is to include treatment status within statistical models of survival. This has not been attempted here, in part because patients receiving and not receiving particular treatments are likely to differ in unmeasured characteristics e.g. their general health. However, further analyses are planned, to take into account available information on co-morbidity (other health conditions in the same patients).

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Table 1 Summary of age-adjusted time-trends in survival and treatment, by region of residence: significant changes in relative survival (1994-97 to 1998-2001 change) or in proportions of patients receiving tumour-directed treatment within six months of diagnosis (1996 to 2001 trend). Trends for colorectal cancer are also adjusted for sex, and for lung cancer for sex and cell-type.

Cancer	Region	Relative survival	Overall treatment	Surgery	Radiotherapy	Chemotherapy	Hormone therapy
Breast	**Total**	+		+		+	-
(female)	East	+		+		+	-
n=13383	Midland						-
	Mid-West						
	North-East	+				+	-
	North-West				-	+	-
	South	+			+	+	-
	South-East				-	+	-
	West				+	+	-
Colorectal	**Total**	+	+	-	+	+	
n=13702	East		+		+	+	
	Midland			-	+		
	Mid-West				+		
	North-East			-	+	+	
	North-West						
	South				+	+	
	South-East		+		+	+	
	West	+			+	+	
Lung	**Total**		+		+	+	
n=11663	East		+			+	
	Midland						
	Mid-West				+		
	North-East				+		
	North-West	-					
	South						
	South-East						
	West						
Prostate	**Total**	+	-	-	+		+
n=10352	East	+	-	-			
	Midland	+		-			+
	Mid-West	+	-	-			
	North-East	+					
	North-West	+	-	-	+		
	South	+		-	+		+
	South-East		-	-	+		
	West	+	-	-			-

+ = significant increase, - = significant decrease.

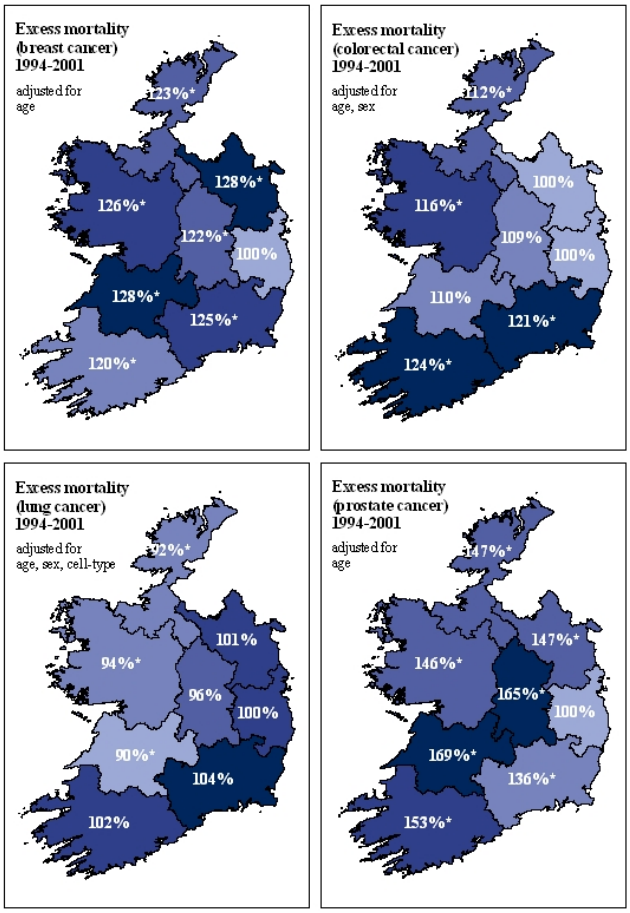
Table 2 Five-year relative survival for Irish cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population (from the same region for regional estimates).

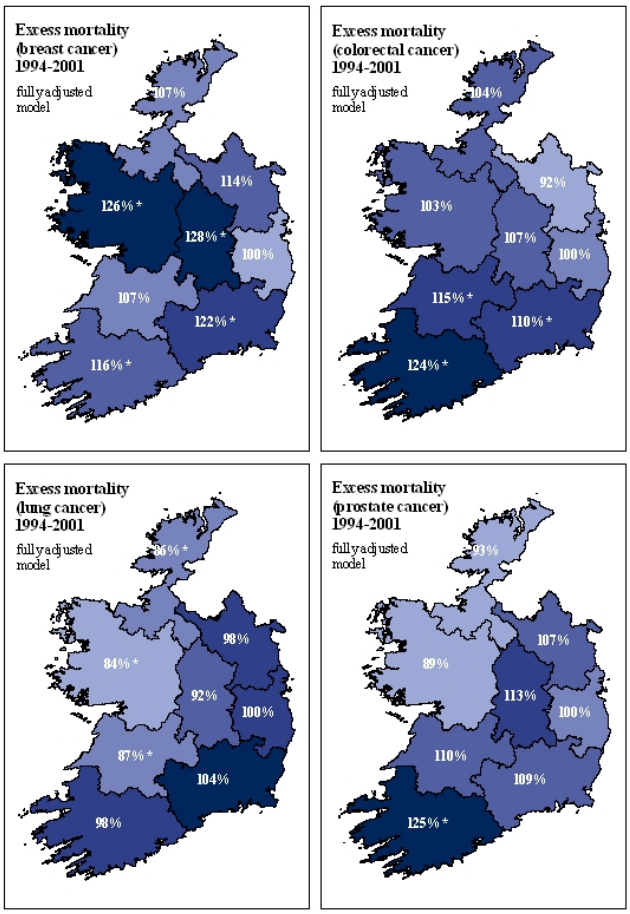
Cancer	Region	1994-2001		1994-1997			1998-2001	
		survival	(95% CI)	survival	(95% CI)		survival	(95% CI)
Breast	**total**	**75.4%**	(74.4%-76.3%)	**72.9%**	(71.6%-74.2%)	+	**78.2%**	(76.8%-79.6%)
(female)	E	78.6%	(77.1%-80.0%)	76.1%	(73.9%-78.1%)	+	81.4%	(79.1%-83.5%)
	M	74.1%	(69.9%-77.9%)	73.2%	(67.5%-78.3%)		76.3%	(69.8%-81.8%)
	MW	73.0%	(69.4%-76.2%)	71.6%	(66.8%-76.0%)		75.1%	(69.5%-80.0%)
	NE	72.3%	(68.5%-75.7%)	68.6%	(63.3%-73.4%)	+	75.6%	(69.9%-80.7%)
	NW	74.1%	(69.8%-78.0%)	71.9%	(66.0%-77.1%)		76.3%	(69.6%-82.1%)
	S	74.7%	(72.2%-77.0%)	70.8%	(67.3%-74.0%)	+	79.3%	(75.6%-82.6%)
	SE	73.5%	(70.3%-76.4%)	72.0%	(67.6%-76.0%)		74.0%	(68.9%-78.5%)
	W	74.1%	(70.8%-77.0%)	71.4%	(67.0%-75.5%)		78.8%	(74.1%-82.8%)
Colorectal	**total**	**49.2%**	(48.1%-50.3%)	**47.7%**	(46.1%-49.1%)	+	**51.0%**	(49.3%-52.6%)
	E	51.9%	(50.0%-53.8%)	50.3%	(47.7%-52.8%)		54.3%	(51.4%-57.1%)
	M	48.8%	(44.2%-53.3%)	47.8%	(41.8%-53.7%)		50.2%	(42.9%-57.2%)
	MW	49.7%	(45.7%-53.6%)	51.0%	(45.4%-56.5%)		48.2%	(42.2%-54.0%)
	NE	52.4%	(48.6%-56.0%)	53.1%	(47.8%-58.3%)		51.5%	(45.9%-56.9%)
	NW	49.3%	(45.1%-53.4%)	45.7%	(40.2%-51.1%)		53.5%	(47.0%-59.9%)
	S	47.1%	(44.4%-49.7%)	46.0%	(42.3%-49.5%)		47.9%	(43.9%-51.8%)
	SE	46.4%	(43.2%-49.6%)	44.6%	(40.2%-48.8%)		48.4%	(43.3%-53.3%)
	W	46.3%	(43.0%-49.6%)	41.0%	(36.7%-45.4%)	+	51.8%	(46.7%-56.8%)
Lung	**total**	**8.6%**	(8.0%-9.2%)	**8.2%**	(7.4%-9.0%)		**9.0%**	(8.1%-9.9%)
	E	9.0%	(8.0%-9.9%)	8.3%	(7.1%-9.5%)		9.6%	(8.1%-11.2%)
	M	9.4%	(6.9%-12.4%)	8.9%	(5.5%-13.2%)		10.1%	(6.6%-14.4%)
	MW	8.2%	(6.2%-10.5%)	7.8%	(5.1%-11.1%)		8.5%	(5.6%-12.2%)
	NE	9.0%	(6.9%-11.2%)	8.6%	(5.8%-11.9%)		9.6%	(6.8%-12.8%)
	NW	9.9%	(7.5%-12.5%)	11.3%	(7.9%-15.3%)		7.9%	(4.7%-11.9%)
	S	7.3%	(5.9%-8.9%)	6.5%	(4.7%-8.5%)		8.7%	(6.4%-11.2%)
	SE	8.7%	(6.9%-10.6%)	9.3%	(6.8%-12.1%)		7.8%	(5.4%-10.7%)
	W	8.1%	(6.2%-10.2%)	7.4%	(5.0%-10.3%)		8.8%	(6.0%-12.1%)
Prostate	**total**	**69.5%**	(67.9%-70.9%)	**63.0%**	(60.8%-65.1%)	+	**75.9%**	(73.7%-77.9%)
	E	77.4%	(74.7%-79.9%)	70.8%	(66.9%-74.6%)	+	84.1%	(80.4%-87.5%)
	M	63.5%	(57.1%-69.7%)	53.1%	(44.5%-61.7%)	+	72.3%	(62.8%-81.2%)
	MW	62.3%	(56.9%-67.5%)	56.9%	(49.9%-63.8%)	+	70.2%	(61.6%-78.2%)
	NE	67.3%	(61.9%-72.5%)	61.0%	(53.6%-68.1%)	+	74.1%	(66.1%-81.4%)
	NW	64.5%	(58.8%-70.0%)	58.2%	(50.1%-66.2%)	+	68.1%	(59.4%-76.3%)
	S	67.8%	(63.9%-71.5%)	59.3%	(53.9%-64.6%)	+	75.7%	(70.1%-80.8%)
	SE	69.0%	(64.8%-73.1%)	65.2%	(59.1%-70.9%)		72.3%	(66.0%-78.2%)
	W	66.4%	(61.8%-70.8%)	60.3%	(54.1%-66.4%)	+	73.7%	(66.9%-80.0%)

+ Significant improvement in survival, based on modelling adjusted for age, or age and sex (*Table 3*).

Explanatory note

Relative survival: This is the *survival observed in a particular group of patients as a percentage or proportion of the survival expected among persons of the same age and sex in the general population*. For example, if the expected five-year survival of a group of persons of a given age is 80%, and the observed survival of a group of cancer patients of the same age is 60%, the five-year relative survival of the cancer patients is expressed as (60/80)% = 75%. Use of relative survival allows assessment of the influence of a given diagnosis (e.g. breast cancer) on survival, over and above other potential causes of death, without needing to know (or rely on) the actual cause of death for any patients who die.





Explanatory note

Excess mortality hazard: This is the 'extra' mortality among a group of patients with a specific disease, having allowed for the expected mortality rate among persons of the same age and sex in the general population. It is the equivalent, for relative survival, of the hazard used in Cox regression modelling of crude or cause-specific survival.

Excess hazard ratio: When comparing two or more patient groups, the ratio of excess mortality hazards is calculated, generally by a statistical model which allows adjustment for age or other patient characteristics – see *Tables 3-4*. Excess hazard ratios thus involve two comparisons: between patients and general population in a given region (to estimate the excess mortality rate), then between patients in different regions (to compare the excess mortality rates, as an excess hazard ratio). Excess hazard ratios in this report are expressed in comparison with patients from the Eastern region. To simplify presentation in *Figures 1-2*, a ratio of 1.21 has been mapped as 121%, for example (compared with 100% for Eastern region).

Figure 1 Regional variation in excess mortality hazards (based on relative survival) adjusted for age, sex and lung cancer cell-type, expressed in comparison to patients from the Eastern region (100%). * = significantly high or low excess mortality (P<0.05). Low excess mortality = high relative survival, high excess mortality = low survival. Excess mortality = in relation to persons of same age and sex in general population. See also *Table 4*.

Explanatory note

Adjustment: In simple terms, adjusting two or more datasets being compared helps ensure that we are comparing like with like. For example, if two groups of patients differ substantially in their average age, survival will tend to be highest for the younger group, other factors being equal.

Figure 2 Regional variation in excess mortality hazards (based on relative survival), fully adjusted for patient and tumour characteristics, expressed in comparison to patients from the Eastern region (100%). * = significantly high or low excess mortality (P<0.05). See also *Table 4*.

Table 3 Changes in relative survival (expressed in terms of excess hazard ratios) between diagnosis periods 1994-97 and 1998-2001, nationally and by region of residence. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant change in excess hazard compared with 1994-97 (<1 = lower excess risk of death i.e. higher survival, >1 = higher excess risk i.e. lower survival). *For example, the excess age-adjusted mortality associated with a breast cancer diagnosis in 1998-2001 was 76.4% that in 1994-1997 (i.e. 23.6% lower).*

Region	Breast cancer [a]EHR (95% CI)	Colorectal cancer EHR (95% CI)	Lung cancer EHR (95% CI)	Prostate cancer EHR (95% CI)
basic model: age-, (lung celltype-), sex-adjusted				
total	**0.764** (0.703-0.831)	**0.903** (0.856-0.952)	0.996 (0.958-1.036)	**0.614** (0.552-0.683)
E	**0.722** (0.623-0.836)	0.923 (0.838-1.017)	0.982 (0.922-1.044)	**0.575** (0.454-0.728)
M	0.994 (0.710-1.391)	0.892 (0.711-1.119)	1.017 (0.853-1.214)	**0.486** (0.335-0.706)
MW	0.853 (0.645-1.128)	1.080 (0.891-1.309)	0.937 (0.812-1.081)	**0.690** (0.493-0.964)
NE	**0.738** (0.551-0.989)	1.063 (0.878-1.285)	**1.172** (1.014-1.353)	**0.697** (0.492-0.987)
NW	0.747 (0.532-1.050)	0.827 (0.675-1.012)	1.091 (0.930-1.280)	**0.588** (0.411-0.842)
S	**0.700** (0.568-0.862)	0.903 (0.797-1.023)	0.964 (0.869-1.069)	**0.639** (0.503-0.811)
SE	0.825 (0.641-1.061)	0.854 (0.730-1.000)	1.043 (0.921-1.181)	0.760 (0.566-1.019)
W	0.811 (0.625-1.051)	**0.710** (0.605-0.832)	0.954 (0.832-1.094)	**0.604** (0.445-0.819)
final multivariate model[b]				
total	**0.906** (0.834-0.985)	**0.781** (0.703-0.867)	0.999 (0.960-1.040)	**0.584** (0.475-0.718)

[a,b]See Table 4.

Table 4 Variation in relative survival, by region of residence (compared to Eastern region), for patients diagnosed with cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (<1 = lower excess hazard thus higher relative survival than in Eastern region, >1 = higher excess hazard thus lower relative survival). *For example, the excess age-adjusted mortality associated with a breast cancer diagnosis was 22.4% higher in patients from the Midland compared to the Eastern region.*

Region	Breast cancer [a]EHR (95% CI)	Colorectal cancer EHR (95% CI)	Lung cancer EHR (95% CI)	Prostate cancer EHR (95% CI)
basic model: age-, (lung celltype-), sex-adjusted				
E	1.000	1.000	1.000	1.000
M	**1.224** (1.022-1.466)	1.087 (0.963-1.227)	0.957 (0.872-1.050)	**1.646** (1.329-2.040)
MW	**1.281** (1.098-1.493)	1.102 (0.990-1.227)	**0.896** (0.828-0.970)	**1.690** (1.391-2.053)
NE	**1.281** (1.092-1.502)	0.995 (0.895-1.106)	1.008 (0.933-1.088)	**1.470** (1.196-1.807)
NW	**1.226** (1.025-1.467)	**1.124** (1.006-1.256)	**0.915** (0.841-0.995)	**1.470** (1.194-1.811)
S	**1.203** (1.062-1.362)	**1.236** (1.143-1.337)	1.017 (0.958-1.080)	**1.529** (1.301-1.798)
SE	**1.248** (1.081-1.440)	**1.205** (1.100-1.321)	1.038 (0.969-1.112)	**1.356** (1.130-1.627)
W	**1.263** (1.091-1.461)	**1.158** (1.055-1.271)	0.939 (0.871-1.011)	**1.455** (1.211-1.749)
final multivariate model[b]				
E	1.000	1.000	1.000	1.000
M	**1.277** (1.068-1.527)	1.066 (0.939-1.210)	0.924 (0.841-1.015)	1.128 (0.923-1.377)
MW	1.069 (0.914-1.250)	**1.152** (1.032-1.286)	**0.871** (0.804-0.943)	1.104 (0.913-1.335)
NE	1.139 (0.971-1.336)	0.917 (0.825-1.020)	0.976 (0.903-1.055)	1.072 (0.889-1.292)
NW	1.066 (0.894-1.271)	1.038 (0.929-1.160)	**0.855** (0.785-0.931)	0.934 (0.772-1.129)
S	**1.162** (1.025-1.317)	**1.240** (1.145-1.343)	0.978 (0.919-1.039)	**1.248** (1.073-1.450)
SE	**1.222** (1.061-1.407)	**1.100** (1.003-1.206)	1.035 (0.966-1.109)	1.086 (0.919-1.284)
W	**1.262** (1.093-1.457)	1.027 (0.935-1.129)	**0.839** (0.779-0.905)	0.894 (0.755-1.057)

[a]EHR = excess hazard ratio estimated by a generalized linear model (GLM).
[b]Final (full) multivariate models, including some or all of the following (if they contributed significantly to model-fit): *sex* (for colorectal and lung cancers); *age-group*; *T, N, M categories*; *tumour grade*; *lung cancer cell-type*; *breast tumour morphology*; *colorectal site*; *microscopic verification status*; *method of presentation*; *smoking status*; *marital status*; individual *year of diagnosis*.

Explanatory note **Why compare hazards, not survival proportions?** Hazards (mortality rates) have technical advantages for statistical modelling to quantify differences in survival, typically with adjustment for patient and tumour characteristics that might complicate comparisons. Model-based comparison of hazards also allows a fuller description of differences in survival between patient groups, throughout follow-up, rather than reflecting simply the percentages of patients who survive to fixed points, e.g. five years, after diagnosis.

Table 5 Breakdown of surgical treatment for cancers diagnosed during 1998-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases.

Region where surgically treated		Region of residence								
		E	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Breast cancer										
Eastern	%	**99.2**	31.2	6.8	35.1	13.6	1.1	17.5	4.6	**46.6**
Midland	%	0.7	**55.8**	1.3	2.3	0.3	0.0	0.2	0.2	3.8
Mid-Western	%	0.0	0.3	**69.3**	0.0	0.0	0.2	0.8	0.0	5.5
North-Eastern	%	0.1	0.6	0.0	**62.7**	1.5	0.0	0.0	0.0	5.1
North-Western	%	0.0	0.0	0.0	0.0	**77.1**	0.0	0.0	0.9	4.3
Southern	%	0.0	0.0	6.2	0.0	0.0	**98.7**	4.3	0.0	15.9
South-Eastern	%	0.0	1.7	4.7	0.0	0.0	0.0	**77.3**	0.0	8.2
Western	%	0.0	10.5	11.7	0.0	4.5	0.0	0.0	**94.3**	10.5
Northern Ireland	%	0.0	0.0	0.0	0.0	3.0	0.0	0.0	0.0	0.2
Colorectal cancer										
Eastern	%	**98.4**	13.0	5.7	21.7	10.7	0.8	8.2	3.7	**37.5**
Midland	%	0.4	**78.5**	0.9	0.4	0.8	0.0	0.7	0.2	4.3
Mid-Western	%	0.0	0.4	**79.3**	0.0	0.0	0.2	0.7	0.0	6.9
North-Eastern	%	0.6	1.1	0.0	**77.0**	4.0	0.0	0.0	0.0	7.6
North-Western	%	0.1	0.0	0.0	0.4	**83.5**	0.0	0.2	2.1	6.1
Southern	%	0.2	0.0	5.5	0.0	0.0	**98.7**	4.1	0.0	17.1
South-Eastern	%	0.3	0.4	4.6	0.2	0.0	0.2	**86.0**	0.0	9.5
Western	%	0.2	6.7	4.1	0.2	0.5	0.0	0.0	**94.1**	10.9
Northern Ireland	%	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0
Lung cancer										
Eastern	%	**100.0**	**100.0**	**54.3**	**95.6**	**92.3**	4.2	**76.5**	**58.1**	**80.2**
Midland	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mid-Western	%	0.0	0.0	6.5	0.0	0.0	0.0	0.0	0.0	0.4
North-Eastern	%	0.0	0.0	0.0	4.4	0.0	0.0	0.0	0.0	0.4
North-Western	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Southern	%	0.0	0.0	30.4	0.0	0.0	**95.8**	19.1	0.0	15.4
South-Eastern	%	0.0	0.0	0.0	0.0	0.0	0.0	4.4	0.0	0.4
Western	%	0.0	0.0	8.7	0.0	7.7	0.0	0.0	41.9	3.3
Prostate cancer										
Eastern	%	**99.3**	**63.2**	17.0	**75.6**	40.4	3.1	**49.2**	30.5	**62.0**
Midland	%	0.4	32.2	0.7	0.0	0.0	0.0	0.0	0.0	2.4
Mid-Western	%	0.1	1.2	**55.1**	0.0	0.0	0.3	0.8	0.0	3.4
North-Eastern	%	0.2	0.0	0.0	23.3	0.0	0.0	0.0	0.0	2.5
North-Western	%	0.0	0.0	0.0	0.8	**53.9**	0.0	0.0	3.7	2.2
Southern	%	0.0	0.0	17.0	0.0	0.0	**96.6**	3.9	0.0	15.0
South-Eastern	%	0.0	1.2	5.4	0.4	0.0	0.0	46.1	0.0	6.9
Western	%	0.0	2.3	4.8	0.0	1.1	0.0	0.0	**65.8**	5.3
Northern Ireland		0.0	0.0	0.0	0.0	4.5	0.0	0.0	0.0	0.2

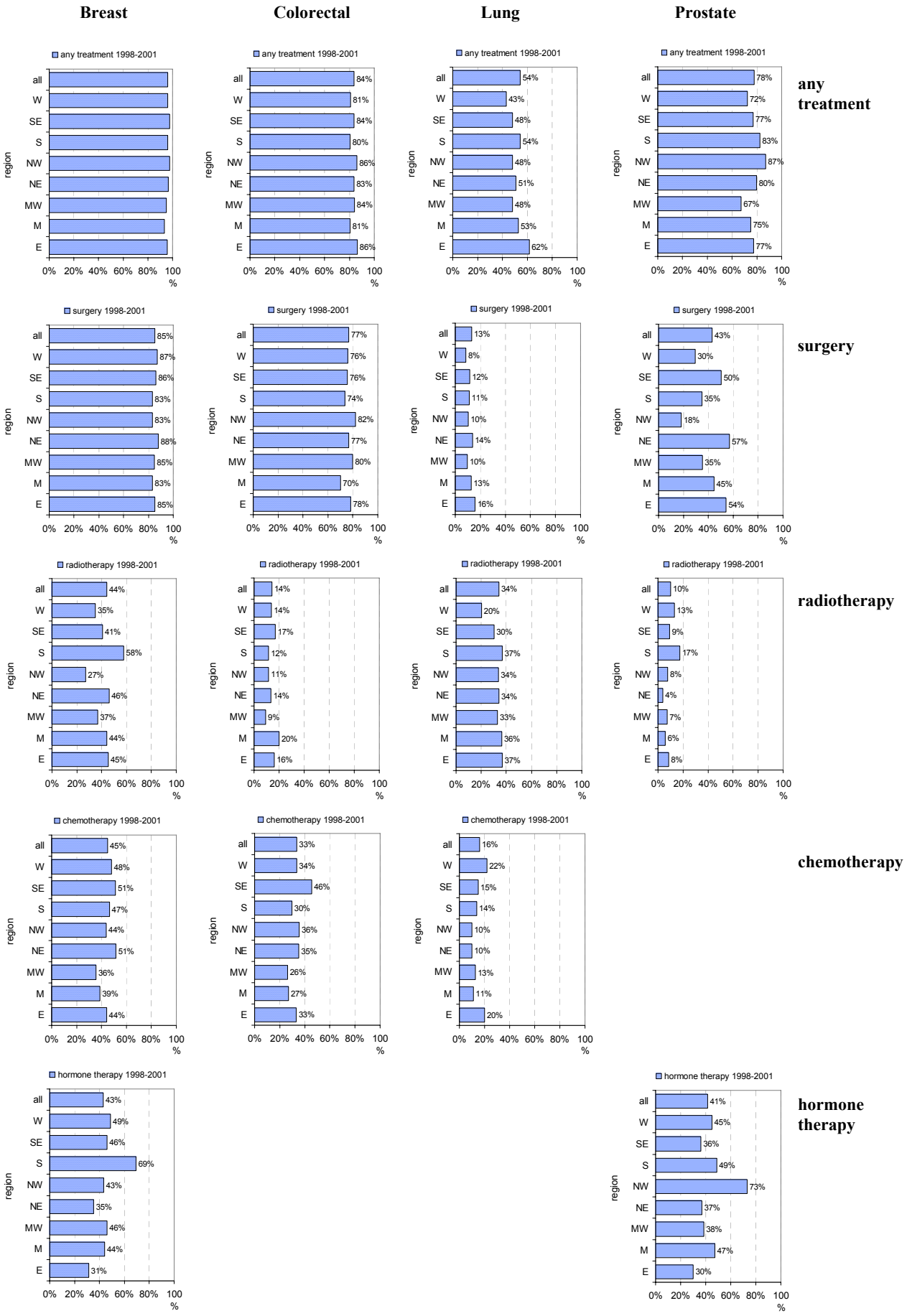


Figure 3 Proportions of cancer patients resident in each region who had tumour-directed treatment within six months of diagnosis, 1998-2001. Note: Results are shown only for standard treatment modalities for a given cancer.

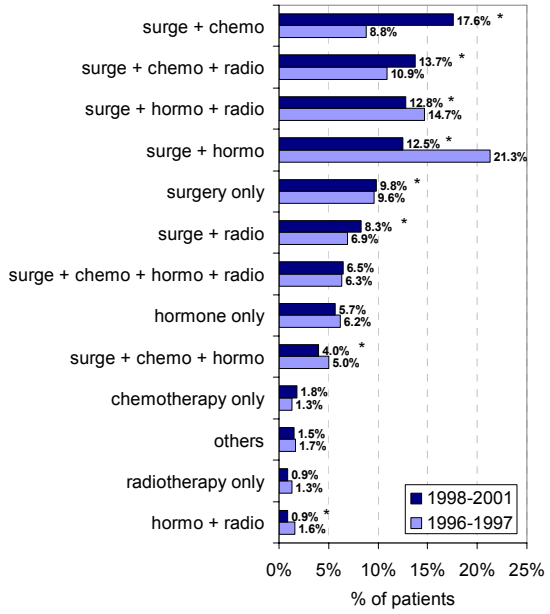


Figure 4 Treatment combinations for breast cancer.
*Significant changes between diagnosis periods.

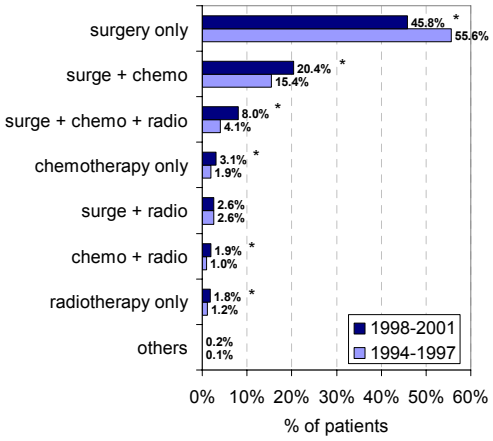


Figure 5 Treatment combinations for colorectal cancer.

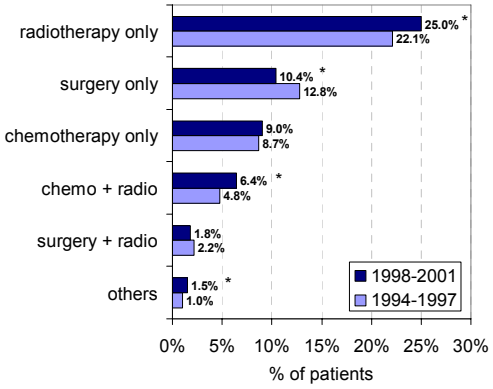


Figure 6 Treatment combinations for lung cancer.

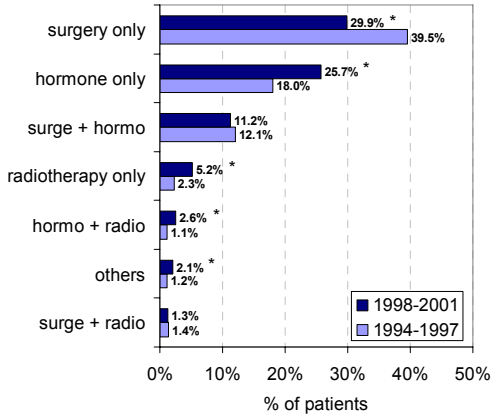


Figure 7 Treatment combinations for prostate cancer.

Table 6 Average annual percentage changes (1996-2001) in proportions of cancer patients having tumour-directed treatment within six months of diagnosis, adjusted for age and sex only (also cell-type for lung cancer). Statistically significant trends are highlighted in bold. In general, further adjustment for stage-related and other variables had only minor effects on the direction, magnitude and statistical significance of these trends.

Treatment modality	Diagnosis period	Breast cancer trend (95% CI)	Colorectal cancer trend (95% CI)	Lung cancer trend (95% CI)	Prostate cancer trend (95% CI)
Overall treatment	1996-2001	-0.1% p.a. (-0.4%, +0.2%)	**+0.6%** p.a. (+0.0%, +1.2%)	**+2.5%** p.a. (+1.1%, +3.9%)	**-1.4%** p.a. (-2.1%, -0.8%)
Surgery	1996-2001	**+0.5%** p.a. (+0.0%, +1.1%)	**-0.7%** p.a. (-1.4%, -0.1%)	**-3.4%** p.a. (-6.5%, -0.2%)	**-7.6%** p.a. (-8.7%, -6.5%)
Radiotherapy	1996-2001	-0.4% p.a. (-1.7%, +1.0%)	**+10.8%** p.a. (+7.4%, +14.2%)	**+2.2%** p.a. (+0.3%, +4.2%)	**+13.2%** p.a. (+8.3%, +18.3%)
Chemotherapy	1996-2001	**+12.6%** p.a. (+10.7%, +14.5%)	**+12.3%** p.a. (+10.1%, +14.6%)	**+6.4%** p.a. (+2.9%, +10.0%)	
Hormone therapy	1996-2001	**-8.9%** p.a. (-9.9%, -7.8%)			**+3.3%** p.a. (+1.5%, +5.0%)

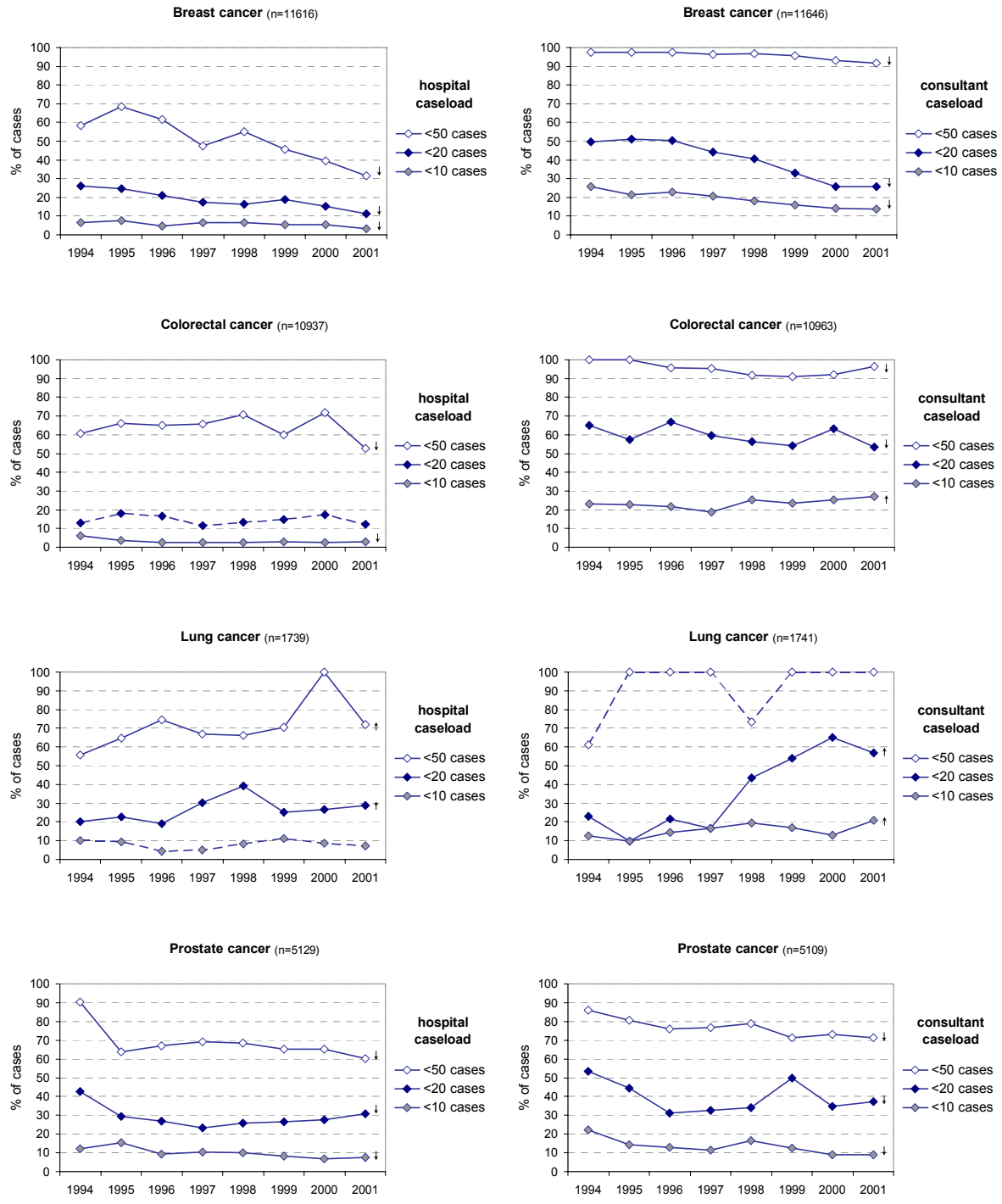
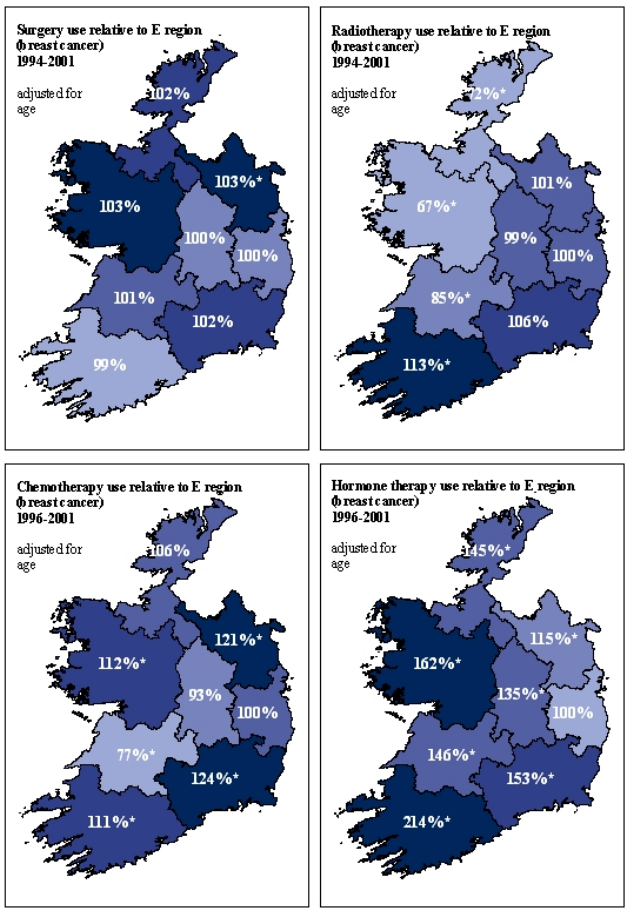


Figure 8 Proportions of surgical patients who had surgery in hospitals which treated, or under a consultant with responsibility for, <10, <20 or <50 surgical patients in a given year, for a given cancer. For this analysis, patients are counted once for each relevant hospital or consultant within six months of diagnosis, for surgical procedures only. Hospitals or consultants outside of the Republic of Ireland are excluded. Significant overall trends (based on Mantel's trend test for proportions) are indicated by solid lines.



Explanatory note

Relative risk (of treatment): In simple terms, if 50% of one group of cancer patients receive a particular treatment within a given time after diagnosis, compared with 40% of another group, the relative risk (RR) for treatment of the first group is (50/40) = 1.25, i.e. patients from the first group are 25% more likely to have been treated. This can be also expressed as a RR of 125% (as in *Figures 9-12*). If the age-composition or other characteristics of two groups of patients differ, those characteristics may also influence the proportion of patient treated. Thus, to examine the effect of, say, region of residence on treatment, it will generally be important to *adjust* for other factors that may complicate comparisons (or help 'explain' some of the apparent differences between regions).

Figure 9 Regional variation in breast cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age.
* = significantly high or low values (P<0.05).

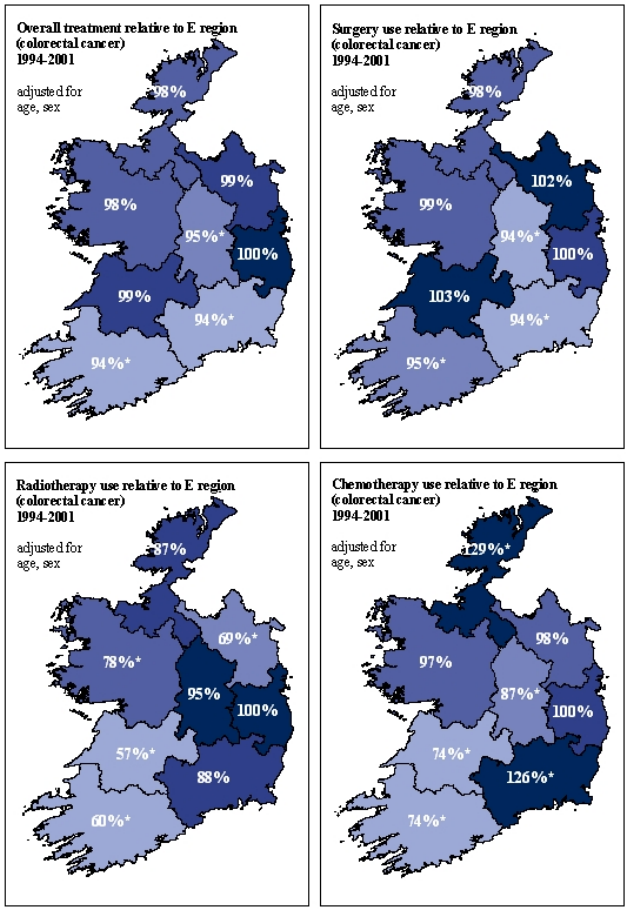


Figure 10 Regional variation in colorectal cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age and sex.
* = significantly high or low values (P<0.05).

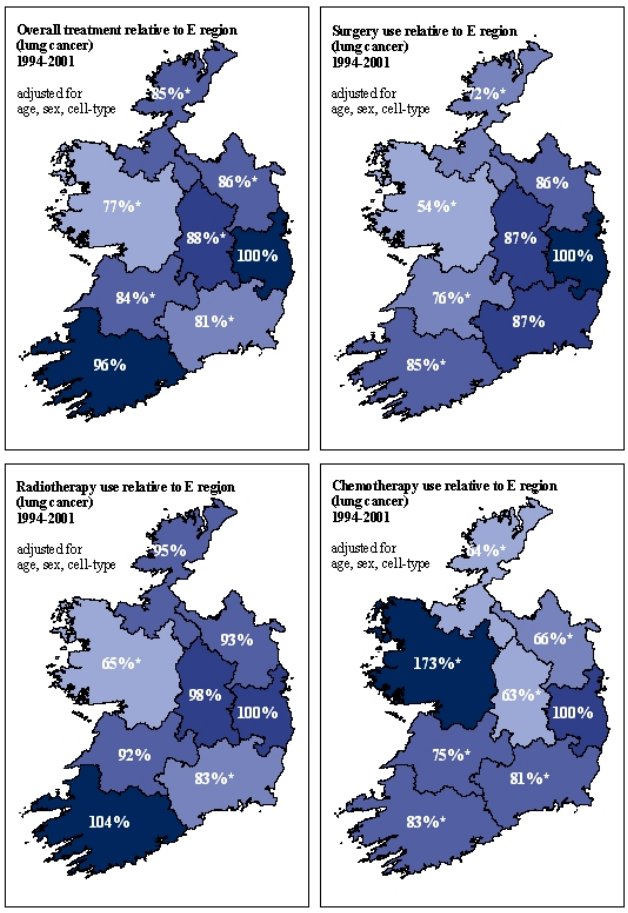


Figure 11 Regional variation in lung cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age, sex and cell-type. * = significantly high or low values (P<0.05).

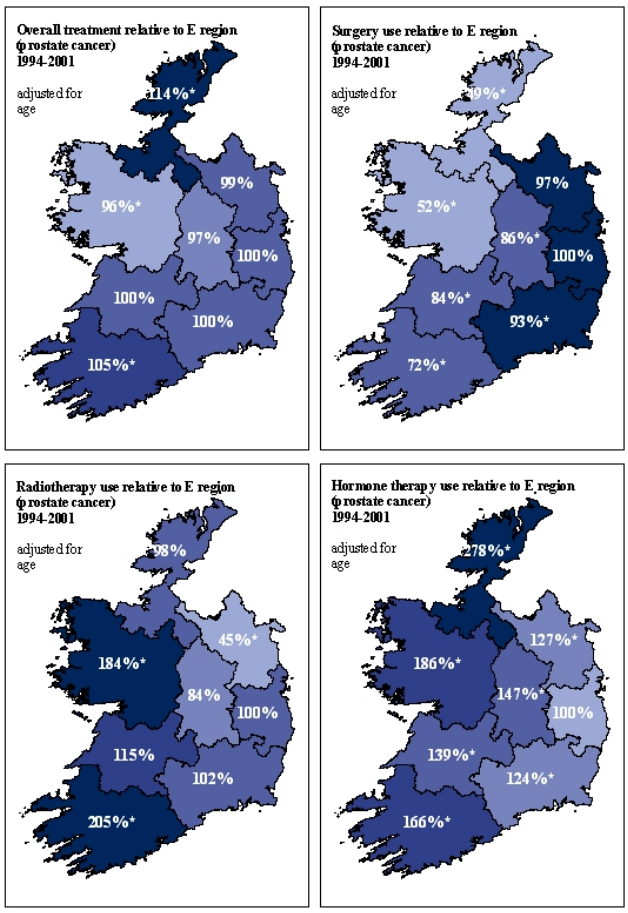


Figure 12 Regional variation in prostate cancer treatment, expressed relative to patients from the Eastern region (100%), adjusted for age.
* = significantly high or low values (P<0.05).

Table 7 Variation in treatment, by region of residence (compared to Eastern region), for patients diagnosed with invasive cancer during 1994-2001, adjusted for age and sex only (also cell-type for lung cancer). Analysis is based on tumour-directed treatments received within six months of diagnosis. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

Treatment modality	Region	Breast cancer [a]RR (95% CI)	Colorectal cancer RR (95% CI)	Lung cancer RR (95% CI)	Prostate cancer RR (95% CI)
Overall treatment	E	1.000	1.000	1.000	1.000
	M	0.989 (0.967-1.006)	**0.950** (0.911-0.984)	**0.878** (0.798-0.958)	0.974 (0.923-1.020)
	MW	1.003 (0.986-1.015)	0.989 (0.957-1.017)	**0.837** (0.767-0.908)	0.999 (0.954-1.040)
	NE	1.007 (0.991-1.019)	0.991 (0.961-1.018)	**0.861** (0.793-0.928)	0.989 (0.944-1.030)
	NW	**1.023** (1.010-1.032)	0.982 (0.949-1.011)	**0.854** (0.780-0.928)	**1.140** (1.105-1.169)
	S	1.009 (0.998-1.018)	**0.936** (0.910-0.961)	0.959 (0.906-1.010)	**1.052** (1.021-1.081)
	SE	**1.022** (1.011-1.030)	**0.937** (0.906-0.965)	**0.805** (0.744-0.866)	0.998 (0.960-1.033)
	W	1.005 (0.990-1.016)	0.977 (0.949-1.002)	**0.773** (0.708-0.839)	**0.960** (0.919-0.998)
Surgery	E	1.000	1.000	1.000	1.000
	M	0.995 (0.957-1.029)	**0.943** (0.898-0.984)	0.868 (0.694-1.077)	**0.862** (0.789-0.936)
	MW	1.009 (0.977-1.036)	1.029 (0.993-1.060)	**0.760** (0.613-0.935)	**0.839** (0.772-0.907)
	NE	**1.034** (1.004-1.059)	1.016 (0.981-1.047)	0.864 (0.716-1.037)	0.974 (0.908-1.039)
	NW	1.016 (0.982-1.045)	0.979 (0.940-1.015)	**0.720** (0.573-0.899)	**0.491** (0.433-0.554)
	S	0.988 (0.963-1.011)	**0.948** (0.919-0.976)	**0.846** (0.733-0.974)	**0.715** (0.665-0.766)
	SE	1.020 (0.992-1.044)	**0.942** (0.907-0.974)	0.865 (0.729-1.021)	**0.929** (0.872-0.985)
	W	1.027 (0.999-1.051)	0.992 (0.960-1.022)	**0.544** (0.433-0.680)	**0.520** (0.469-0.574)
Radiotherapy	E	1.000	1.000	1.000	1.000
	M	0.986 (0.901-1.074)	0.952 (0.778-1.157)	0.975 (0.857-1.099)	0.839 (0.584-1.196)
	MW	**0.853** (0.781-0.928)	**0.565** (0.454-0.700)	0.920 (0.821-1.026)	1.149 (0.869-1.508)
	NE	1.007 (0.930-1.085)	**0.692** (0.570-0.836)	0.928 (0.831-1.030)	**0.452** (0.299-0.680)
	NW	**0.724** (0.645-0.808)	0.865 (0.710-1.048)	0.949 (0.843-1.062)	0.983 (0.716-1.339)
	S	**1.127** (1.068-1.186)	**0.600** (0.512-0.702)	1.036 (0.958-1.117)	**2.049** (1.720-2.428)
	SE	1.057 (0.987-1.127)	0.882 (0.753-1.029)	**0.832** (0.749-0.921)	1.021 (0.798-1.300)
	W	**0.667** (0.605-0.733)	**0.783** (0.661-0.923)	**0.649** (0.568-0.737)	**1.836** (1.491-2.246)
Chemotherapy[b]	E	1.000	1.000	1.000	-
	M	0.932 (0.820-1.049)	**0.867** (0.751-0.994)	**0.626** (0.472-0.822)	-
	MW	**0.769** (0.679-0.866)	**0.738** (0.646-0.839)	**0.750** (0.598-0.934)	-
	NE	**1.205** (1.099-1.312)	0.982 (0.878-1.092)	**0.664** (0.530-0.826)	-
	NW	1.060 (0.939-1.184)	**1.285** (1.154-1.420)	**0.641** (0.497-0.820)	-
	S	**1.105** (1.024-1.187)	**0.735** (0.665-0.811)	**0.834** (0.713-0.971)	-
	SE	**1.241** (1.143-1.338)	**1.255** (1.148-1.365)	**0.808** (0.669-0.971)	-
	W	**1.120** (1.022-1.220)	0.972 (0.876-1.075)	**1.725** (1.493-1.976)	-
Hormone therapy[b]	E	1.000	-	-	1.000
	M	**1.346** (1.215-1.478)	-	-	**1.474** (1.314-1.642)
	MW	**1.463** (1.348-1.577)	-	-	**1.385** (1.241-1.537)
	NE	**1.148** (1.038-1.262)	-	-	**1.268** (1.130-1.415)
	NW	**1.453** (1.321-1.585)	-	-	**2.777** (2.630-2.913)
	S	**2.139** (2.063-2.212)	-	-	**1.662** (1.543-1.783)
	SE	**1.534** (1.430-1.638)	-	-	**1.236** (1.118-1.361)
	W	**1.617** (1.509-1.723)	-	-	**1.859** (1.722-1.997)

[a]Risk ratios, compared with Eastern region, were derived using the method of Zhang & Yu (1998) from adjusted odds ratios calculated by logistic regression adjusted for the following patient and tumour variables: *sex* (for colorectal and lung cancers); *age-group* 15-44, 45-54, 55-64, 65-74, or 75+ (ages 15-54 to 85+ for prostate cancer); *lung tumour morphology* - non-small-cell (NSCLC), small- cell (SCLC), or other/unspecified.
[b]For breast cancer, data on use of chemotherapy and hormone therapy are for 1996-2001 only.

Table 8 Variation in treatment, by region of residence (compared to Eastern region), for patients diagnosed with invasive cancer during 1994-2001, adjusted for detailed patient and tumour characteristics. Analysis is based on tumour-directed treatments received within six months of diagnosis. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

Treatment modality	Region	Breast cancer [a]RR (95% CI)	Colorectal cancer RR (95% CI)	Lung cancer RR (95% CI)	Prostate cancer RR (95% CI)
Overall treatment	E	1.000	1.000	1.000	1.000
	M	**0.971** (0.937-0.995)	**0.916** (0.852-0.971)	**0.867** (0.783-0.950)	0.972 (0.918-1.021)
	MW	**1.015** (1.000-1.026)	1.013 (0.971-1.047)	**0.835** (0.762-0.908)	**1.073** (1.032-1.110)
	NE	1.005 (0.985-1.019)	0.992 (0.951-1.027)	**0.882** (0.811-0.952)	0.992 (0.944-1.036)
	NW	**1.025** (1.010-1.035)	0.992 (0.946-1.030)	**0.856** (0.778-0.934)	**1.161** (1.127-1.189)
	S	1.006 (0.991-1.017)	0.989 (0.955-1.018)	0.965 (0.910-1.020)	**1.061** (1.027-1.092)
	SE	**1.021** (1.007-1.031)	**0.944** (0.900-0.982)	**0.762** (0.699-0.826)	0.994 (0.952-1.032)
	W	1.002 (0.983-1.016)	1.030 (0.999-1.057)	**0.788** (0.720-0.857)	0.996 (0.955-1.034)
Surgery	E	1.000	1.000	1.000	1.000
	M	0.965 (0.907-1.013)	**0.880** (0.801-0.951)	0.774 (0.577-1.024)	**0.916** (0.833-0.999)
	MW	**1.059** (1.025-1.087)	**1.091** (1.047-1.127)	**0.715** (0.543-0.931)	1.052 (0.972-1.129)
	NE	1.037 (0.996-1.070)	1.032 (0.983-1.075)	0.863 (0.676-1.090)	1.054 (0.979-1.126)
	NW	1.031 (0.982-1.069)	0.950 (0.885-1.006)	**0.641** (0.477-0.851)	**0.509** (0.443-0.582)
	S	**0.954** (0.913-0.991)	0.988 (0.944-1.028)	0.840 (0.699-1.005)	**0.754** (0.695-0.815)
	SE	1.006 (0.965-1.040)	**0.952** (0.900-0.999)	**0.778** (0.625-0.962)	0.955 (0.890-1.020)
	W	**1.057** (1.024-1.084)	**1.069** (1.029-1.104)	**0.549** (0.415-0.719)	**0.523** (0.466-0.584)
Radiotherapy	E	1.000	1.000	1.000	1.000
	M	0.982 (0.895-1.071)	1.046 (0.826-1.313)	0.969 (0.850-1.096)	0.821 (0.567-1.179)
	MW	**0.890** (0.815-0.967)	**0.508** (0.395-0.651)	0.936 (0.833-1.044)	1.229 (0.918-1.631)
	NE	1.003 (0.923-1.083)	**0.729** (0.587-0.899)	0.950 (0.850-1.055)	**0.491** (0.323-0.742)
	NW	**0.727** (0.647-0.813)	0.997 (0.801-1.231)	0.934 (0.826-1.049)	0.953 (0.684-1.319)
	S	**1.136** (1.075-1.198)	**0.552** (0.461-0.660)	1.055 (0.972-1.140)	**2.093** (1.730-2.516)
	SE	1.063 (0.991-1.135)	0.852 (0.712-1.017)	**0.834** (0.749-0.926)	1.117 (0.868-1.430)
	W	**0.684** (0.619-0.751)	**0.681** (0.561-0.822)	**0.636** (0.555-0.725)	**1.831** (1.472-2.262)
Chemotherapy[b]	E	1.000	1.000	1.000	-
	M	0.871 (0.750-1.000)	0.883 (0.751-1.030)	**0.606** (0.451-0.805)	-
	MW	**0.751** (0.651-0.858)	**0.714** (0.612-0.827)	**0.767** (0.609-0.959)	-
	NE	**1.153** (1.031-1.275)	1.014 (0.897-1.140)	**0.706** (0.561-0.882)	-
	NW	0.941 (0.811-1.078)	**1.315** (1.169-1.467)	**0.640** (0.493-0.824)	-
	S	1.041 (0.947-1.136)	**0.762** (0.682-0.849)	0.854 (0.725-1.001)	-
	SE	**1.143** (1.033-1.255)	**1.257** (1.139-1.380)	**0.800** (0.658-0.967)	-
	W	1.089 (0.978-1.203)	0.920 (0.816-1.032)	**1.743** (1.503-2.003)	-
Hormone therapy[b]	E	1.000	-	-	1.000
	M	**1.305** (1.167-1.446)	-	-	**1.407** (1.235-1.589)
	MW	**1.482** (1.357-1.606)	-	-	**1.488** (1.321-1.664)
	NE	**1.184** (1.063-1.308)	-	-	**1.209** (1.061-1.367)
	NW	**1.344** (1.206-1.485)	-	-	**2.814** (2.654-2.960)
	S	**2.120** (2.034-2.200)	-	-	**1.658** (1.523-1.797)
	SE	**1.491** (1.378-1.604)	-	-	**1.279** (1.146-1.420)
	W	**1.581** (1.464-1.697)	-	-	**2.015** (1.860-2.169)

[a]Risk ratios, compared with Eastern region, were derived using the method of Zhang & Yu (1998) from adjusted odds ratios calculated by logistic regression adjusted for the following patient and tumour variables (if they contributed significantly to model-fit): *sex* (for colorectal and lung cancers); *age-group*; *T, N and M categories of stage*; *tumour grade*; *tumour morphology* (for lung and breast cancers); *colorectal site*; *microscopic verification status; method of presentation*; *smoking status*; *marital status*; individual *year of diagnosis*.
[b]For breast cancer, data on use of chemotherapy and hormone therapy are for 1996-2001 only.

Chapter 1. INTRODUCTION

This is the second in a series of reports focusing on treatment and survival for the four most important cancers in healthcare terms in Ireland: breast cancer (in women), colorectal cancer, lung cancer and prostate cancer. The previous report covered the period 1994 to 1998 (NicAmhlaoibh *et al*. 2004). Coverage here is extended to 2001, with follow-up of patient survival to the end of 2003.

The level of detail available for treatment data has increased since earlier years, and a number of analyses are only reliable for more recent years - in particular, the use of chemotherapy and hormone therapy for breast cancer (1996-2001). However, for many of the basic measures (e.g. receipt of tumour-directed surgery within six-months of treatment), it has been possible to assess patterns over the whole period 1994-2001. The four-year period 1998-2001 has been selected for presentation of recent data, for comparison with the period 1994-97. The current report provides assessments of changes over time, and involves re-analysis and (where necessary) re-coding of all data for the period 1994-2001. Thus direct comparisons between the current report and the previous report are not necessary.

The availability of eight years of treatment data and ten years of survival follow-up data provides an improved basis for assessment of time trends compared with previous National Cancer Registry publications. The timing of this report is also opportune, given the recent publication of Ireland's second National Cancer Control Strategy (National Cancer Forum 2006). This report can thus be seen as part of the process of assessing improvements in cancer care and outcomes since publication of the first Cancer Strategy in 1996. This report will also provide a baseline, and a framework, for assessment of expected further improvements, and will, it is hoped, inform evidence-based implementation of improvements in cancer care.

More definitive assessments of trends in cancer care and survival will be possible as further years' data become available. In particular, in the current report, we are not yet in a position to examine in detail the potential interaction between screening and treatment for breast cancer (following the introduction of the BreastCheck screening programme from 2000/2001 onwards). Future reports will also have the potential to look at treatment and survival in relation to a number of data items whose collection did not start until very recently, e.g. tumour receptor status for breast cancer. Other treatment-related data items are likely to be added over time, providing potentially greater explanatory power to the analyses presented.

Registration of cancer cases, and collection of detailed and reliable data on treatment and outcomes, is a time-consuming process. The National Cancer Registry is aware that publication even of basic data on cancer diagnoses lags several years behind the experiences of cancer patients and healthcare professionals in Ireland. We hope that improvements in the timeliness of data-collection will be possible, within the framework of expected wider improvements in the infrastructure, organization and quality of healthcare data collection in Ireland.

Planned further analyses

Although the analyses presented in this report are quite comprehensive, coverage of some aspects has been deferred to publication in further reports or scientific papers. This is partly is to facilitate comparable coverage across cancer sites here, and partly to allow collation of more comprehensive data on some aspects (in particular, comorbidity and deprivation). Further aspects for potential coverage (or for which analyses are already underway) include:

- Influence of hospital and consultant caseload or specialization on outcomes.
- Regional variation in use of breast-conserving surgery for breast cancer.
- Influence of deprivation and comorbidity on treatment and survival.
- Influence of breast cancer screening on treatment (cf. Walsh *et al*. 2006).
- Comparisons of treatments administered with national or international guidelines on treatment (cf. the European Cancer Health Indicators Project, or EUROCHIP: http://www.tumori.net/eurochip/).

Chapter 2. METHODS

2.1 Summary of data inclusions and exclusions

Table 2.1 summarizes the inclusion and exclusion criteria used to identify cancers for inclusion in this report. Overall, of 54 341 registered tumours for the cancer sites involved (breast, colorectal sites, lung and prostate), 49 100 were retained for both survival and treatment analyses. Among the cases excluded were those lacking follow-up (e.g. death-certificate-only diagnoses), non-invasive tumours, and second or less serious cancers in the same patients.

Table 2.1 Summary of inclusions and exclusions for cancers included in this report. Numbers of cases dropped at each step are shown in grey. See site-chapters for further details of patient and tumour characteristics.

	cancer site (ICD-10 definitions)				
Case definition	**breast**	**colorectal**	**lung**	**prostate**	**total**
all registered tumours[a]	14,974	15,685	12,686	10,996	54,341
	-4	-29	-4	-2	-39
ages 15-99 only	14,970	15,656	12,682	10,994	54,302
	-117	-0	-0	-0	-117
excluding male breast	14,853	15,656	12,682	10,994	54,185
	-241	-450	-637	-338	-1,666
excluding DCO & autopsy-only cases	14,612	15,206	12,045	10,656	52,519
	-865	-888	-43	-22	-1,818
invasive tumours only	13,747	14,318	12,002	10,634	50,701
	-364	-616	-339	-282	-1,601
first or most-serious-synchronous tumours[b]	13,383	13,702	11,663	10,352	49,100

[a]Including in situ carcinomas, and tumours of unspecified behaviour, but excluding primary lymphomas or other morphologies (e.g. Kaposi's sarcoma) that are classifiable separately within ICD-10.
[b]For a given cancer site, a patient was only counted if the cancer was the first 'serious' malignancy in that patient (ignoring neoplasms not fully invasive or malignant, and also ignoring non-melanoma skin cancers); for a patient with more than once cancer diagnosed on the same date, the more serious cancer was counted (typically lung > colorectal > breast/prostate), based on average survival for the cancer types involved (by reference to EUROCARE-3 data: Sant *et al*., 2003).

2.2 General methodology and case definitions

Tumour behaviour

Only neoplasms classed as behaviour 3 (invasive or malignant) in the second edition of the International Classification of Diseases for Oncology (ICD-O-2) (Percy *et al*. 1990) are included.

Tumour sites and morphologies

Four main cancer sites are examined, defined on the basis of their classification in ICD-10 (WHO 1992): breast cancer (ICD-10 code C50, but females only); colorectal cancer (C18-C21, including anus); lung cancer (C34); and prostate cancer (C61). Almost all cancers of these sites are classifiable as carcinomas, but some other morphologies (e.g. sarcomas) are included under the ICD-10 definition and in this report. [Non-carcinoma morphologies were excluded from the previous NCR report covering 1994-98: NicAmhlaoibh *et al*. 2004.] Substantial numbers of cancers of unspecified morphology also occur, although for the sites considered in this report they can generally be assumed to be carcinomas (albeit not confirmed histologically). Lymphomas of these sites are not included, as they are coded separately under ICD-10. Summary data on annual incidence and mortality rates and trends, for each main cancer, are provided for the period 1994-2001, derived from incident cases registered by the National Cancer Registry and mortality data provided by the Central Statistics Office.

Age at diagnosis

Only cancer cases diagnosed within the age-range 15 to 99 years are included. This is standard international practice for cancer survival analyses. The cancers covered in this report are rare in children, while, above age 99, expected rates of survival (used for computation of relative survival of cancer patients) are not available in some countries.

Method of presentation

Cases for which the only information on diagnosis came from a death certificate ("death certificate only" or DCO cases) or from autopsy (autopsy-only cases) were excluded from all treatment and survival analyses presented here. This is in line with standard international practice, e.g. the EUROCARE project (Capocaccia *et al*. 2003).

Collection of data

Data on diagnoses and on managements (treatments and other hospital 'encounters') are abstracted from hospital records, pathology notes and other relevant sources by NCR Tumour Registration Officers. Fuller details on methods and scope of NCR data-collection are given elsewhere (National Cancer Registry 2001, available at http://www.ncri.ie). Data are collated and quality-checked centrally by the NCR's Data and Information Technology teams. Once data-collection is considered complete, data are included in a central database of 'closed' cases, with attached patient, tumour, management and follow-up data. Follow-up data include the results of matching of patients against death certificate data to provide information on the patient's status (alive or known to be dead) at a given censoring date. (This is typically a year or more after the most recent complete year of incidence data – 31 December 2003 is used in this report.)

2.3 Patient and tumour variables

Treatment and survival analyses are presented by, or adjusted for, various combinations of the variables summarized below. The main analyses compare different regions of residence and between diagnosis years. The most important potential confounding or explanatory variables are the patient's age and variables that describe the stage or extent of disease at diagnosis. Other variables having a potential confounding or explanatory role are also considered, where available from existing Registry data. Cases with "unknown" status for a given variable have been coded as such, rather than the variable left blank, as such cases may make up substantial numbers of cases and potentially may differ in survival or treatment from other patients. Proportional changes in patient and tumour characteristics between years were assessed using χ^2 tests.

Region of residence

Treatment and survival data are compared between patients resident in eight regions of Ireland, corresponding to the areas covered by the former Eastern Regional Health Authority and Midland, Mid-Western, North-Eastern, North-Western, Southern, South-Eastern and Western Health Boards. These definitions no longer exist (having being replaced with a smaller number of Health Service Executive areas), but the equivalent regions are used in this report for geographic convenience as much as for their relationship to former administrative boundaries. The neutral term "region" is deliberately used. The counties and populations included are shown in *Table 2.2* (national census data from Central Statistic Office 1997, 2003).

Table 2.2 Regions used for analysis of treatment and survival.

Region	Counties	1996 population			2002 population		
		males	females	total	males	females	total
Eastern (E)	Dublin, Kildare, Wicklow	627,796	668,143	1,295,939	683,610	717,831	1,401,441
Midland (M)	Laois, Longford, Offaly, Westmeath	104,230	101,312	205,542	114,070	111,293	225,363
Mid-Western (MW)	Clare, Limerick, Tipperary (N) Tipperary (north)	159,625	157,444	317,069	170,558	169,033	339,591
North-Eastern (NE)	Cavan, Louth, Meath, Monaghan Monaghan	154,420	151,735	306,155	174,043	170,922	344,965
North-Western (NW)	Donegal, Leitrim, Sligo	106,312	104,560	210,872	111,111	110,463	221,574
Southern (S)	Cork, Kerry	272,978	273,662	546,640	288,889	291,467	580,356
South-Eastern (SE)	Carlow, Kilkenny, Tipperary (S), Waterford, Wexford	197,276	194,241	391,517	212,784	210,832	423,616
Western (W)	Galway, Mayo, Roscommon Roscommon	177,595	174,758	352,353	191,099	189,198	380,297
Total		1,800,232	1,825,855	3,626,087	1,946,164	1,971,039	3,917,203

Year of diagnosis

All treatments for a given patient are assigned to the year of diagnosis (1994-2001). To allow for possible under-recording of treatments during 1994 and 1995, trends in treatment are assessed as average annual changes during the period 1996-2001 only. Survival comparisons are made between the diagnosis periods 1994-97 and 1998-2001, using follow-up to December 2003.

Age

Age-groups as defined for the EUROCARE-3 cancer survival project (Capocaccia *et al*. 2003) have been used here. For most cancers, these groups are ages 15-44, 45-54, 55-64, 65-74 and 75+. For prostate cancer, the groups are 15-54, 55-64, 65-74, 75-84 and 85+. Note that these age-groups differ from the non-standard groupings used in the previous patterns of care report (NicAmhlaoibh *et al*. 2004).

Sex

This is examined as a potential confounding variable for colorectal and lung cancers, and for presentation of some descriptive results. Analyses for breast cancer are restricted to women.

Stage

For descriptive analyses of treatment and survival, overall stage of disease was coded, where possible, using the 4th edition of the TNM system (Beahrs *et al*. 1992), based on the combination of data on the T, N and M categories of stage (also tumour grade for prostate cancer). Where necessary, more recent data coded to the 5th edition of TNM were recoded to the 4th edition, for consistency across the period examined. One or more of T, N and M categories was missing or unknown for a large proportion of cases, thus overall stage is substantially incomplete. Stage "unknown" has been recoded to include tumour morphologies for which the TNM system is not strictly applicable, e.g. sarcomas of the breast. For statistical modelling, the components of stage (T, N and M categories and, for prostate, also tumour grade) were used as separate variables.

T category

This describes the size, or the extent of local invasion or direct regional extension, of the primary tumour (Beahrs *et al*. 1992). For analyses here, data have been coded as T category 1, 2, 3, 4 or unknown, although finer subdivision is possible for some sites.

N category

This describes the presence (and extent) or absence of spread of secondary cancer to lymph nodes considered regional to the primary sites (e.g. axillary and internal mammary lymph-nodes of the same side for breast cancer). For simplicity, data have been recoded as N positive, N negative or N unknown, although finer subdivision is possible.

M category

This describes the recorded presence or absence of distant spread of metastases or secondary cancer, to organs or tissues other than those considered regional to the primary site. This is the most poorly recorded component of stage, as it is often not clear from hospital notes whether or not sufficient investigations have been done to confirm the absence of at least the more obvious evidence of distant metastases have been.

Tumour grade

This describes the degree of differentiation of individual tumour cells, and has been coded here as grade 1 (well-differentiated), 2 (moderately differentiated), 3+ (poorly differentiated plus undifferentiated) or unknown. Cancer cells in grades 3-4 least resembling normal cells of the relevant primary site. Cases originally reported as grade 4 (undifferentiated) in pathology notes have been included in grade 3+. For prostate cancer, grade (derived from Gleason scores) is taken into account when assigning overall TNM stage to a case and in stage-based models. Grade can also be examined as a prognostic or explanatory variable in its own right, for all cancers considered in this report.

Morphology (cell type)

For colorectal and prostate cancers, no sub-grouping of morphologies was used; most invasive cancers of these sites are adenocarcinomas, although many were recorded only as non-specific carcinomas or cancers.

For primary invasive lung cancer, three broad groupings of cell types or morphologies are used for presentation or adjustment of survival and treatment analyses:

1. NSCLC (non-small-cell lung carcinomas): carcinomas of the lung other than those in ICD-O-2 morphology range 8040-8045.
2. SCLC (small-cell lung carcinomas): carcinoma morphologies in the range 8040-8045 (Parkin *et al*. 1998).
3. Other and unspecified morphologies: mainly cancers of unspecified morphology (range 8000-8004), most of which represent

carcinomas that have not been confirmed histologically, and small numbers of any further morphologies (mainly sarcomas).

For invasive breast cancer, six groupings of morphological types have been identified for potential adjustment of survival and treatment analyses:

1. Adenocarcinomas of breast-specific types: carcinomas in ICD-O-2 morphology ranges 8500-8506 or 8520-8543, i.e. ductal and lobular carcinomas, inflammatory carcinoma and Paget's disease (but not medullary carcinomas, not classed as adenocarcinomas by Parkin *et al*. 1998).
2. Other adenocarcinomas: those in morphology ranges 8140-8147, 8160-8162, 8180-8221, 8250-8490, 8550, or 8570-8573 (adenocarcinomas as classed by Parkin *et al*.1998, but excluding group 1).
3. Other specified carcinoma types: those in morphology range 8010-8671, other than groups 1, 2 and 4. Includes papillary carcinoma (8050), medullary carcinoma (8510-8512), and carcinoid tumours (8240-8245).
4. Carcinomas of unspecified type: those in morphology range 8010-8022.
5. Cancers of unspecified type: cancers in morphology range 8000-8004, the majority of which will be carcinomas that have not been confirmed histologically.
6. Other specified cancer types (non-carcinomas): all remaining morphologies, including malignant phyllodes tumours (9020), sarcomas and others.

Site

For colorectal cancer, account is also taken of potential influences of the detailed site of the primary tumour – colon, rectosigmoid junction, and rectum or anus.

Method of diagnosis

This was recoded to indicate whether or not a diagnosis was microscopically verified (by histological or cytological methods) or not. Note that, for the cancer sites considered in this report, specific morphologies (other than "cancer, not otherwise specified") are coded only for cases having microscopic verification.

Method of presentation

This describes how a case originally presented, and is summarized here as: symptomatic; screen-detected (found by deliberate screening or examination for a particular cancer type in a non-symptomatic patient); incidental (found during examination for other purposes); or unknown.

Most cases in the period considered presented symptomatically (or were coded as such). There were no national screening programmes during the period covered, although population-based screening for breast cancer was introduced to eastern parts of Ireland during 2000-2001 (the BreastCheck programme). Screen-detected cases also include patients screened for a given cancer outside the context of a population-based programme, but such cases are likely to have been under-recorded (if mis-coded as symptomatic). Substantial numbers of screen-detected cases were recorded only in the most recent years (>100 breast cancer cases annually 2000-2001, >50 prostate cancer cases 2001).

Smoking status

This is coded as non-smoker (never smoker), ex-smoker, current smoker or unknown.

Marital status

This has been re-coded as ever married, never married (single) or unknown.

Region of treatment

See under **Treatment: data-definition and analytical approach** below. This field has not been incorporated in the main analyses of survival or treatment, but data are tabulated to summarize numbers and proportions of cases treated by region of surgical treatment in relation to region of residence.

Hospital and consultant caseloads

See under **Treatment: data-definition and analytical approach** below. Again, this field has not been incorporated in the main analyses of survival or treatment. However, data are tabulated to summarize the proportions of cases having surgical treatment in hospitals in relation to average surgical caseloads for those hospitals. Equivalent tabulations are provided in relation to surgical consultant workloads. Further analyses are planned, however.

Deprivation

This has <u>not</u> been included in statistical models in this report, but further analyses are planned. Area-based deprivation is derivable for patients whose address data allow coding of their place of residence to the level of Electoral Divisions (EDs). For Irish EDs, material deprivation scores can be allocated the majority of EDs based on relevant variables from national Censuses (Small Area Health Research Unit 1997). For the previous patterns of care report covering 1994-98

(NicAmhlaoibh *et al*. 2004), patients were allocated to deprivation categories on this basis, for those addresses that had been geocoded. A detailed revision of this geocoding process is currently underway, with the intention of more complete and more accurate assignment of patient addresses to EDs. Pending completion of this revision, deprivation influences on survival and treatment were not examined here.

Comorbidity

The present report has not attempted to incorporate and adjust for comorbidity measures in regional comparisons, but planned further analyses will do so. Patient and tumour variables currently recorded by the NCR may not adequately explain why particular patients did not have treatment or had poor outcomes. In some cases, it may be that stage of disease was not adequately recorded in the hospital or pathology notes. In others it may be that the patient's general health was poor for other reasons, thus treatment options may have been limited or survival influenced by more than the cancer. Information on general patient condition or on non-cancer conditions is not, currently, abstracted routinely by NCR staff from hospital notes. In part, this is because such information tends to be recorded in an incomplete or non-standardized way. Linkage of patient data to HIPE, the Hospital In-Patient Enquiry computer system used by public hospitals in Ireland, potentially provides a means of obtaining data on significant non-cancer conditions recorded during a cancer patient's stay in hospital. For the previous patterns-of-care report (1994-98), HIPE linkage was used to check for such information for a substantial proportion (up to 70%) of patients (including private patients treated in public hospitals). This was used to derive a measure of comorbidity (the Charlson index: Charlson *et al*. 1987). However, it was noted in that report (NicAmhlaoibh *et al*. 2004) that the main reason for lack of linkage to HIPE was treatment in a private hospital, most of which were in the Eastern region, thus inclusion of comorbidity data could potentially bias regional comparisons of treatment and survival. It was also noted that: "The sensitivity of the Charlson index may also be limited; only 9% of patients had non-zero scores. While this index is of value in predicting death, it may be insufficiently sensitive to give information on the fitness of patients for surgery, radiotherapy and chemotherapy, and treatment choices may have been influenced by levels of comorbidity not recorded by the Charlson index." The process of linkage to HIPE and extraction of co-diagnosis data is also quite complex and difficult to standardize, in part because the same patient may have multiple inpatient episodes, sometimes in different hospitals.

2.4 Survival analysis

Survival analysis provides an estimate of the probability (or percentage) of patients diagnosed with a specific condition surviving to various times after diagnosis, e.g. one-year survival, five-year survival. Because patients may die of unrelated causes, 'net' survival (excluding unrelated deaths) is generally of interest. For population-based studies of cancer patients, this is typically calculated as *relative survival* (compared with the general population) but can also be calculated as *cause-specific survival*. Differences in survival (or its inverse) between patient groups can also be examined using modelling techniques. adjusted for potential confounders. Typically, Cox regression is used to derive *hazard ratios* (for observed and cause-specific survival) comparing different groups. Equivalent modelling approaches can be applied using relative survival, to derive *excess hazard ratios* (for relative survival) – the approach taken in this report.

Relative survival

This is the *survival observed in a particular group of patients as a percentage or proportion of the survival expected among persons of the same age and sex in the general population*. For example, if the expected five-year survival of a group of persons of a given age is 80%, and the observed survival of a group of cancer patients of the same age is 60%, the relative survival is expressed as (60/80)% = 70%. Relative survival is the typical measure computed by population-based cancer registries. Calculations here are based on the Ederer II approach (Ederer & Heise 1959), using modifications of Stata commands originally written by Dr Paul Dickman *et al*. (www.pauldickman.com/). Follow-up for each patient was split into intervals of three months for the first year after diagnosis, six months for the second and third years, and whole years for the fourth year of follow-up onwards. This allows for the risk of death generally being highest soon after diagnosis. In addition to deriving estimates of relative survival, data were also used for relative survival modelling (Dickman *et al*. 2003), again using modifications of Stata commands by Dickman *et al*.

Life tables

Calculation of relative survival requires does not require information on cause of death, but does require age- and sex-specific estimates of the annual survival probabilities of persons in the general population from which patients are drawn.

These estimates are obtained from *life tables*, derived from census population and annual mortality data.

For Ireland, official national life tables of annual survival and mortality probabilities were obtained for 1991, 1996 and 2002 (Central Statistics Office 1995, 2001). Age-specific survival and mortality probabilities were interpolated to derive estimated life tables for other individual years 1994-95 and 1997-2001, to avoid 'stepped' transitions between broader-period life tables. National life tables were used for assessment of relative survival at national scale (i.e. patients matched against "average" surrvival probabilities for Irish persons of the same age and sex), but regional life tables for analyses at regional scale.

Regional life tables

To allow correct estimation and comparison of relative survival for cancer patients resident in different regions, it was also necessary to derive region-specific life tables. These were prepared using detailed mortality data for the years 1994-2002 and detailed population data for the years 1996 and 2002, coded to county and single years of age (CSO, unpublished data). Regional age-specific populations for 2001 were derived by simple linear interpolation between 1996 and 2002, and life tables were prepared for 1996 and 2001, using mortality data for the three-year periods 1995-97 and 2000-2002, respectively.

The methods used to construct these regional life tables were essentially as described by Anderson (1999), and involved the use of Beer's "ordinary minimized fifth difference formula" to derive smooth curves of annual mortality probabilities. Because of small regional populations and numbers of deaths between ages 85 and 99, further smoothing and adjustment was done for this age-range by reference to national life tables for 1996 and 2001. (This was equivalent to the approach to used for U.S. life tables, where Medicare data provided a reference group for ages 85-99 [Anderson 1999].) Regional life-table data computed for ages 0-14 were less reliable, but did not require further adjustment as these ages were not required for relative survival analysis purposes in this report. The methods used to derive regional life tables had some features in common with those used by the CSO, but differed in some respects (particularly in relation to derivation and smoothing of survival probabilities for children and for the very oldest age-groups). However, comparison with the CSO's own unpublished life tables for local authority regions (some of which match the regional definitions used in this report) indicate a good match within the age-range 15-99.

Excess hazard ratio (EHR) [ratio of excess hazards]

This is derived by modelling techniques (Dickman *et al*. 2004) based on *relative survival* and provides an alternative to the more traditional approach of deriving hazard ratios based on cause-specific or crude survival. As for hazard ratios, calculation of excess hazard ratios is most straightforward if the proportional risk differences between patient groups are constant across the range of variables considered. Where this does not hold true, interaction terms are introduced into the model (Dickman *et al*. 2004) – typically between age and year of follow-up (year 1 to year 5) and between stage and year of follow-up. Relative survival modelling of data for this report was done using modifications of Stata do-files written by Dickman *et al*. (www.pauldickman.com/). Although those authors have shown that various approaches to relative survival modelling give essentially similar results, they recommended use of a "generalized linear model based on collapsed data using exact survival times and a Poisson assumption." This has been done here.

Excess hazard ratios, comparing patients resident in different regions during 1994-2001 as a whole (initially), were first computed using a *basic model* adjusting for *age* (EUROCARE age-classes) as a potential confounder. Likelihood-ratio testing was used to assess if including other potential confounders (or interactions between follow-up interval and age or stage-related variables) significantly improved the fit of the basic model. These additional variables or interactions were added to the basic model in the following sequence (with only those which improved goodness of fit being retained in successive models): (1) age*follow-up interaction; (2) *sex*, for colorectal and lung cancers; (3) *cell-type*, for lung cancer [later in sequence for breast cancer]; (4) *grade*, for prostate cancer [later in sequence for other cancers]; (5) grade*follow-up interaction, for prostate cancer; (6) *T category* of stage; (7) T category*follow-up interaction; (8) *N category*; (9) N category*follow-up interaction; (10) *M category*; (11) M category*follow-up interaction; (12) *cell-type*, for breast cancer; (13) cancer *site*, for colorectal cancers; (14) *method of diagnosis* (microscopic verification status); (15) *method of presentation*; (16) *smoking status*; (17) *marital status*; and (18) individual *year of diagnosis*. This sequence was decided based on prior knowledge of or assumptions about the likely relevance of particular variables (overall or for particular cancers), although we recognize that testing of variables in a different sequence might lead to a different 'choice' of variables for the final models used.

Up to three sets of models are presented for regional comparisons.

i. Age-group and age-group/follow-up interaction (plus sex for colorectal and lung cancers, and cell-type for lung cancer) significantly improved model-fit for all cancers included in this report, and are used in *basic models* (as distinct from the baseline model with just age-group and no interaction term).
ii. Additional variables considered for *fuller (stage-adjusted) models* were the T category of stage, N category, M category, grade (for prostate cancer only), and interaction between follow-up interval and age, and follow-up interval and stage-related variables (including grade for prostate cancer). All these variables significant improved model-fit, but the T-category/follow-up and N-category/follow-up interactions did not improve fit for prostate cancer and were excluded.
iii. All variables and interactions examined which significantly improved goodness of fit were retained in the *final (full) model*. For comparability, precisely the same variables and interactions were used in equivalent models restricted to shorter periods (mainly 1994-97 and 1998-2001).

For assessment of time-trends in survival (comparing 1994-97 and 1998-2001 diagnosis periods), the same variables (except year of diagnosis) and interactions were also used in *basic*, *stage-adjusted* and *final models*.

2.5 Treatment: data-definition and analytical approach

Time since diagnosis

Collection of treatment data by the National Cancer Registry is primarily intended to cover 'first-course' treatments, rather than treatments for subsequent recurrences. In practice it is sometimes difficult to distinguish first-course from later treatments. A working definition of "treatments administered or planned within six months after diagnosis" has thus been broadly adopted for data-collection purposes, to allow for collection of treatment data planned at an early stage but not administered until later. However, some of the later treatments recorded for particular patients may, in fact, relate to treatment for recurrences, and it is not always possible to distinguish such treatments on the basis of hospital notes or other information available. For pragmatic reasons, therefore, *the main analyses of treatment data for this report are confined to treatments actually administered within six months after diagnosis*. (For prostate cancer, we recognize that a longer 'window' might also be informative, given that a higher proportion of 'initial' treatment for this cancer takes place more than six months after diagnosis. However, such data may be less complete for earlier years, and if the initial management of a prostate cancer is 'watchful waiting', it may not be strictly valid to count later treatments as 'first course'.)

Definitive or tumour-directed treatment

Analyses were confined to definitive or *tumour-directed treatment, i.e. any treatment or therapy with aim or effect of removing, destroying or preventing growth of tumour tissue, whether "curative" or "palliative" in intent*. This includes surgery (and related destructive therapies), chemotherapy (and related therapies e.g. biological response modifiers and immunotherapy), hormone therapy and radiotherapy. Any treatments or therapies that do not remove or destroy tissue, or prevent growth of tumour, are not counted here as tumour-directed treatment. See also *Treatment intent* below.

Surgery and related treatments

This heading includes a number of quasi-surgical destructive techniques (e.g. cryotherapy, cauterization etc). Biopsy procedures (removal of small samples of tissue for diagnostic or prognostic purposes) and any surgical procedures that do not remove or destroy tissue (e.g. incisions, bypasses, insertion of stents) were <u>not</u> included in analyses of surgical treatment. Removal of one or more complete lymph nodes was, however, included as surgery (but biopsy of lymph nodes was not), in line with SEER practice. For the purposes of analyses presented in this report, in general no distinction was made between surgery of the primary cancer site and surgery of other sites (e.g. regional lymph-nodes or distant metastases). However, for breast cancer, oophorectomy (removal of one or both ovaries) has been counted as hormonal rather than surgical treatment, as has orchiectomy (removal of testicles) for prostate cancer. Oophorectomy and orchiectomy could not be identified (specifically) for the years 1994-97, but were not were included in the NCR definition of "(tumour-directed) surgery" for those years, thus assessment of trends in surgery should not be affected. (See also under *Hormonal therapy* below.) For some specific analyses planned, for example to assess the relative frequency of breast-conserving surgery versus mastectomy for breast cancer, surgery of other than the primary site would be excluded.

'Main' surgery (main hospital, consultant, region of treatment)

This was defined on the basis of detailed treatment codes from the 9th edition of the International Classification of Diseases and Related Health Problems, Clinical Modification (ICD-9-CM: Puckett 1998). The most 'advanced' or relevant procedure, within six months of diagnosis, was coded as the main surgical treatment for a given case. The "main surgical hospital" was coded as the hospital in which the most advanced procedure was done (or first done), and this was also used to allocate a "main region of surgical treatment". The "main surgical consultant" was coded as the consultant who was coded (or first coded) in registry records against the relevant procedure.

Chemotherapy and related treatment

This category includes directly cytotoxic chemical agents, administered singly or in combination, to kill or reduce growth of cancer cells. It excludes hormonal or anti-hormonal agents. For the purposes of analyses here, small numbers of related treatments are also included, in particular immunotherapy or biological response modifiers (BRMs) such as Herceptin (for breast cancer).

Hormone therapy

For NCR data collection, this is defined to cover hormonal treatments intended to reduce or prevent tumour growth, and to exclude hormonal therapies that do not have a direct anti-tumour effect. Of the cancers covered here, hormonal therapy is an important anti-cancer therapy for breast and prostate only. For the period 1994-95, NCR treatment data did not differentiate between hormonal therapy and chemotherapy. These modalities cannot be analyzed for those years for breast cancer, for which both modalities are important. For prostate cancer, where chemotherapy is administered to only a small proportion of patients, relevant treatments during 1994-95 have been recoded as hormonal therapy. For colorectal and lung cancers, relevant treatments during 1994-95 have been recoded as chemotherapy, as hormonal therapy is rare for those cancers.

Oophorectomy ((for treatment of breast cancer) and orchiectomy (for prostate cancer) have been counted as hormonal therapy. Oophorectomy and orchiectomy could not be identified as specific treatments in NCR data for the years 1994-97. Assessments of trends in hormonal therapy (presented for 1996-2001) could thus potentially be biased (decreases overestimated or increases underestimated). However, trends in hormonal therapy were virtually identical whether or not 'endocrine surgery' was included in the definition of hormonal therapy.

Radiotherapy

This is the main anti-tumour therapy for some cancers, while for others it may be considered an adjuvant treatment (e.g. irradiation of the tumour site after breast-conserving surgery for breast cancer). Substantial numbers of cancer patients also receive radiotherapy for palliative purposes, to alleviate pain by reducing growth of secondary tumours. As noted earlier, this is also counted here as definitive or tumour-directed treatment.

No treatment

This refers to cases that did not have surgery, chemotherapy, hormone therapy, radiotherapy or related treatments as defined above. Many of these cases will have had biopsy procedures and various other investigative, supportive or palliative procedures – but note that "palliative" treatments that have the effect or removing or destroying tumour tissue are counted here as tumour-directed treatments. During the period covered by this report, the NCR did not collect information on reasons why particular patients were not treated, in part because this information was generally not available or was not amenable to standardized recording. It is hoped that it will be possible to collect such information (where available from hospital notes) in future.

Multiple treatments

For each main treatment modality described above, only one treatment episode was counted per case. (However, for some analyses, surgical caseloads were derived by counting one episode of surgery per hospital or consultant, where the same patient had relevant surgery coded for more than one hospital or consultant.) Treatment analyses are also presented for "any treatment" (if tumour-directed as defined earlier) and summaries are provided of the main combinations of treatments given within six months of diagnosis, along with numbers of patients having single treatment modalities only.

Treatment 'intent'

For this report, no distinction is made between treatments stated (or assumed) to have "curative" as opposed to "palliative" intent – instead, the concept of "*definitive treatment*" is adopted. This is in line with practice in the SEER cancer registry program in the United States: "For the SEER Program, the concept of definitive treatment is limited to procedures directed toward cancer tissues whether of the primary site or metastases. If a specific therapy normally

affects, controls, changes, removes, or destroys cancer tissue, it is classified as definitive treatment even if it cannot be considered curative for a particular patient in view of the extent of disease, incompleteness of treatment, lack of apparent response, size of dose, operative mortality, or other criteria. … The term 'palliative' may be used in two senses: (a) as meaning non-curative and (b) as meaning the alleviation of symptoms. Thus, some treatments termed palliative fall within the definition of cancer-directed treatment and some treat the patient but not the cancer. For example, radiation therapy to bony metastases is considered cancer-directed treatment because in addition to alleviating pain, the radiation also kills cancer cells in the bone" (Fritz & Ries 1998).

Region where treated

It was not straightforward to define this for treatment as a whole (or, indeed, for diagnosis of a given patient). Instead, a "main region" was defined for surgical treatments (see under *Main surgery* definition), and this was cross-tabulated against region of residence to provide a basic indicator of patient movement between regions. No attempt was made here to assign region of treatment for other modalities, but it radiotherapy was known to be largely confined to hospitals in the Eastern and Southern regions. Region where treatment took place was <u>not</u> included in the statistical models in this report, but further analyses may be published elsewhere.

Hospital and consultant caseloads

These were defined *for surgical patients only*, annually and for combined periods 1994-2001, 1994-97 and 1998-2001, on the basis of patients receiving *tumour-directed surgery* within six months of diagnosis. Data on caseloads (a proxy for hospital or consultant specialization or experience) are presented here for each cancer, and in planned further analyses (but not here) will be assessed for their possible influence on treatment and survival. For caseload calculations but not for the main treatment analyses, surgical treatments were counted whether or not they were the patient's "main" surgery, as long as they met the criteria for surgery and related destructive treatments (see *Surgery* subheading). Caseload calculations for a given invasive cancer (breast, colorectal, lung or prostate) were based on *patients* (rather than tumours), to provide some consistency with the main treatment analyses (which were restricted to the first primary cancer, of any type, in a given patient). However, patients diagnosed (and registered) with two or more cancers of the same type in different years were counted once for <u>each</u> hospital and consultant for <u>each</u> diagnosis year, if surgically treated within six months of a given tumour. For caseload analyses based on multi-year periods (1995-97, 1998-2001 and 1994-2001), surgically-treated patients were counted once for each hospital and consultant for the period as whole. (Note, however, that caseload calculations excluded hospitals or consultants that were coded "unknown" or missing, or that were based in Northern Ireland or elsewhere outside the Republic of Ireland.)

Major public and private hospitals were analyzed as separate hospitals, but a small number of public hospitals or hospital-names were combined as single hospitals if they had either merged or effectively operated as single hospitals within the period 1994-2001.

Consultant codes used by the NCR were checked in detail by reference to the Irish Medical Directory, online sources and NCR staff based regionally and any 'duplicate' codes were corrected. Where the same consultant was involved in treating patients in multiple hospitals (or regions), as far as possible the same code was used for analyses here. Otherwise, details of consultants abstracted by NCR staff from hospital records have been taken at face value, although it is recognized that (a) some named consultants recorded against a given treatment may not have been surgical consultants and (b) some consultants may no longer have been in-post at the time of a given surgical treatment (even though the relevant code for their post was used).

For descriptive analyses of caseloads, numbers of hospitals and surgical consultants responsible for <10, <20 and <50 cases were summarized for each year and (based on average caseloads) for the four-year periods 1994-97 and 1998-2001. Trends in the proportions of surgical patients treated by hospitals or consultants of a given caseload were assessed using Mantel's trend test (Szklo & Nieto, 2000) and χ^2 tests.

Logistic regression of treatment data, and derivation of risk ratios from odds ratios

Logistic regression was used to model and estimate differences (based on *odds ratios*) in the *odds* of treatment between different patient groups. Note, however, that for treatments and other frequent outcomes, odds ratios will tend to overestimate true differences in the 'risk' of treatment. For example, if 90 out of 100 patients in group B are treated (90%), compared with 80 out of 100 patients in group A, the *risk ratio (RR)* for treatment, comparing group B v A, is (90/100)/(80/100) = 1.125 i.e. patients in group B are 1.125 times (or 12.5%) more likely to have treatment than group A. However, the odds ratio (OR) for treatment, comparing B v A, is (90/10)/(80/20) = 2.25.

Calculation of odds ratios for treatment has a number of statistical advantages over calculation of risk ratios, and statistical conclusions based on odds ratios are valid. Thus ORs and their 95% confidence limits correctly identify differences in the odds of treatment between different groups and whether or not the differences are likely to be due to chance. However, ORs for treatment should not be taken, at face value, as quantitative estimates of the relative risk (or proportional frequency) of treatment when comparing patient groups.

For comparisons of treatment among patient-groups, equivalent risk ratios (RRs) were derived from adjusted ORs using a correction method proposed for studies of frequent outcomes:

$$\text{derived RR} = \text{adjusted OR}/((1-P_0)+(P_0*\text{OR})$$

where P_0 is the proportion of cases treated in the baseline group (Zhang and Yu 1998).

As for relative survival modelling (see above), comparisons of patients resident in different regions during 1994-2001 were first computed using a *basic model* adjusted for *age* (EUROCARE age-classes) as a potential confounder. Likelihood-ratio testing was then used to assess if including other potential confounders significantly improved the fit of the basic model. These additional variables were added to the basic model in the following sequence (with only those which improved goodness of fit being retained in successive models): (1) *sex*, for colorectal and lung cancers; (23) *cell-type*, for lung cancer [later in sequence for breast cancer]; (3) *grade*, for prostate cancer [later in sequence for other cancers]; (4) *T category* of stage; (5) *N category*; (6) *M category*; (7) *cell-type*, for breast cancer; (8) cancer *site*, for colorectal cancers; (9) *method of diagnosis* (microscopic verification status); (10) *method of presentation*; (11) *smoking status*; (12) *marital status*; and (13) individual *year of diagnosis*.

Results of three sets of logistic models are presented for regional comparisons.

i. Age-group (plus sex for colorectal and lung cancers, and cell-type for lung cancer) were used in *basic models* (although sex did not significantly improve model-fit for surgical treatment of lung cancers or for overall and surgical treatment of colorectal cancers).
ii. Additional variables considered for *fuller (stage-adjusted) models* were the T category of stage, N category, M category, and (for prostate cancer only) grade. These variables significant improved model-fit for each of the four cancers.
iii. All variables and interactions examined which significantly improved goodness of fit were retained in the *final (full) model*. For comparability, precisely the same variables were used in equivalent models restricted to shorter periods (mainly 1994-97 and 1998-2001).

For assessment of time-trends in treatment (average annual changes 1996 to 2001), the same variables (but year of diagnosis as a continuous variable) were also used in *basic* and *stage-adjusted logistic models*.

Time-trends in treatment (by year of diagnosis)

For overall treatment, and the man treatment modalities, logistic regression was used to assess average annual changes in relative odds of treatment (re-expressed as relative risk of treatment as described above), as a summary measure of time-trends. To allow for the possibility that treatment data may have been under-recorded in earlier years (1994 and 1995), trends have been assessed for the six-year period 1996-2001. Trends were adjusted for age, sex (where relevant), morphological subtype (for lung cancer) and stage-related variables (including grade for prostate cancer), but not for other variables. No formal tests for linearity of trend, or for whether year as a continuous variable was a better fit to data than individual year, were done.

Comparison of risk ratios between analyses

In some instances where two independent estimates of risk ratios (RR) are available, e.g. for effect of region on treatment for males and females, or for different diagnosis periods, a *test of interaction* has been applied to assess whether or not the RRs differ significantly between the two groups (Altman & Bland 2003). For large sample sizes, the ratio of the difference in the natural logs of the RR between two groups to the standard error of the difference in the natural logs of the RR provides the *z*-statistic:

$$z = (\ln(RR1)-\ln(RR2))/\text{SQRT}(\text{SE}(\ln(RR1))^2+(\text{SE}(\ln((RR2))^2)$$

The *z*-statistic is compared with a table of the normal distribution to determine the significance of the difference in RR estimates between groups.

Chapter 3. BREAST CANCER (female)

Summary

Trends in incidence, mortality and patient/tumour characteristics

Numbers of invasive cases showed significant upward trends between 1994 and 2001, but numbers of deaths showed no significant trends. Age-standardized incidence rates increased, but mortality rates declined significantly.

During this period, there were increases in the proportions of patients aged 55-64, in T1, node-negative and non-metastatic cancers, and in screen-detected cases. These changes are consistent with expected trends towards earlier detection.

Survival

1994-2001 average

Relative survival to five years after diagnosis was estimated as 75.4% (95% CI 74.4-76.3%).

Survival trends

National estimates of five-year survival were 72.9% (95% CI 71.6-74.2%) for cases diagnosed during 1994-97 and 78.2% (76.8-79.6%) for 1998-2001. The improvement represented a 24% reduction in age-adjusted excess risk of death (i.e. the risk having allowed for expected background mortality), or a 9% reduction in excess risk after adjustment for other tumour and patient variables. Relative survival also improved significantly for the Eastern, North-Eastern and Southern regions between diagnosis-periods 1994-97 and 1998-2001. These changes amounted to a 26-30% reduction in age-adjusted excess risk of death.

Most of the improvements seen in breast cancer survival between the two periods considered seem likely to reflect improved treatment. This may involve greater or more appropriate use of specific treatments. Changes seen in the proportions of patients receiving particular treatments seem to support this. Improvements in survival overall and in some individual regions may also reflect, in part, increases in early diagnosis. Further improvements in recorded survival are expected to result from the introduction of population-based breast cancer screening, from 2000/2001 onwards. However, the possibility of 'lead-time' bias, whereby patients diagnosed earlier appear to survive longer even if no true survival benefit occurs, will need to be taken into account.

Regional variation in survival

After adjusting for a range of patient and tumour characteristics, four regions had a significantly high excess risk of death for cases diagnosed during 1994-2001 as a whole: Midland (28% higher than Eastern), Southern (16% higher), South-Eastern (22% higher) and Western (26% higher). Regional variations in relative survival were not fully consistent between the two diagnosis periods. Only the Western region showed a significant excess risk for both 1994-97 (+24%) and 1998-2001 (+33%). Other regions with significantly high excess risks (lower survival) in the full model for 1998-2001 were Midland (+38%) and South-Eastern (+41%). Survival improvements in the Eastern, North-Eastern and Southern regions reduced differences in survival between those regions, but accentuated differences between the Eastern region and other regions. As for the interpretation of survival trends, the relative roles of treatment quality and early detection are difficult to quantify.

International comparison of survival

Average five-year relative survival for female breast cancer patients diagnosed in Ireland during 1994-97 was slightly lower than the European average for patients diagnosed during 1990-94.

Treatment

Proportions of patients treated: main modalities and combinations

96% of patients diagnosed during 1996-2001 had some form of definitive or tumour-directed treatment within six months of diagnosis, 85% had surgical treatment, 47% had hormonal therapy, 44% had radiotherapy and 42% had chemotherapy. (1994-95 data are excluded form these figures as chemotherapy and hormonal therapy were not recorded separately for those years.)

The most frequent treatments or combinations were surgery plus hormonal therapy (15% of cases 1996-2001), surgery plus chemotherapy (also 15%), surgery plus hormonal therapy plus radiotherapy (13%), surgery plus chemotherapy plus radiotherapy (13%), and surgery only (10%).

Region of treatment versus region of residence

Most patients resident in each region had their main surgical treatment in the same region, ranging

from 60% of surgical patients from the Midland region to 99% of those from the Eastern region.

Hospital caseloads

Breast cancers were surgically treated in a total of 60 hospitals during 1994-2001. There was no strong evidence of any trend in numbers of hospitals providing surgical treatment. About one-third of hospitals involved in surgery in any given year treated fewer than 10 surgical cases each; over half treated fewer than 20 surgical cases each in a given year and about three-quarters treated fewer than 50 cases. There was a general tendency for average hospital caseload to increase during the period 1994-2001, with significant declines in the proportions of surgical cases treated in 'low volume' hospitals. For example, the proportion of surgical cases treated in hospitals treating 50+ cases per year rose from 36% during 1994-97 to 58% during 1998-2001.

Surgical consultant caseloads

At least 221 individual consultants were responsible for surgical managements of female breast cancers during 1994-2001, increasing from 147 in 1994-97 to 181 in 1998-2001. About two-thirds of surgical consultants in any given year treated fewer than 10 surgical cases each; more than three-quarters treated fewer than 20 surgical cases each in a given year and almost all treated fewer than 50 cases. Average annual caseloads increased over time, and significant declines were seen in the proportions of surgical patients treated by 'low volume' consultants.

Treatment trends

Age-adjusted trends during 1996-2001 showed a minor, albeit statistically significant, increase in surgery use nationally (by an average 0.5% annually in relative terms). At regional scales, only patients from the Eastern region showed any significant trend, equivalent to a 1% annual increase in relative terms.

There was no significant national trend in use of radiotherapy during 1996-2001. However, significant trends in radiotherapy were seen for patients from four regions: significant increases for the Southern and Western, significant decreases for the North-Western and South-Eastern regions.

Nationally, age-adjusted trends indicated a substantial and significant increase in chemotherapy use during 1996-2001, by about 13% annually in relative terms. Patients from seven of the eight regions also showed significant increases, by between 10% and 20% annually.

There was a significant overall decline in hormonal use during 1996-2001 by about 9% annually in relative terms. Significant declines were also seen for patients from all regions, by between 6% and 13% annually. One possible interpretation is that this indicates more appropriate use, i.e. reduction in use of hormonal-therapy for patients who were negative for both oestrogen-receptor and progesterone-receptor status.

Regional variation in treatment

Overall treatment and use of surgery varied comparatively little between regions. For 1994-2001 as a whole, there was significantly high use of surgery in patients from the Mid-Western and Western regions, but significantly low use in those from the Southern region, after adjustment for a rasnge of patient and tumour characteristics.

More substantial variation was apparent for radiotherapy, with patients from the Mid-Western, North-Western and Western regions significantly less likely, but patients from Southern region significantly more likely, to have radiotherapy than patients from the Eastern region. Radiotherapy use was consistently similar (and high) among patients from the Eastern, Midland and North-Eastern regions throughout the period. Radiotherapy use was highest for patients from the Southern region. These patterns suggests that geographic proximity to Dublin and Cork, the locations of the main radiotherapy centres in Ireland during those years, was an important factor.

Significantly high use of chemotherapy was seen in two regions (North-Eastern and South-Eastern), compared with the Eastern region. Significantly low use of chemotherapy was apparent for the Mid-Western and (during 1998-2001) Midland region.

Regional variation in hormonal therapy was also marked, but involved significantly higher use for patients from outside the Eastern region. Patients from the North-Eastern and, to a lesser extent, Midland region were most similar to those from the Eastern region in terms of hormonal use. Although this was less marked than for radiotherapy use, it may support geographic or institutional factors, rather than variation in patient or tumour characteristics, having been a crucial determinant of the extent to which hormonal therapy was used.

International comparison of treatment

Patients in Ireland were significantly less likely to have surgery, or to a lesser extent radiotherapy, than in the USA. The proportion of patients having chemotherapy or hormonal therapy appeared to be higher in Ireland.

3.1 Incidence and mortality statistics

On average, there were 1725 cases of and 644 deaths from invasive breast cancer annually in Irish women during 1994-2001 (*Table 3.1.1*). Over this period, numbers of cases showed significant upward trends, but numbers of deaths showed no significant trends. Age-standardized incidence rates increased, but mortality rates declined significantly.

Table 3.1.1 Incidence of and mortality from invasive breast cancer, Republic of Ireland, 1994-2001.

	annual average numbers		age-standardized rate[a]	
1994-2001	**female**		**female**	
Incidence (cases)	1725		100.2	
Incidence trend (per year)[b]	+4.0%	***	+2.1%	***
Mortality (deaths)	644		35.3	
Mortality trend (per year)	+0.4%	ns	-1.3%	*

[a]European age-standardized rate per 100,000 persons per year.
[b]Estimated annual percentage change (ns not significant, * P<0.05, **P<0.01, ***P<0.001).

3.2 Cases included for treatment and survival analyses; patient and tumour characteristics

Analyses cover invasive breast cancers (ICD-10 code C50) diagnosed in 13,383 women aged 15-99 years during 1994-2001. Full details of inclusion and exclusion criteria are shown in *Table 3.2.1*.

Table 3.2.1 Summary of inclusions and exclusions for breast cancer analyses.

Case definition	total
all registered tumours[a]	14 974
ages 15-99 only	14 970
excluding male breast	14 853
excluding death-certificate-only & autopsy-only cases	14 612
invasive tumours only	13 747
first tumours only[b]	**13 383**

[a] Including in situ carcinomas, and tumours of unspecified behaviour, but excluding lymphomas (classified separately within ICD-10.)
[b] Or most serious tumour diagnosed same date.

A breakdown of basic patient and tumour characteristics is given in *Table 3.2.2*, including comparisons between diagnosis periods 1994-97 and 1998-2001. The variables and category-values shown are those considered, later in this chapter, for inclusion in statistical models aimed at describing and if possible explaining regional variation and time-trends in survival and treatment.

Statistically significant changes between 1994-97 and 1998-2001 in proportions of patients or tumours with particular characteristics were as follows:

- Increase in patients aged 55-64, decrease in those aged 65-74 years at diagnosis.
- Increase in tumours in T1 category, decrease in T3 and T unknown.
- Increase in node-negative cancers, decrease in 'nodal status unknown' cases.
- Increase in non-metastatic cancers.
- Increase in breast-specific adenocarcinoma morphologies, decrease in non-specific carcinomas and cancers.
- Increase in grade 1 and grade 2 tumours, decrease in grade unknown.
- Increase in microscopically verified (MV) cases, decrease in non-MV cases.
- Decrease in symptomatic cases, increase in screen-detected cases and unknown method of presentation.
- Decrease in patients with marital status unknown.
- Decrease in patients recorded as non-smokers, increase in ex-smokers and unknown smoking status.

In general, these changes are consistent with expected trends towards earlier detection and more specific or complete diagnoses and investigations.

Variation in patient and tumour characteristics by region of residence is summarized in *Table 3.2.3*.

Table 3.2.2 Summary of patient and tumour characteristics for female breast cancer patients included in survival and treatment analyses, 1994-2001.

	diagnosed 1994-2001		diagnosed 1994-1997		diagnosed 1998-2001	
	number	% of cases	number	% of cases	number	% of cases
total	13383		6216		7167	
age 15-44	1975	14.8%	930	15.0%	1045	14.6%
age 45-54	3277	24.5%	1514	24.4%	1763	24.6%
age 55-64	3167	23.7%	1397	22.5%	1770	*24.7%
age 65-74	2593	19.4%	1262	20.3%	1331	*18.6%
age 75+	2371	17.7%	1113	17.9%	1258	17.6%
stage I	1462	10.9%	653	10.5%	809	11.3%
stage II	3525	26.3%	1603	25.8%	1922	26.8%
stage III	817	6.1%	385	6.2%	432	6.0%
stage IV	955	7.1%	452	7.3%	503	7.0%
stage X[a]	6624	49.5%	3123	50.2%	3501	48.8%
T1	4257	31.8%	1822	29.3%	2435	*34.0%
T2	5581	41.7%	2563	41.2%	3018	42.1%
T3	1304	9.7%	697	11.2%	607	*8.5%
T4	1190	8.9%	567	9.1%	623	8.7%
T X	1051	7.9%	567	9.1%	484	*6.8%
N negative	5825	43.5%	2603	41.9%	3222	*45.0%
N positive	5463	40.8%	2507	40.3%	2956	41.2%
N X	2095	15.7%	1106	17.8%	989	*13.8%
M negative	6279	46.9%	2855	45.9%	3424	*47.8%
M positive[b]	959	7.2%	453	7.3%	506	7.1%
M X	6145	45.9%	2908	46.8%	3237	45.2%
grade 1	1078	8.1%	439	7.1%	639	*8.9%
grade 2	3356	25.1%	1250	20.1%	2106	*29.4%
grade 3+	3983	29.8%	1822	29.3%	2161	30.2%
grade X	4966	37.1%	2705	43.5%	2261	*31.5%
ductal/lobular	10829	80.9%	4874	78.4%	5955	*83.1%
other adenocarc	979	7.3%	470	7.6%	509	7.1%
other carcinoma	146	1.1%	59	0.9%	87	1.2%
carcinoma NOS	854	6.4%	478	7.7%	376	*5.2%
cancer NOS	512	3.8%	310	5.0%	202	*2.8%
other cancer	63	0.5%	25	0.4%	38	0.5%
MV[c] yes	12932	96.6%	5937	95.5%	6995	*97.6%
MV no	388	2.9%	249	4.0%	139	*1.9%
MV X	63	0.5%	30	0.5%	33	0.5%
symptomatic	11706	87.5%	5762	92.7%	5944	*82.9%
incidental	310	2.3%	144	2.3%	166	2.3%
screen detected	552	4.1%	121	1.9%	431	*6.0%
presentation X	815	6.1%	189	3.0%	626	*8.7%
non-smoker	6445	48.2%	3072	49.4%	3373	*47.1%
ex-smoker	1107	8.3%	455	7.3%	652	*9.1%
smoker	2712	20.3%	1301	20.9%	1411	19.7%
smoking X	3119	23.3%	1388	22.3%	1731	*24.2%
ever married	10875	81.3%	5007	80.6%	5868	81.9%
never married	2032	15.2%	961	15.5%	1071	14.9%
marital status X	476	3.6%	248	4.0%	228	*3.2%

[a]Unknown values shown as "X" for stage and other variables. [b]Minor discrepancies between stage IV and M positive cases reflect morphologies for which TNM staging is not strictly applicable. [c]MV = microscopic verification (histology or cytology).
*Significant change in the proportion of cases in this category (χ^2 test, 1 df, $P<0.05$); but note that some further changes may be significant if cases in "unknown" categories are excluded.

Table 3.2.3 Summary of patient and tumour characteristics, by region of residence, for female breast cancer patients included in survival and treatment analyses, 1994-2001. Account is taken of the potential confounding affect of these variables in statistical models of regional variation in survival (*section 3.4.4*) and treatment (*section 3.6.3*).

	Eastern	Mid-Western	Midland	North-Eastern	North-Western	Southern	South-Eastern	Western
total cases	5087	767	1079	1002	776	2098	1326	1248
age 15-44	15.1%	15.6%	14.2%	14.3%	14.9%	13.8%	15.5%	14.4%
age 45-54	25.4%	23.6%	25.7%	24.9%	*20.9%	25.2%	*21.6%	24.3%
age 55-64	25.0%	26.2%	*22.0%	23.2%	21.9%	21.8%	23.7%	22.6%
age 65-74	18.6%	19.9%	19.8%	20.1%	18.7%	19.3%	19.7%	*21.6%
age 75+	15.9%	14.6%	18.4%	17.7%	*23.6%	*19.9%	*19.5%	17.1%
stage I	10.6%	12.9%	11.8%	*5.4%	*14.9%	9.7%	*13.3%	11.6%
stage II	28.4%	27.8%	*24.3%	*15.4%	30.7%	*20.6%	*33.0%	27.5%
stage III	7.5%	6.1%	*5.0%	*4.2%	7.1%	*3.4%	7.8%	*5.0%
stage IV	7.1%	5.5%	7.3%	6.0%	8.4%	7.0%	7.3%	8.6%
stage X	46.4%	47.7%	*51.6%	*69.1%	*38.9%	*59.3%	*38.5%	47.3%
T1	32.3%	31.4%	32.6%	*25.2%	*28.6%	34.6%	31.1%	32.9%
T2	41.4%	42.0%	*38.1%	*47.4%	43.0%	41.7%	42.5%	39.7%
T3	10.4%	9.3%	*7.6%	*13.1%	9.1%	*8.5%	*8.5%	10.3%
T4	7.6%	8.1%	8.3%	8.3%	*13.3%	*9.7%	*10.9%	*9.5%
T X	8.4%	9.3%	*13.3%	*6.0%	*5.9%	*5.5%	7.0%	7.7%
N negative	43.5%	42.5%	44.2%	41.7%	41.8%	43.0%	*47.4%	42.9%
N positive	39.1%	*45.1%	39.1%	41.8%	41.5%	*43.2%	*42.7%	39.5%
N X	17.4%	*12.4%	16.7%	16.5%	16.8%	*13.8%	*9.9%	17.6%
M negative	50.9%	50.2%	*46.0%	*26.7%	*54.9%	*34.8%	*58.5%	48.8%
M positive	7.1%	5.5%	7.4%	6.0%	8.5%	7.0%	7.3%	8.6%
M X	42.0%	44.3%	*46.6%	*67.3%	*36.6%	*58.2%	*34.2%	42.6%
grade 1	11.0%	*7.6%	*4.6%	*7.7%	*7.1%	*6.9%	*4.4%	*5.9%
grade 2	27.7%	25.8%	*19.7%	27.2%	*33.5%	26.4%	*19.2%	*15.5%
grade 3+	28.4%	27.1%	25.9%	*35.8%	28.2%	*32.4%	*36.1%	*25.0%
grade X	32.8%	*39.5%	*49.7%	*29.2%	31.2%	34.3%	*40.3%	*53.5%
ductal/lobular	82.2%	*78.9%	*70.3%	83.0%	82.1%	*85.1%	80.0%	*77.4%
other adenocarc	6.3%	*14.6%	*9.2%	5.8%	6.6%	5.7%	*8.6%	*8.5%
other carcinoma	0.7%	0.8%	1.0%	0.9%	*1.7%	*1.5%	1.1%	*1.8%
carcinoma NOS	7.4%	*3.1%	*13.2%	*5.4%	*3.5%	*2.8%	*5.3%	8.1%
cancer NOS	2.8%	2.1%	*5.8%	*4.3%	*5.8%	*4.7%	*4.5%	3.6%
other cancer	0.5%	0.5%	0.5%	0.6%	0.4%	0.3%	0.5%	0.6%
MV yes	97.7%	98.7%	*95.0%	*96.2%	*94.5%	*95.4%	*95.8%	97.1%
MV no	1.7%	*0.7%	*4.3%	*3.4%	*5.3%	*4.5%	*3.4%	*2.7%
MV X	0.6%	0.7%	0.7%	0.4%	0.3%	*0.1%	0.8%	0.2%
symptomatic	82.3%	*88.3%	*89.1%	*87.5%	*95.1%	*90.4%	*92.8%	*91.4%
incidental	1.6%	0.9%	*2.7%	2.0%	1.2%	*5.6%	1.1%	2.5%
screen detected	5.9%	6.0%	*1.6%	5.2%	*1.8%	*3.3%	*2.3%	*1.8%
presentation X	10.2%	*4.8%	*6.7%	*5.3%	*1.9%	*0.7%	*3.8%	*4.2%
non-smoker	39.0%	*48.6%	*51.5%	*43.9%	*49.1%	*63.1%	*49.3%	*59.0%
ex-smoker	9.5%	8.3%	*5.5%	9.8%	9.7%	*5.8%	*6.6%	9.6%
smoker	20.9%	19.3%	21.5%	19.0%	21.9%	*18.1%	20.7%	20.5%
smoking status X	30.7%	*23.7%	*21.5%	*27.3%	*19.3%	*13.0%	*23.4%	*10.9%
ever married	78.5%	*82.1%	*81.6%	*84.5%	*82.2%	*82.6%	*82.4%	*84.8%
never married	16.9%	*13.2%	*13.8%	*11.5%	16.4%	15.4%	*14.4%	*13.2%
marital status X	4.6%	4.7%	4.5%	4.0%	*1.4%	*2.0%	*3.2%	*2.0%

*Significant difference in proportion of cases, compared with Eastern region (χ^2 test, 1 df, P<0.05)

3.3 Relative survival: descriptive analysis

Five-year relative survival estimates for national population, by period of diagnosis, age and other patient or tumour characteristics, are shown in *Table 3.3.1*. Survival curves, to five years after diagnosis, are plotted for the same variables in *Figure 3.3.1*. One-year, three-year and five-year survival estimates, nationally and regionally by diagnosis period, are shown in *Table 3.3.2*, and five-year estimates, by treatment status, in *Table 3.3.3*.

Results and comparisons presented in this section are not adjusted for potential confounding variables, thus are potentially open to misinterpretation if taken at face value. More formal (multivariate) comparisons are made in *section 3.4*.

3.3.1 General summary

For breast cancer cases diagnosed in Irish women during 1994-2001 as a whole, relative survival to five years after diagnosis was estimated as 75.4% (95% CI 74.4-76.3%) (*Table 3.3.1*). Relative survival to one year averaged 93.1% (92.6-93.6%), and to three years 82.5% (81.7-83.2%) (*Table 3.3.2*).

3.3.2 Variation by patient and tumour characteristics

In general, relative survival (to five years) was highest for cases among young or middle-aged women, or, for other specific variables, cases of early or unknown stage; T category 1; node-negative; grade 1; carcinomas or other specific morphologies; microscopically verified; or screen-detected (*Table 3.3.1*, *Figure 3.3.1*). Survival was lowest among women in the oldest age-group (75+), and, for other variables, cases that were stage IV; T category 4; node-positive or nodal status unknown; metastatic; grade 3+ or unknown; of unspecified morphology; lacking microscopic verification (or with MV status unknown); or incidentally detected. Smoking status and marital status also appeared to be associated with survival, which was highest for patients who were ever married or who were non-smokers or ex-smokers. Note however that patients in a given univariate category may differ with respect to other characteristics - see section *3.4.1* for multivariate comparisons.

3.3.3 Variation by treatment status

Patients who received any tumour-directed treatment, or surgery, within six months of diagnosis had substantially higher five-year survival than patients who did not receive these treatments: averaging 77% v 41% for treatment v no treatment, and 81% v 42% for surgery v no surgery for 1994-2001 as a whole (*Table 3.3.3*). A smaller difference was seen for patients who had or did not have radiotherapy (78% v 73%), with apparently the opposite effect for chemotherapy (75% v 78%) and little or no difference for hormonal therapy (both 77%). However, patients given or not given particular treatments may have differed greatly in disease stage or other characteristics (prognostic, treatment-predictive or otherwise). Thus these figures do not provide any measure of treatment effectiveness.

3.3.4 National and regional trends

National estimates of five-year survival were 72.9% (95% CI 71.6-74.2%) for cases diagnosed during 1994-97 and 78.2% (76.8-79.6%) for 1998-2001 (*Table 3.3.1, Figure 3.3.1*) – a clear improvement in survival. At regional scale, significant improvements in survival were evident for at least two regions: from 76.1% (73.9-78.1%) to 81.4% (79.1-83.5%) for patients from the Eastern region, and from 70.8% (67.6-74.0%) to 79.3% (75.6-82.6%) for the Southern region (*Table 3.3.2*). See sections *3.4.2-3* for more formal comparisons, adjusted for age or other factors.

3.3.5 Regional variation

Five-year relative survival estimates during 1994-2001 ranged from 72.3% (95% CI 68.5-75.7%) for patients from the North-Eastern region to 78.6% (74.4-76.3%) for the Eastern region (*Table 3.3.2*). See *section 3.4.4* for more formal comparisons.

Table 3.3.1 National five-year relative survival for female breast cancer patients, by patient and tumour characteristics, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population.

	1994-2001		1994-1997		1998-2001	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	75.4%	(74.4%-76.3%)	72.9%	(71.6%-74.2%)	*78.2%	(76.8%-79.6%)
age 15-44	78.2%	(76.1%-80.1%)	75.3%	(72.3%-77.9%)	*82.5%	(79.4%-85.1%)
age 45-54	81.2%	(79.6%-82.6%)	78.4%	(76.2%-80.5%)	*84.9%	(82.6%-86.8%)
age 55-64	75.7%	(73.8%-77.4%)	72.9%	(70.3%-75.3%)	77.7%	(74.7%-80.3%)
age 65-74	72.1%	(69.8%-74.2%)	70.0%	(66.8%-73.0%)	74.3%	(70.7%-77.6%)
age 75+	68.5%	(65.0%-71.9%)	67.1%	(62.4%-71.7%)	70.3%	(64.9%-75.5%)
stage I	95.4%	(93.3%-97.2%)	93.5%	(90.4%-96.0%)	97.5%	(94.2%-99.8%)
stage II	82.6%	(80.8%-84.1%)	80.1%	(77.7%-82.3%)	*85.6%	(83.0%-87.9%)
stage III	63.3%	(59.2%-67.2%)	60.2%	(54.7%-65.4%)	66.6%	(60.2%-72.3%)
stage IV	20.0%	(17.1%-23.0%)	17.2%	(13.7%-21.1%)	24.0%	(19.4%-28.8%)
stage X[a]	76.7%	(75.2%-78.0%)	74.5%	(72.5%-76.4%)	*79.0%	(76.9%-81.0%)
T1	90.4%	(89.0%-91.7%)	87.3%	(85.2%-89.2%)	*94.1%	(92.1%-95.8%)
T2	77.9%	(76.4%-79.3%)	76.3%	(74.2%-78.2%)	79.6%	(77.4%-81.7%)
T3	61.1%	(57.9%-64.2%)	59.9%	(55.6%-63.9%)	62.6%	(57.2%-67.5%)
T4	36.9%	(33.4%-40.3%)	35.2%	(30.7%-39.6%)	39.2%	(33.5%-45.0%)
T X	62.1%	(58.2%-65.7%)	64.1%	(59.1%-68.8%)	58.7%	(52.3%-64.8%)
N negative	88.8%	(87.5%-89.9%)	86.9%	(85.1%-88.5%)	*91.1%	(89.2%-92.7%)
N positive	65.8%	(64.2%-67.3%)	62.3%	(60.1%-64.3%)	*69.7%	(67.3%-71.9%)
N X	63.6%	(60.7%-66.3%)	64.4%	(60.7%-68.0%)	62.1%	(57.5%-66.5%)
M negative	82.8%	(81.5%-83.9%)	80.6%	(78.7%-82.2%)	*85.2%	(83.2%-86.9%)
M positive[b]	20.1%	(17.2%-23.1%)	17.4%	(13.8%-21.3%)	24.0%	(19.4%-28.8%)
M X	76.5%	(75.0%-77.9%)	74.1%	(72.0%-76.0%)	*79.4%	(77.2%-81.5%)
grade 1	92.8%	(89.9%-95.2%)	90.5%	(86.1%-94.2%)	94.4%	(90.1%-97.7%)
grade 2	83.4%	(81.5%-85.1%)	80.5%	(77.6%-83.0%)	*86.1%	(83.4%-88.5%)
grade 3+	69.4%	(67.6%-71.1%)	66.8%	(64.3%-69.1%)	*72.1%	(69.4%-74.6%)
grade X	71.3%	(69.6%-72.8%)	70.8%	(68.7%-72.8%)	72.4%	(69.8%-74.9%)
ductal/lobular	78.3%	(77.2%-79.3%)	75.8%	(74.3%-77.1%)	*81.1%	(79.5%-82.5%)
other adenocarc	76.7%	(73.0%-80.1%)	76.2%	(71.1%-80.8%)	76.8%	(71.0%-81.9%)
other carcinoma	85.8%	(77.4%-92.0%)	88.8%	(75.1%-97.3%)	83.4%	(71.7%-91.5%)
carcinoma NOS	63.5%	(59.4%-67.4%)	65.2%	(59.8%-70.1%)	62.5%	(55.7%-68.9%)
cancer NOS	26.0%	(21.0%-31.2%)	27.1%	(20.9%-33.7%)	25.1%	(17.2%-34.3%)
other cancer	80.0%	(65.3%-90.2%)	95.8%	(73.2%-104%)	68.1%	(46.6%-83.6%)
MV yes	77.2%	(76.2%-78.1%)	75.1%	(73.7%-76.4%)	*79.6%	(78.1%-80.9%)
MV no	19.6%	(14.6%-25.4%)	21.6%	(15.3%-28.8%)	16.9%	(8.5%-28.4%)
MV X	31.6%	(18.5%-46.3%)	30.8%	(13.6%-52.0%)	33.6%	(15.9%-53.6%)
symptomatic	74.8%	(73.8%-75.8%)	73.1%	(71.7%-74.4%)	*77.0%	(75.4%-78.5%)
incidental	55.9%	(48.4%-63.0%)	48.4%	(38.7%-57.8%)	66.3%	(55.1%-76.3%)
screen detected	92.3%	(87.7%-95.7%)	90.1%	(82.1%-95.3%)	94.2%	(86.5%-98.6%)
presentation X	81.9%	(77.9%-85.4%)	74.6%	(66.2%-81.9%)	84.6%	(80.0%-88.5%)
non-smoker	76.7%	(75.3%-78.0%)	74.1%	(72.1%-75.9%)	*79.8%	(77.6%-81.8%)
ex-smoker	77.0%	(73.4%-80.2%)	73.7%	(68.4%-78.4%)	80.4%	(75.4%-84.8%)
smoker	73.7%	(71.6%-75.6%)	70.9%	(68.0%-73.5%)	*76.8%	(73.6%-79.6%)
smoking X	73.8%	(71.7%-75.7%)	72.2%	(69.2%-75.0%)	75.6%	(72.6%-78.4%)
ever married	76.5%	(75.4%-77.5%)	74.1%	(72.6%-75.4%)	*79.2%	(77.6%-80.7%)
never married	70.8%	(68.1%-73.3%)	68.2%	(64.5%-71.6%)	73.9%	(69.9%-77.6%)
marital status X	70.8%	(65.2%-75.8%)	68.6%	(61.3%-75.2%)	73.7%	(64.8%-81.4%)

[a]Unknown values shown as "X" for stage, T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status. [b]Minor discrepancies between stage IV and M positive cases are because some M positive cases were of morphologies for which TNM staging is not strictly applicable for this site. *Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

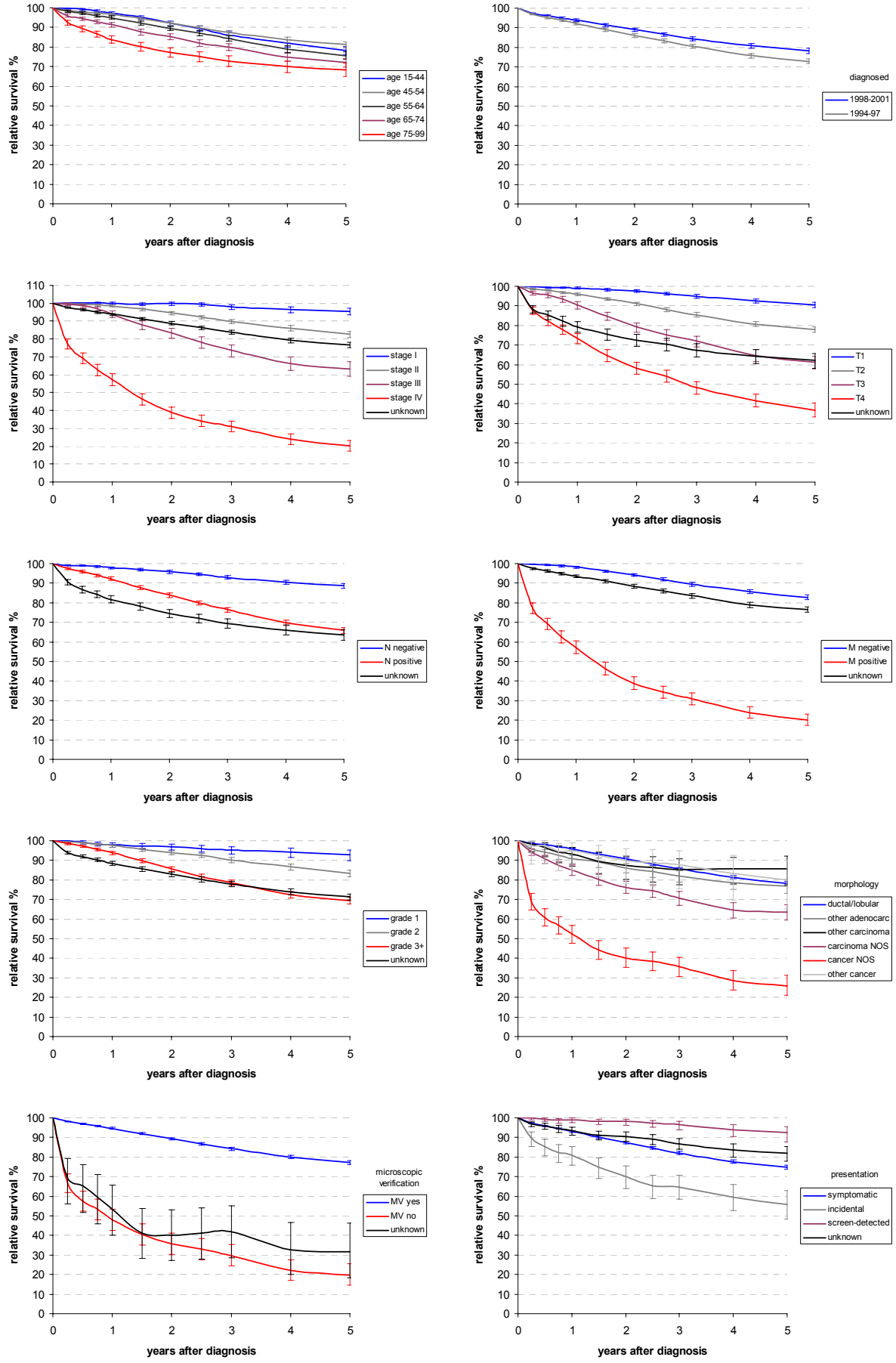


Figure 3.3.1 Relative survival up to five years after diagnosis for female breast cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown.

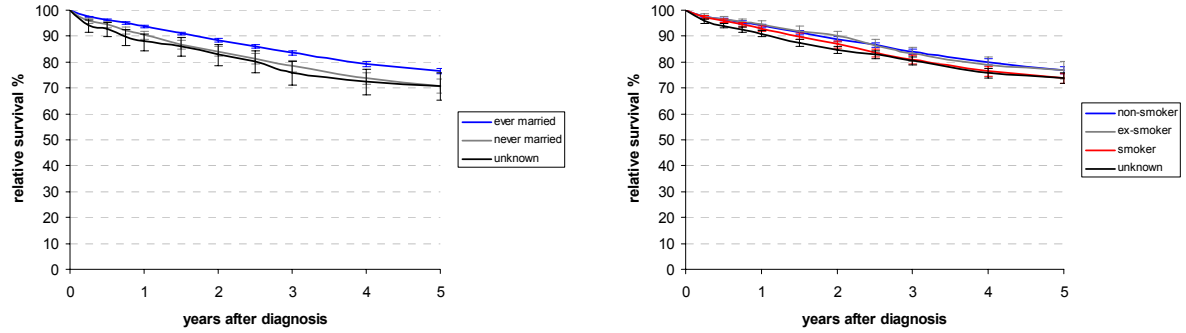


Figure 3.3.1 (continued)

Table 3.3.2 One-year, three-year and five-year relative survival for female breast cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001.

Region	1994-2001		1994-1997		1998-2001	
	1-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	93.1%	(92.6%-93.6%)	92.2%	(91.4%-92.9%)	*93.9%	(93.2%-94.5%)
E	94.0%	(93.2%-94.7%)	93.1%	(91.8%-94.1%)	94.9%	(93.8%-95.7%)
M	92.9%	(90.6%-94.7%)	93.4%	(89.9%-95.9%)	92.5%	(89.3%-94.9%)
MW	92.1%	(90.0%-93.7%)	91.2%	(88.2%-93.6%)	92.9%	(90.0%-95.0%)
NE	94.3%	(92.3%-95.7%)	91.8%	(88.5%-94.3%)	96.3%	(93.9%-97.9%)
NW	91.8%	(89.3%-93.7%)	90.1%	(86.2%-93.0%)	93.4%	(90.1%-95.8%)
S	92.3%	(90.9%-93.5%)	90.9%	(88.6%-92.7%)	93.6%	(91.7%-95.1%)
SE	92.4%	(90.6%-93.8%)	92.5%	(89.8%-94.6%)	92.3%	(89.8%-94.3%)
W	92.9%	(91.1%-94.3%)	92.8%	(90.1%-94.8%)	93.0%	(90.4%-94.9%)
	1994-2001		**1994-1997**		**1998-2001**	
	3-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	82.5%	(81.7%-83.2%)	80.6%	(79.4%-81.7%)	*84.3%	(83.2%-85.3%)
E	85.1%	(83.9%-86.2%)	83.0%	(81.1%-84.7%)	*87.0%	(85.4%-88.5%)
M	82.7%	(79.3%-85.6%)	82.9%	(77.9%-87.0%)	82.5%	(77.7%-86.5%)
MW	81.4%	(78.5%-84.0%)	80.8%	(76.6%-84.4%)	82.2%	(78.1%-85.6%)
NE	80.5%	(77.4%-83.2%)	76.3%	(71.5%-80.4%)	84.0%	(79.9%-87.4%)
NW	81.0%	(77.5%-84.1%)	78.7%	(73.5%-83.2%)	83.0%	(78.0%-87.1%)
S	81.3%	(79.2%-83.2%)	78.8%	(75.6%-81.5%)	83.7%	(80.9%-86.1%)
SE	80.8%	(78.2%-83.1%)	79.0%	(75.1%-82.5%)	82.4%	(78.8%-85.5%)
W	80.4%	(77.7%-82.8%)	79.3%	(75.3%-82.7%)	81.8%	(78.0%-85.0%)
	1994-2001		**1994-1997**		**1998-2001**	
	5-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	75.4%	(74.4%-76.3%)	72.9%	(71.6%-74.2%)	*78.2%	(76.8%-79.6%)
E	78.6%	(77.1%-80.0%)	76.1%	(73.9%-78.1%)	*81.4%	(79.1%-83.5%)
M	74.1%	(69.9%-77.9%)	73.2%	(67.5%-78.3%)	76.3%	(69.8%-81.8%)
MW	73.0%	(69.4%-76.2%)	71.6%	(66.8%-76.0%)	75.1%	(69.5%-80.0%)
NE	72.3%	(68.5%-75.7%)	68.6%	(63.3%-73.4%)	75.6%	(69.9%-80.7%)
NW	74.1%	(69.8%-78.0%)	71.9%	(66.0%-77.1%)	76.3%	(69.6%-82.1%)
S	74.7%	(72.2%-77.0%)	70.8%	(67.3%-74.0%)	*79.3%	(75.6%-82.6%)
SE	73.5%	(70.3%-76.4%)	72.0%	(67.6%-76.0%)	74.0%	(68.9%-78.5%)
W	74.1%	(70.8%-77.0%)	71.4%	(67.0%-75.5%)	78.8%	(74.1%-82.8%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

Table 3.3.3 National five-year relative survival for female breast cancer patients, by treatment status (within six months of diagnosis) and period of diagnosis, 1994-2001. Patients treated and not treated are likely to differ markedly in disease stage, age or other characteristics, thus *differences in survival between treated and untreated patients below should not be interpreted as reflecting the effect of treatment*. For chemotherapy and hormone therapy, survival is only presented for 1996-2001 as these treatments were not fully recorded separately during 1994-95.

	1994-2001		**1994-1997**		**1998-2001**	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	75.4%	(74.4%-76.3%)	72.9%	(71.6%-74.2%)	*78.2%	(76.8%-79.6%)
treatment	77.0%	(76.0%-77.9%)	74.5%	(73.1%-75.7%)	*79.9%	(78.4%-81.2%)
no treatment	40.6%	(35.5%-45.8%)	41.1%	(34.1%-48.1%)	38.2%	(29.9%-46.7%)
surgery	81.5%	(80.5%-82.4%)	79.2%	(77.8%-80.4%)	*84.1%	(82.6%-85.4%)
no surgery	41.9%	(39.0%-44.7%)	41.1%	(37.4%-44.8%)	42.8%	(38.2%-47.4%)
radiotherapy	78.2%	(76.7%-79.4%)	73.8%	(71.8%-75.7%)	82.6%	(80.6%-84.4%)
no radiotherapy	73.4%	(72.0%-74.7%)	72.4%	(70.5%-74.1%)	74.7%	(72.6%-76.7%)
	1996-2001		**1996-1997**		**1998-2001**	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
chemotherapy	74.9%	(73.2%-76.4%)	71.0%	(68.0%-73.6%)	*76.7%	(74.6%-78.5%)
no chemotherapy	78.3%	(76.8%-79.7%)	76.1%	(73.7%-78.4%)	79.7%	(77.6%-81.6%)
hormone therapy	77.4%	(75.6%-78.9%)	74.6%	(72.0%-77.0%)	79.2%	(76.8%-81.3%)
no hormone	76.5%	(75.0%-77.9%)	73.7%	(71.0%-76.2%)	77.7%	(75.8%-79.4%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

3.4 Relative survival: modelling

3.4.1 Variation by patient and tumour characteristics

For assessment of regional variation in relative survival during 1994-2001, a full relative survival model was run, potentially incorporating and adjusting for available patient and tumour characteristics. These included year of follow-up (years 1 to 5 after diagnosis), age-group, stage-related variables (T, N and M categories), grade, interaction between those variables and year of follow-up, and additional patient and tumour variables without interaction terms (celltype, microscopic verification status, method of presentation, marital status, smoking status, year of diagnosis). Excluding region and year (covered later), and variables that did not contribute significantly to model-fit, statistically significant excess hazard ratios (EHRs) were recorded as follows:

- During year 1 of follow-up (for variables assessed using an interaction term for follow-up year):
  - Higher EHR (lower relative survival) for age-groups 55-64 years (1.437 [95% CI 1.050-1.965]), 65-74 (2.164 [1.597-2.931]) and 75+ (2.821 [2.082-3.821]), compared with age-group 15-44 years.
  - Higher EHR for T categories 2 (2.470 [1.719-3.550]), 3 (3.898 [2.638-5.760], 4 (5.2184 [3.608-7.548]) and unknown or non-applicable (4.523 [3.096-6.609]), compared with T category 1.
  - Higher EHR for N positive (1.751 [1.376-2.229]) and N unknown cases (2.259 [1.746-2.921]), compared with N negative cases.
  - Higher EHR for M positive (10.61 [8.155-13.81]) and M unknown cases (2.113 [1.630-2.739], compared with M negative cases.
  - Higher EHR for grade 3+ (1.734 [1.059-2.841] and grade unknown cases (1.699 [1.045-2.764]), compared with grade 1.
- For age, stage-related and grade variables, EHRs varied significantly during subsequent follow-up and cannot readily be summarized beyond year 1.
- Overall (for variables assessed without an interaction term for follow-up year):
  - Higher EHR (lower relative survival), averaged across follow-up years, for non-specific carcinomas (1.237 [95% CI 1.070-1.430]) and non-specific cancers (2.471 [2.109-2.894]), compared with ductal and lobular adenocarcinomas.
  - Higher EHR for cases presenting incidentally (1.345 [1.080-1.675]), and lower EHR (higher relative survival) for screen-detected cases (0.473 [0.302-0.741]) and cases with unknown method of presentation (0.719 [0.587-0.879]), compared with cases presenting symptomatically.
  - Higher EHR for current smokers (1.245 [1.121-1.382]) and patients of unknown smoking status (1.206 [1.086-1.339]), compared with non-smokers (never-smokers).
- Microscopic verification (MV) status, marital status and year of diagnosis did not significantly improve model fit, after adjustment for other variables, and were excluded from the full model.

In general these findings confirmed the variations noted earlier for unadjusted relative survival (*section 3.3.2*), for the overall period 1994-2001. Note, however, that unadjusted relative survival figures were significantly low for a number of categories – including grade 2, no MV, unknown MV status, never married – that did not show significant variation in the fully-adjusted model.

3.4.2 National and age-specific trends

Relative survival improved significantly (i.e. excess hazard ratios fell significantly) for Ireland as a whole between diagnosis periods 1994-97 and 1998-2001 (*Table 3.4.1*). The improvement represented a 24% reduction in age-adjusted excess risk of death, or a 9% reduction in excess risk after adjustment for other tumour and patient variables (including stage). Significant improvements in relative survival, equivalent to 19-30% reductions in excess risk of death, were also seen for individual age-groups 15-44 to 65-74, but not for age-group 75+ (unadjusted models, *Table 3.4.1*).

3.4.3 Regional trends

Relative survival improved significantly for the Eastern, North-Eastern and Southern regions between diagnosis periods 1994-97 and 1998-2001 (*Table 3.4.1*). These changes amounted to a 26-30% reduction in age-adjusted excess risk of death. Other regions showed no significant changes in relative survival, although similar reductions were apparent for the North-Western region in particular, with weaker or less consistent indications of improvements in the remaining regions.

3.4.4 Regional variation

This was very marked for the period 1994-2001 as a whole, with significantly higher (by 20-28%) excess risk of death (lower relative survival) in regions other than the Eastern region, based on age-adjusted comparisons (*Figure 3.4.1*, *Table 3.4.2*). This variation appeared to be more marked during 1998-2001 than during 1994-97. Adjustment for stage-related variables appeared to reduce these

differences somewhat for most regions, although the opposite effect was seen for others.

In the fully adjusted model, taking account of a wider range of patient and tumour characteristics, four regions had a significantly high excess risk of death during 1994-2001: Midland (28% higher than Eastern), Southern (16% higher), South-Eastern (22% higher) and Western (26% higher) (*Figure 3.4.1*, *Table 3.4.2*). Again, regional variations in relative survival were not fully consistent between the two diagnosis periods, although for the fully adjusted results there was no overall tendency towards less or more variation. Only the Western region showed a significant excess risk in both 1994-97 (+24%) and 1998-2001 (+33%). Other regions with significantly high excess risks (lower survival) in the full model for 1998-2001 were Midland (+38%) and South-Eastern (+41%) (*Table 3.4.2*).

While these analyses may imply, to some extent, that variation in patient and tumour characteristics 'explain' some of the regional variation seen – e.g. if cases are detected at an earlier average stage in some regions – cautious interpretation is needed.

Table 3.4.1 Changes in relative survival between diagnosis-years 1994-97 and 1998-2001, stratified by age and region of residence, for female patients diagnosed with breast cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from baseline (1994-1997). (EHR <1 = reduction in excess hazard thus improvement in relative survival, EHR >1 = increase in excess hazard thus reduction in relative survival). Only the basic model is shown for individual regions as regional sample sizes are generally too small too allow complex modelling.

	1998-2001 v 1994-97	
	[a]**EHR (95% CI)**	**P**
basic model: age-specific		
age 15-44	**0.712** (0.576-0.879)	0.002
age 45-54	**0.704** (0.589-0.842)	0.000
age 55-64	**0.743** (0.629-0.878)	0.001
age 65-74	**0.808** (0.673-0.970)	0.022
age 75+	0.891 (0.724-1.096)	0.277
basic model: age-adjusted[b]		
total	**0.764** (0.703-0.831)	0.000
E	**0.722** (0.623-0.836)	0.000
M	0.994 (0.710-1.391)	0.974
MW	0.853 (0.645-1.128)	0.267
NE	**0.738** (0.551-0.989)	0.042
NW	0.747 (0.532-1.050)	0.094
S	**0.700** (0.568-0.862)	0.001
SE	0.825 (0.641-1.061)	0.135
W	0.811 (0.625-1.051)	0.114
fuller model: age-, stage-adjusted[b]		
total	**0.832** (0.766-0.903)	0.000
final multivariate model[b]		
total	**0.906** (0.834-0.985)	0.021

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]See *Table 3.4.2* but region and diagnosis year excluded here.

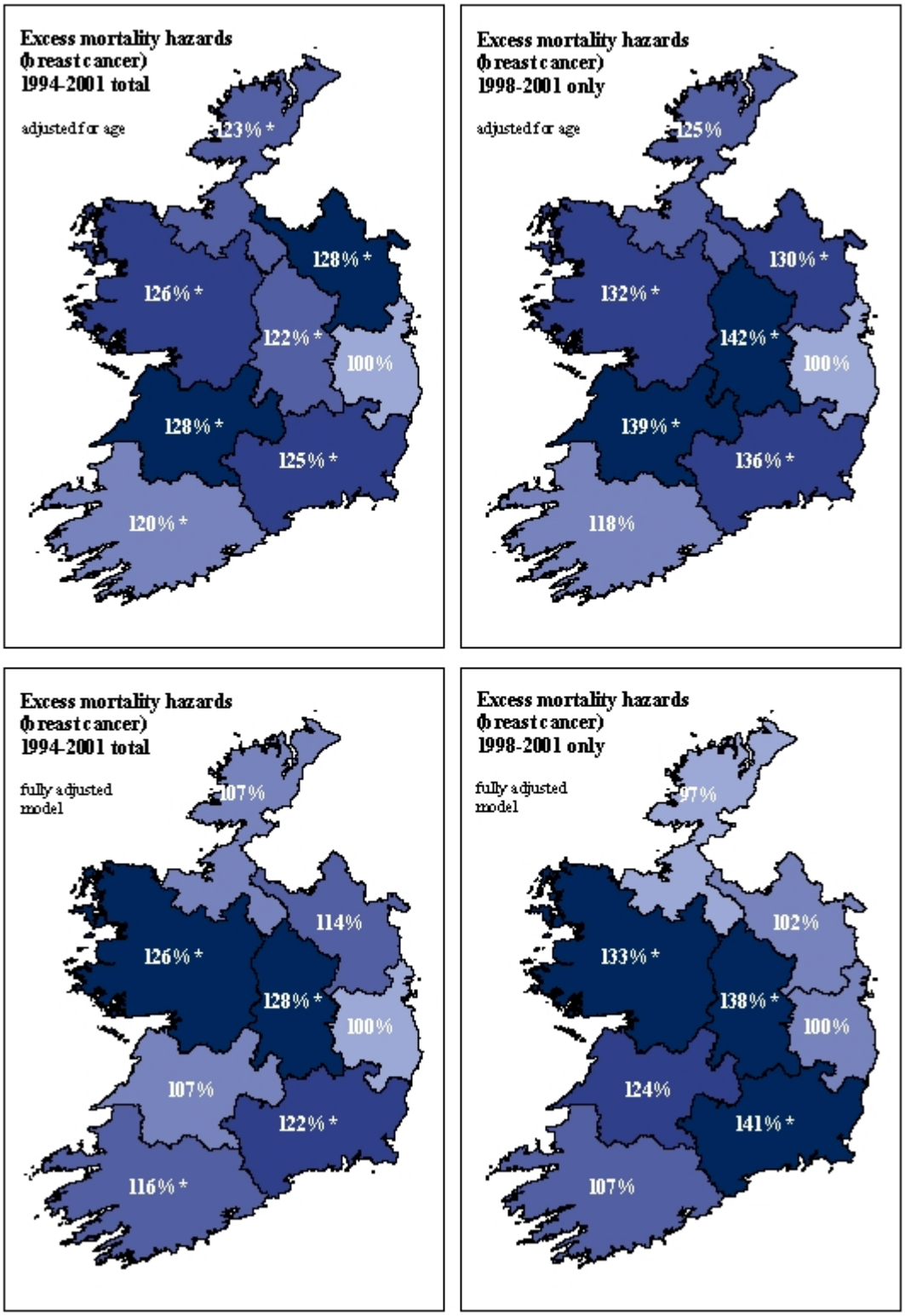


Figure 3.4.1 Regional variation in excess mortality hazards (based on relative survival) for breast cancer, expressed in comparison with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 6.4.2* for further details. * = significantly high or low excess risk (P<0.05).

Table 3.4.2 Variation in relative survival, by region of residence, for female patients diagnosed with breast cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (EHR <1 = lower excess hazard thus higher relative survival than in Eastern region, EHR >1 = higher excess hazard thus lower relative survival).

	1994-2001		1994-1997		1998-2001	
	[a]EHR (95% CI)	P	EHR (95% CI)	P	EHR (95% CI)	P
basic model: age-adjusted[b,c]						
E	1.000		1.000		1.000	
M	**1.224** (1.022-1.466)	0.028	1.068 (0.830-1.375)	0.605	**1.421** (1.096-1.842)	0.008
MW	**1.281** (1.098-1.493)	0.002	1.182 (0.964-1.449)	0.106	**1.394** (1.102-1.762)	0.005
NE	**1.281** (1.092-1.502)	0.002	**1.277** (1.033-1.579)	0.023	**1.298** (1.018-1.654)	0.035
NW	**1.226** (1.025-1.467)	0.026	1.191 (0.941-1.507)	0.144	1.252 (0.949-1.652)	0.111
S	**1.203** (1.062-1.362)	0.003	**1.215** (1.034-1.429)	0.018	1.180 (0.972-1.433)	0.093
SE	**1.248** (1.081-1.440)	0.002	1.161 (0.957-1.408)	0.128	**1.360** (1.098-1.686)	0.005
W	**1.263** (1.091-1.461)	0.002	1.199 (0.990-1.452)	0.062	**1.323** (1.056-1.658)	0.015
fuller model: age-, stage-adjusted[b,c,d]						
E	1.000		1.000		1.000	
M	**1.212** (1.014-1.449)	0.035	1.040 (0.808-1.337)	0.760	**1.442** (1.116-1.861)	0.005
MW	**1.250** (1.072-1.456)	0.004	1.171 (0.956-1.435)	0.125	**1.338** (1.058-1.692)	0.015
NE	**1.224** (1.044-1.436)	0.013	**1.311** (1.060-1.622)	0.012	1.141 (0.897-1.452)	0.282
NW	1.131 (0.950-1.346)	0.166	1.176 (0.933-1.481)	0.169	1.087 (0.831-1.421)	0.541
S	**1.213** (1.073-1.370)	0.002	**1.236** (1.054-1.451)	0.009	1.174 (0.971-1.420)	0.097
SE	**1.360** (1.181-1.565)	0.000	**1.233** (1.017-1.494)	0.033	**1.573** (1.278-1.937)	0.000
W	**1.281** (1.112-1.477)	0.001	**1.206** (0.999-1.455)	0.050	**1.405** (1.127-1.751)	0.003
final multivariate model[b,e]						
E	1.000		1.000		1.000	
M	**1.277** (1.068-1.527)	0.007	1.171 (0.908-1.510)	0.221	**1.379** (1.068-1.780)	0.014
MW	1.069 (0.914-1.250)	0.399	0.986 (0.800-1.216)	0.900	1.240 (0.979-1.570)	0.074
NE	1.139 (0.971-1.336)	0.109	**1.240** (1.000-1.537)	0.049	1.015 (0.796-1.293)	0.903
NW	1.066 (0.894-1.271)	0.471	1.134 (0.897-1.434)	0.290	0.973 (0.742-1.277)	0.849
S	**1.162** (1.025-1.317)	0.019	**1.242** (1.052-1.466)	0.010	1.067 (0.878-1.297)	0.513
SE	**1.222** (1.061-1.407)	0.005	1.146 (0.944-1.392)	0.168	**1.407** (1.142-1.735)	0.001
W	**1.262** (1.093-1.457)	0.002	**1.239** (1.022-1.503)	0.029	**1.332** (1.067-1.662)	0.011

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]Models included interaction terms between follow-up interval (years 1-5) and age (plus stage/grade variables in fuller and final models), equivalent to stratification by these variables, to allow for non-proportional hazards across follow-up time.
[c]Age-categories: EUROCARE age-groups 15-44, 45-54, 55-64, 65-74, 75+.
[d]Stage-related variables: T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[e]Final (full) multivariate model, also including: grade 1, 2, 3+ or unknown (with grade/follow-up interaction); tumour morphology (six categories); method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown). [Microscopic verification status, marital status and year of diagnosis did not significantly improve model fit and were excluded from the full model.]

3.5 Treatment: descriptive analysis

3.5.1 General comment

Analyses here are restricted to *treatments administered within six months after diagnosis*. Variations noted in treatment between patient groups may thus, to some extent, reflect variations in timing of treatment. However, the majority of first-line treatments for this cancer should be included.

3.5.2 General summary of treatment

Treatments and treatment-combinations during 1996-2001 are summarized in *Table 3.5.1*. This excludes 1994-95 data, which did not distinguish between chemotherapy and hormonal therapy. Of the 13,383 cases included in overall analyses, 10,352 were diagnosed during 1996-2001. Of these, 96% had some form of definitive or tumour-directed treatment within six months of diagnosis, 85% had surgical treatment (excluding oophorectomy), 47% had hormonal therapy (including oophorectomy), 44% had radiotherapy and 42% had chemotherapy. Equivalent figures for the most recent period, 1998-2001, were 7167 cases, of which 96% were treated, 85% had surgery, 43% had hormonal therapy (a significant decrease compared with 1996-97), 44% had radiotherapy, and 45% had chemotherapy (a significant increase) (*Table 3.5.1*, *Figure 3.5.2*). A further breakdown by age is shown in *Table 3.5.1* and *Figure 3.5.1*.

The most frequent treatments or combinations were surgery plus hormonal therapy (15% of cases 1996-2001), surgery plus chemotherapy (also 15%), surgery plus hormonal therapy plus radiotherapy (13%), surgery plus chemotherapy plus radiotherapy (13%), and surgery only (10%). For the most recent period (1998-2001), equivalent figures were 13%, 18%, 13%, 14%, and 10%, representing a notable decrease since 1996-97 for surgery plus hormonal therapy and a notable increase for surgery plus chemotherapy (*Table 3.5.1*).

Table 3.5.1 Summary of main treatment modalities and combinations (within six months of diagnosis) for female breast cancer patients, by age and diagnosis period, 1996-2001. Only treatments or combinations making up at least 1% of cases in any period are listed. Data for 1994 & 1995 are excluded as chemotherapy was not coded separately from hormonal therapy for those years.

	1996-2001						1996-97	1998-2001	
	age 15-44	44-54	55-64	65-74	75+	total	subtotal	subtotal	
total cases	1529	2531	2523	1933	1836	10 352	3185	7167	
any treatment	98.0%	97.4%	97.9%	96.7%	87.9%	95.8%	95.4%	96.0%	
no treatment	2.0%	2.6%	2.1%	3.3%	12.1%	4.2%	4.6%	4.0%	
any surgery[a]	93.9%	92.4%	91.1%	85.7%	56.0%	84.6%	83.4%	85.1%	*
any hormonal therapy	26.0%	36.2%	46.9%	60.4%	66.6%	47.2%	56.1%	43.3%	*
any radiotherapy	48.7%	48.6%	50.9%	44.9%	21.5%	43.7%	42.6%	44.1%	
any chemotherapy[b]	74.0%	61.6%	45.4%	20.2%	4.8%	41.7%	33.9%	45.2%	*
surgery + hormone	4.0%	8.1%	13.7%	24.4%	26.7%	15.2%	21.3%	12.5%	*
surgery + chemo	27.7%	22.0%	15.7%	7.0%	1.5%	14.9%	8.8%	17.6%	*
surge + hormo + radio	4.1%	9.4%	17.3%	23.0%	10.8%	13.3%	14.7%	12.8%	*
surge + chemo + radio	26.4%	19.1%	12.6%	5.8%	0.7%	12.9%	10.9%	13.7%	*
surgery only	8.1%	9.2%	8.9%	11.1%	11.4%	9.7%	9.6%	9.8%	
surgery + radio	6.7%	7.6%	9.9%	9.6%	4.4%	7.8%	6.9%	8.3%	*
sur + che + hor + rad	9.7%	10.1%	8.0%	2.7%	0.4%	6.4%	6.3%	6.5%	
hormone only	0.2%	0.4%	1.1%	5.6%	24.9%	5.9%	6.2%	5.7%	
surge + chemo + horm	7.1%	7.0%	5.0%	1.9%	0.2%	4.3%	5.0%	4.0%	*
chemotherapy only	1.8%	1.6%	2.1%	1.0%	1.5%	1.6%	1.3%	1.8%	
hormone + radio	0.2%	0.2%	0.6%	1.7%	3.2%	1.1%	1.6%	0.9%	*
radiotherapy only	0.6%	0.9%	1.0%	1.0%	1.7%	1.0%	1.3%	0.9%	
others	1.4%	1.9%	2.0%	1.7%	0.6%	1.6%	1.7%	1.5%	

[a]Surgery and related treatments. [b]Chemotherapy and related treatments (excluding hormonal therapy).
*Significant difference between diagnosis periods in percentage having this treatment (χ^2 tests), unadjusted for age or other variables.

3.5.3 Region of surgical treatment v. region of residence

Based on surgical treatment within six months of diagnosis, the majority of breast cancer patients during 1994-2001 had their main surgical treatment within their region of residence (*Table 3.5.2*). The proportion was highest for the Eastern and Southern regions (98-99%), lowest for the Midland (60%) and North-Eastern region (66%). Patterns based on the most recent four years (1998-2001) were similar to the longer-term average, with the proportion again highest for the Eastern and Southern regions (99%), lowest for the Midland (56%) and North-Eastern region (63%) (*Table 3.5.2*).

Table 3.5.2 Breakdown of breast cancer surgery, 1994-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases (female). Only surgical procedures within 6 months of diagnosis are included.

		Region of residence																	
Region where		**1994-2001 total**									**1998-2001 subtotal**								
treated		**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**	**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Eastern	%	**99.3**	26.6	7.1	32.7	11.6	1.3	18.7	4.4	**45.6**	**99.2**	31.2	6.8	35.1	13.6	1.1	17.5	4.6	**46.6**
Midland	%	0.5	**60.1**	1.8	1.3	0.2	0.0	0.4	0.1	4.0	0.7	**55.8**	1.3	2.3	0.3	0.0	0.2	0.2	3.8
Mid-Western	%	0.0	0.2	**72.0**	0.0	0.0	0.2	1.4	0.0	6.0	0.0	0.3	**69.3**	0.0	0.0	0.2	0.8	0.0	5.5
North-Eastern	%	0.2	0.5	0.0	**65.9**	1.6	0.0	0.0	0.1	5.2	0.1	0.6	0.0	**62.7**	1.5	0.0	0.0	0.0	5.1
North-Western	%	0.0	0.0	0.0	0.1	**80.3**	0.0	0.0	0.7	4.6	0.0	0.0	0.0	0.0	**77.1**	0.0	0.0	0.9	4.3
Southern	%	0.0	0.2	6.0	0.0	0.0	**98.5**	4.6	0.0	16.0	0.0	0.0	6.2	0.0	0.0	**98.7**	4.3	0.0	15.9
South-Eastern	%	0.0	1.1	3.4	0.0	0.0	0.1	**74.9**	0.0	7.8	0.0	1.7	4.7	0.0	0.0	0.0	**77.3**	0.0	8.2
Western	%	0.0	11.4	9.8	0.0	4.4	0.0	0.0	**94.7**	10.7	0.0	10.5	11.7	0.0	4.5	0.0	0.0	**94.3**	10.5
Northern Ireland	%	0.0	0.0	0.0	0.0	2.0	0.0	0.0	0.1	0.1	0.0	0.0	0.0	0.0	3.0	0.0	0.0	0.0	0.2

3.5.4 Hospital caseloads (surgical cases)

Female breast cancer cases were surgically treated (within six months of diagnosis) in a total of 60 hospitals in the Republic of Ireland during 1994-2001. There was no strong evidence of any trend in numbers of hospitals providing surgical treatment, although fewer hospitals were involved for cases diagnosed in 2000 (51) and 2001 (50) compared with earlier years (*Table 3.5.3*).

About one-third (12-19 annually) of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each, accounting for between 3.3%-7.4% of annual totals. Over half (25-34) the hospitals treated fewer than 20 surgical cases each in a given year (11%-26% of annual totals), and about three-quarters (37-47) treated fewer than 50 cases (31%-68% of annual totals).

There was a general tendency for average hospital caseload to increase during the period 1994-2001, with significant declines in the proportions of surgical cases treated in 'low volume' hospitals. This is broadly supported by surgical caseloads averaged over four-year periods, with an increase from 23 annual cases per hospital during 1994-97 to 28 cases per hospital during 1998-2001. Most notably, the proportion of surgical cases treated in hospitals treating 50+ cases per year rose from 36% during 1994-97 to 58% during 1998-2001.

3.5.5 Consultant caseloads (surgical cases)

At least 221 individual consultants were coded as responsible for surgical managements of female breast cancers during 1994-2001. Annual data gave only a slight indication of an increase in numbers of 'surgical consultants' involved over this period, but this was more obvious from comparisons of the numbers of consultants recorded during 1998-2001 (181) compared with 1994-97 (147) (*Table 3.5.4*).

About two-thirds of surgical consultants in any given year treated fewer than 10 surgical cases each, accounting for 14%-26% of annual totals. More than three-quarters of the consultants treated fewer than 20 surgical cases each in a given year (26%-51% of annual totals), and almost all treated fewer than 50 cases (54%-85% of annual totals).

Average annual caseloads increased over time, and significant declines were seen in the proportions of surgical patients treated by 'low volume' consultants. A very marked increase was seen in the proportion treated by consultants with annual caseloads of 50 or more surgical cases, from 15% of surgical patients in 1994 to 46% in 2001 (*Table 3.5.4*). These trends could be exaggerated somewhat, however, if recording of multiple surgical treatments has been more complete in recent years.

Table 3.5.3 Summary of surgical caseloads by year of diagnosis and hospital, based on female breast cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* hospital where surgical treatment received, excluding unidentified hospitals and those outside the Republic of Ireland.

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
hospitals (1+ case)	54	52	53	55	55	54	51	50		58	57	
case average	23	24	25	25	27	29	31	35		23	28	
<10 cases/year[a]	17	15	12	19	19	16	18	15		22	21	
% of cases	*6.5*	*7.4*	*4.9*	*6.5*	*6.5*	*5.3*	*5.6*	*3.3*	***	*8.4*	*5.5*	***
<20 cases/year	34	31	28	30	29	30	28	25		36	35	
% of cases	*26.0*	*24.5*	*21.1*	*17.5*	*16.2*	*18.8*	*15.3*	*11.1*	***	*23.8*	*19.4*	***
<50 cases/year	47	47	46	45	47	43	40	37		52	46	
% of cases	*58.2*	*68.3*	*61.8*	*47.3*	*55.2*	*45.6*	*39.5*	*31.5*	***	*63.6*	*42.3*	***
50+ cases/year	7	5	7	10	8	11	11	13		6	11	
% of cases	*41.8*	*31.7*	*38.2*	*52.7*	*44.8*	*54.4*	*60.5*	*68.5*	***	*36.4*	*57.7*	***

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated in hospitals of a given caseload.

Table 3.5.4 Summary of surgical caseloads by year of diagnosis and surgical consultant, based on female breast cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* surgical consultant involved, excluding unknown consultants and those based outside the Republic of Ireland

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
consultants (1+ case)	115	114	115	112	118	116	115	118		147	181	
case average	11	11	12	12	13	13	14	15		9	9	
<10 cases/year[a]	75	69	70	69	73	71	75	78		106	138	
% of cases	*25.9*	*21.6*	*23.0*	*20.8*	*18.2*	*16.1*	*14.2*	*13.6*	***	*26.7*	*18.5*	***
<20 cases/year	97	97	97	93	98	90	88	93		130	159	
% of cases	*49.6*	*51.2*	*50.3*	*44.3*	*40.4*	*33.0*	*25.6*	*25.7*	***	*51.2*	*36.7*	***
<50 cases/year	112	111	112	108	114	111	107	108		144	174	
% of cases	*85.2*	*83.4*	*82.6*	*76.9*	*75.7*	*74.0*	*59.9*	*54.2*	***	*83.3*	*67.4*	***
50+ cases/year	3	3	3	4	4	5	8	10		3	7	
% of cases	*14.8*	*16.6*	*17.4*	*23.1*	*24.3*	*26.0*	*40.1*	*45.8*	***	*16.7*	*32.6*	***

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated by surgical consultants of a given caseload.

3.5.6 Variation by patient and tumour characteristics

More detailed comparisons are made under the section covering logistic regression analysis (*section 3.6.1*). Basic tabulations of treatment for each category of patient or tumour are shown in *Table 3.5.5* for diagnosis period 1998-2001. It is noteworthy that cases lacking information on a given characteristic tend to be less likely to receive a given treatment. It should also be noted that these tabulations are based on unadjusted data – i.e. patients or tumours compared under a given variable may also differ in other characteristics, some of which may be more important determinants of treatment.

See also *Table 3.5.1* and *Figure 3.5.1* for further summaries of treatments in relation to age.

Table 3.5.5 Summary of treatment of breast cancer cases, 1998-2001, by patient and tumour characteristics: unadjusted percentages receiving treatment within six months of diagnosis. See *Table 3.2.2* for sample sizes.

	Overall treatment	Surgery	Radiotherapy	Chemotherapy	Hormone
total cases	96.0%	85.1%	44.1%	45.2%	43.3%
age 15-44[a]	98.3%	94.3%	46.3%	76.4%	23.9%
age 45-54	97.7%	93.6%	49.7%	64.6%	32.8%
age 55-64	97.9%	91.1%	50.6%	50.9%	40.8%
age 65-74	96.8%	86.6%	47.4%	24.9%	55.0%
age 75+	88.0%	55.7%	22.0%	5.3%	65.1%
stage I	99.6%	97.3%	56.0%	28.9%	53.2%
stage II	99.8%	97.5%	45.1%	62.5%	38.0%
stage III	99.1%	86.1%	40.3%	67.6%	33.6%
stage IV	86.5%	39.4%	31.2%	45.9%	43.1%
stage X	94.0%	82.0%	43.2%	36.5%	45.1%
T1	98.5%	94.3%	52.0%	36.4%	46.3%
T2	98.6%	93.5%	44.8%	54.0%	42.8%
T3	97.5%	85.3%	42.0%	60.5%	36.2%
T4	91.3%	46.4%	33.1%	43.2%	49.3%
T X	70.5%	36.2%	17.8%	17.6%	31.8%
N negative	98.7%	92.8%	49.1%	33.4%	49.0%
N positive	98.3%	89.8%	44.7%	66.3%	37.9%
N X	80.2%	46.2%	26.5%	20.3%	41.0%
M negative	99.3%	94.5%	45.8%	52.8%	41.4%
M positive	86.4%	39.1%	31.2%	45.7%	43.1%
M X	93.9%	82.4%	44.5%	36.9%	45.3%
grade 1	98.7%	93.1%	54.9%	29.1%	49.4%
grade 2	98.4%	92.5%	48.3%	44.5%	45.5%
grade 3+	97.8%	91.4%	46.5%	61.2%	36.5%
grade X	91.1%	70.1%	35.0%	34.9%	46.0%
ductal/lobular	97.9%	90.2%	46.2%	48.5%	42.9%
other adenocarcinoma	94.9%	77.8%	44.4%	28.1%	52.7%
other carcinoma	98.9%	92.0%	57.5%	43.7%	37.9%
carcinoma NOS	89.4%	56.4%	27.9%	37.5%	41.0%
cancer NOS	52.5%	5.0%	10.4%	8.9%	42.1%
other cancer	94.7%	89.5%	23.7%	15.8%	18.4%
MV yes	97.2%	87.2%	45.0%	46.1%	43.4%
MV no	51.1%	0.7%	5.8%	5.0%	46.8%
MV X	27.3%	6.1%	15.2%	3.0%	9.1%
symptomatic	96.6%	85.1%	43.3%	46.6%	46.2%
incidental	88.6%	59.6%	29.5%	31.3%	58.4%
screen detected	97.9%	95.6%	58.7%	36.7%	40.4%
presentation X	90.3%	85.1%	45.7%	41.1%	13.7%
non-smoker	97.7%	88.1%	44.1%	45.6%	49.0%
ex-smoker	96.8%	86.3%	43.6%	47.1%	42.8%
smoker	97.7%	89.0%	46.4%	52.4%	45.0%
smoking status X	90.9%	75.7%	42.6%	37.7%	30.9%
ever married	96.9%	86.8%	45.4%	46.8%	43.3%
never married	94.8%	81.3%	40.1%	39.4%	45.8%
marital status X	76.8%	60.1%	29.8%	28.9%	29.8%

[a]See *Table 3.5.1* for a further breakdown by age, for the period 1996-2001.

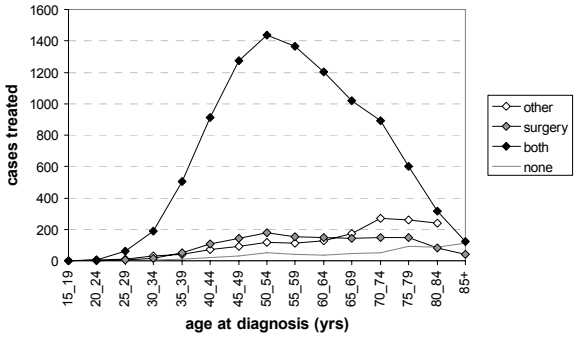


Figure 3.5.1 Age-profiles for tumour-directed treatments within six months of diagnosis for female breast cancer cases diagnosed 1994-2001: numbers of cases having surgery (only), other treatments (radiotherapy, chemotherapy or hormone therapy but not surgery), both surgery and other treatments, or no treatment.

3.5.7 National trends

See *section 3.5.2*.

3.5.8 Regional variation

Regional variations in treatment, unadjusted for patients or tumour characteristics, are summarized for the period 1998-2001 in *Figure 3.5.2*. Overall treatment and use of surgery varied comparatively little between regions. More substantial variation was apparent for radiotherapy (range 27-58% of regional cases, lowest in North-Western, highest in Southern region), hormone therapy (range 31-69%, lowest in North-Eastern, highest in Southern region) and, to a lesser extent, chemotherapy (range 36-51%, lowest in Mid-Western, highest in North-Eastern and South-Eastern regions). The degree of variation was broadly similar during earlier years (not presented). More rigorous comparisons of treatments between regions, taking account of age and where possible other patient and tumour characteristics, are presented in *section 3.6.3*.

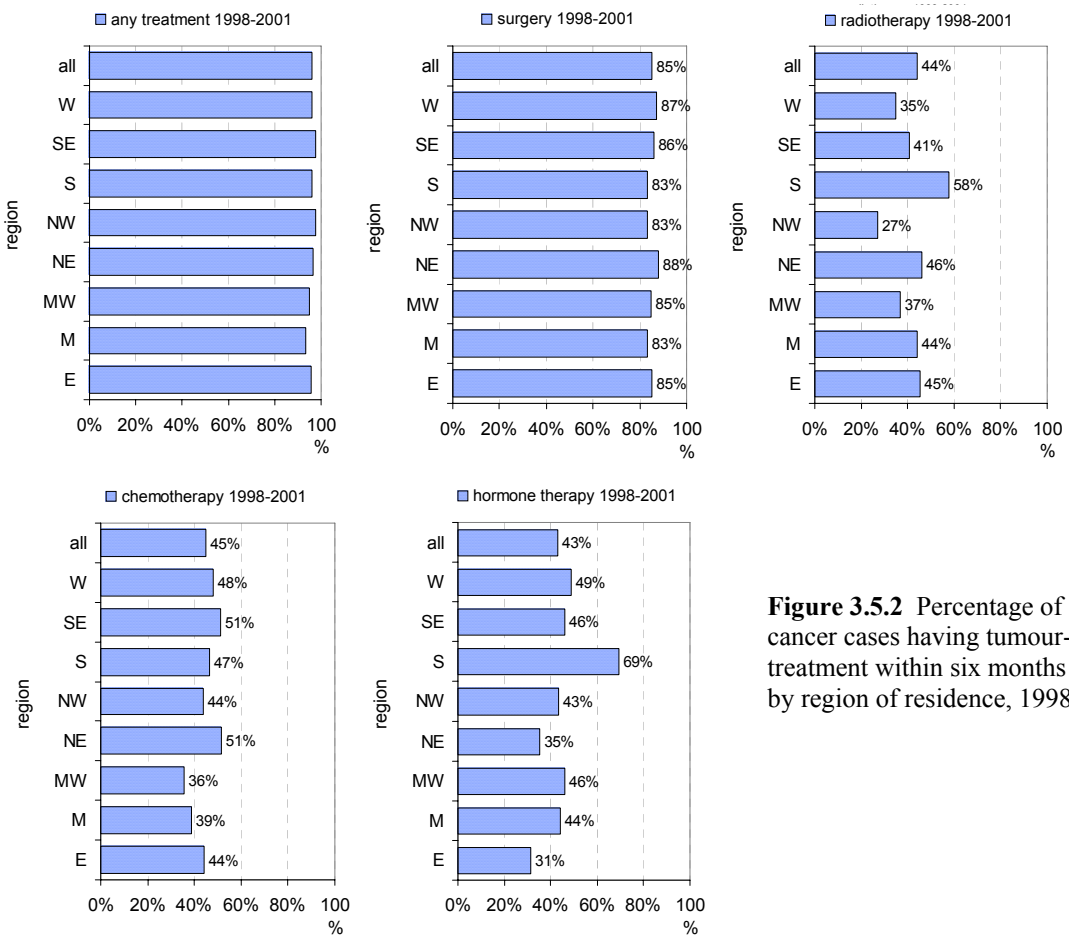


Figure 3.5.2 Percentage of female breast cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence, 1998-2001.

3.6 Treatment: logistic regression analysis

3.6.1 Variation by patient and tumour characteristics

Preliminary multivariate logistic regression models were used to assess variation in treatments in relation to patient and tumour characteristics other than region of residence and year of diagnosis (before examining those). Comparisons here are with baseline groups for relevant variables – diagnosis age 15-44, T category 1 (smallest size/local extension), N negative (no nodal involvement), M negative (no distant metastasis), tumour grade 1, ductal or lobular adenocarcinoma, microscopically verified (MV), symptomatic method of presentation, non-smoker and ever married – having adjusted for all variables shown in the relevant table (*Tables 3.6.1-5*). The main comparisons are based on data for 1994-2001 as a whole (or 1996-2001 for chemotherapy and hormonal therapy). However, attention is drawn to any significant differences in patterns between the diagnosis periods 1994-97 (or 1996-97) and 1998-2001 (details also tabulated).

Overall treatment

Although the differences involved were small, treatment was significantly less likely, compared with baseline groups, for patients aged 75 or above; T category 4 or unknown; N category unknown; M category positive or unknown; grade unknown; 'other' adenocarcinomas, non-specific carcinomas or non-specific cancers; cases lacking microscopic verification (MV); method of presentation unknown; ex-smokers or smoking status unknown; and marital status unknown (*Table 3.6.1*). There were no significant differences in the magnitude of relative risk values between earlier and later diagnosis periods, i.e. the patterns were broadly similar, although treatment use was significantly low for some groups of patients in one but not the other period.

Surgical treatment

Variation between patient groups was more marked (and of greater magnitude) than for overall treatment, with surgery use significantly lower in patients aged 65; T category 3, 4 or unknown; M category positive or unknown; grade unknown; 'other' adenocarcinomas, non-specific carcinomas and non-specific cancers; cases lacking MV; incidental presentation; smoking status unknown; and never married or marital status unknown (*Table 3.6.2*). Use of surgery was significantly higher for non-carcinoma morphologies. The relative risk of surgery for cases of unknown M category differed significantly between diagnosis periods, otherwise there were no significant changes for any variable.

Radiotherapy

Radiotherapy was used significantly less for patients aged 65 or over; T category 2, 3 or unknown; N category unknown; grade 2, 3+ or unknown; non-carcinoma morphologies; incidental presentation; and never married (*Table 3.6.3*). Patients of unknown M category, unknown smoking status or whose cancer was screen-detected were significantly more likely to have radiotherapy. Differences in patterns between diagnosis periods were more marked than for surgery, including significantly different relative risks of radiotherapy for age-groups 45-54 to 75+ (all low for 1994-97 but only 75+ for 1998-2001). Other differences involved cases that were T category 4 or unknown; N category positive or unknown; grade unknown; non-specific carcinomas; and marital status unknown.

Chemotherapy

Chemotherapy use was significantly lower for patients aged 45 or over; M category unknown; 'other' adenocarcinomas and non-carcinomas; cases lacking MV; screen-detected cases; and never married or marital status unknown (*Table 3.6.4*). Chemotherapy use was higher, compared with baseline groups, for T category 2, 3 or 4; N category positive or unknown; and grade 2, 3+ or unknown. The main differences between diagnosis periods 1996-97 and 1998-2001 were significant changes in relative risks of chemotherapy for patients aged 55-64 and 65-74, and for cases that were N category positive or unknown, M category unknown, or incidentally detected.

Hormonal therapy

Hormonal use was significantly less likely in cases that were T category 3 or unknown; N category positive or unknown; grade 3+; non-carcinomas and non-specific carcinomas; unknown MV status; screen-detected, and method of presentation unknown; marital status unknown; and ex-smokers and smoking status unknown (*Table 3.6.5*). Hormonal use was more likely for patients aged 45 or over, and for 'other' adenocarcinomas. Patterns were broadly similar between diagnosis periods, but with significant differences in relative risks of treatment for age-groups 55-64 and 75+, cases that were T category 3, N positive, M category unknown, lacking MV, or screen-detected, and patients of unknown marital status.

Table 3.6.1 Risk ratios for overall treatment of female breast cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
age 15-44	1.000		1.000		1.000	
age 45-54	0.995 (0.983-1.003)	0.298	0.995 (0.976-1.005)	0.471	0.996 (0.978-1.005)	0.494
age 55-64	1.001 (0.992-1.007)	0.714	1.000 (0.985-1.008)	0.931	1.003 (0.990-1.009)	0.547
age 65-74	0.994 (0.982-1.002)	0.218	0.986 (0.961-1.000)	0.059	1.003 (0.991-1.009)	0.490
age 75+	**0.980** (0.963-0.992)	0.000	**0.974** (0.942-0.993)	0.002	0.989 (0.968-1.001)	0.092
T1	1.000		1.000		1.000	
T2	1.001 (0.996-1.006)	0.466	1.002 (0.993-1.008)	0.542	1.001 (0.992-1.006)	0.765
T3	0.998 (0.988-1.004)	0.653	0.999 (0.984-1.008)	0.992	0.997 (0.980-1.005)	0.600
T4	**0.987** (0.975-0.996)	0.002	0.989 (0.969-1.000)	0.077	**0.985** (0.965-0.997)	0.009
T X	**0.962** (0.942-0.977)	0.000	**0.961** (0.930-0.982)	0.000	**0.960** (0.930-0.980)	0.000
N negative	1.000		1.000		1.000	
N positive	1.000 (0.994-1.004)	0.910	0.999 (0.990-1.006)	0.974	1.000 (0.993-1.005)	0.756
N X	**0.980** (0.968-0.988)	0.000	**0.986** (0.971-0.997)	0.009	**0.972** (0.952-0.985)	0.000
M negative	1.000		1.000		1.000	
M positive	**0.955** (0.934-0.971)	0.000	**0.950** (0.915-0.973)	0.000	**0.959** (0.929-0.978)	0.000
M X	**0.987** (0.979-0.992)	0.000	**0.990** (0.979-0.997)	0.005	**0.983** (0.969-0.991)	0.000
grade 1	1.000		1.000		1.000	
grade 2	0.996 (0.981-1.005)	0.490	1.000 (0.973-1.012)	0.973	0.993 (0.970-1.004)	0.322
grade 3+	0.993 (0.977-1.003)	0.262	1.001 (0.977-1.012)	0.881	0.988 (0.958-1.001)	0.100
grade X	**0.986** (0.967-0.998)	0.027	0.992 (0.962-1.007)	0.404	**0.983** (0.950-0.998)	0.030
ductal/lobular	1.000		1.000		1.000	
other adenocarc	**0.986** (0.972-0.996)	0.004	**0.984** (0.962-0.998)	0.022	0.987 (0.967-1.000)	0.067
other carcinoma	0.989 (0.941-1.008)	0.398	0.974 (0.885-1.005)	0.160	1.003 (0.902-1.019)	0.850
carcinoma NOS	**0.974** (0.958-0.985)	0.000	**0.970** (0.946-0.987)	0.000	**0.976** (0.952-0.991)	0.001
cancer NOS	**0.963** (0.911-0.991)	0.003	**0.933** (0.824-0.984)	0.001	0.989 (0.930-1.010)	0.466
other cancer	1.000 (0.938-1.016)	0.950	-		0.998 (0.923-1.016)	0.933
MV yes	1.000		1.000		1.000	
MV no	**0.967** (0.909-0.998)	0.036	0.989 (0.929-1.014)	0.540	**0.906** (0.721-0.986)	0.009
MV X	0.975 (0.906-1.006)	0.171	0.996 (0.921-1.020)	0.854	0.922 (0.701-1.000)	0.052
symptomatic	1.000		1.000		1.000	
incidental	0.994 (0.970-1.010)	0.575	1.009 (0.978-1.025)	0.471	0.970 (0.918-1.000)	0.055
screen detected	0.982 (0.933-1.009)	0.258	1.019 (0.897-1.038)	0.522	0.971 (0.907-1.004)	0.116
presentation X	**0.957** (0.929-0.978)	0.000	**0.932** (0.870-0.973)	0.000	**0.971** (0.939-0.993)	0.005
non-smoker	1.000		1.000		1.000	
ex-smoker	**0.986** (0.967-1.000)	0.050	0.978 (0.941-1.001)	0.071	0.991 (0.968-1.005)	0.306
smoker	0.995 (0.983-1.003)	0.313	0.996 (0.976-1.009)	0.613	0.994 (0.977-1.004)	0.327
smoking status X	**0.983** (0.972-0.993)	0.000	0.990 (0.973-1.003)	0.163	**0.978** (0.961-0.991)	0.000
ever married	1.000		1.000		1.000	
never married	0.990 (0.978-1.000)	0.053	0.993 (0.975-1.007)	0.409	**0.983** (0.964-0.997)	0.021
marital status X	**0.958** (0.929-0.979)	0.000	**0.955** (0.909-0.986)	0.001	**0.956** (0.912-0.984)	0.000

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
There were no significant differences in RR between diagnosis periods.

Table 3.6.2 Risk ratios for surgical treatment of female breast cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.992 (0.970-1.009)	0.398	0.986 (0.950-1.012)	0.349		0.999 (0.971-1.018)	0.932
age 55-64	0.986 (0.964-1.004)	0.165	0.984 (0.947-1.011)	0.297		0.990 (0.960-1.012)	0.443
age 65-74	**0.955** (0.925-0.979)	0.000	**0.932** (0.880-0.971)	0.000		0.975 (0.939-1.001)	0.068
age 75+	**0.758** (0.700-0.811)	0.000	0.744 (0.657-0.821)	0.000		**0.785** (0.705-0.852)	0.000
T1	1.000		1.000			1.000	
T2	1.002 (0.989-1.012)	0.731	1.003 (0.983-1.019)	0.702		0.998 (0.980-1.012)	0.871
T3	**0.917** (0.883-0.945)	0.000	**0.901** (0.848-0.943)	0.000		**0.931** (0.884-0.967)	0.000
T4	**0.701** (0.645-0.752)	0.000	**0.706** (0.625-0.780)	0.000		**0.685** (0.605-0.757)	0.000
T X	**0.810** (0.762-0.852)	0.000	**0.818** (0.750-0.876)	0.000		**0.783** (0.708-0.846)	0.000
N negative	1.000		1.000			1.000	
N positive	1.010 (0.996-1.021)	0.126	1.004 (0.981-1.022)	0.709		1.012 (0.995-1.026)	0.134
N X	0.858 (0.823-0.888)	0.000	**0.872** (0.821-0.915)	0.000		**0.821** (0.768-0.868)	0.000
M negative	1.000		1.000			1.000	
M positive	**0.592** (0.534-0.649)	0.000	**0.621** (0.537-0.702)	0.000		**0.559** (0.477-0.639)	0.000
M X	**0.975** (0.961-0.987)	0.000	0.996 (0.977-1.011)	0.637	*	**0.949** (0.925-0.969)	0.000
grade 1	1.000		1.000			1.000	
grade 2	0.997 (0.971-1.017)	0.843	0.996 (0.950-1.026)	0.831		1.000 (0.965-1.025)	0.960
grade 3+	0.998 (0.972-1.018)	0.918	0.987 (0.939-1.019)	0.490		1.008 (0.976-1.030)	0.535
grade X	**0.923** (0.880-0.958)	0.000	**0.919** (0.850-0.970)	0.000		**0.922** (0.861-0.968)	0.000
ductal/lobular	1.000		1.000			1.000	
other adenocarc	**0.944** (0.910-0.973)	0.000	**0.944** (0.895-0.982)	0.003		**0.935** (0.882-0.977)	0.001
other carcinoma	0.995 (0.910-1.046)	0.882	0.982 (0.845-1.053)	0.716		0.992 (0.859-1.058)	0.867
carcinoma NOS	**0.788** (0.739-0.834)	0.000	**0.792** (0.725-0.851)	0.000		**0.789** (0.712-0.856)	0.000
cancer NOS	**0.406** (0.232-0.618)	0.000	**0.420** (0.193-0.706)	0.000		**0.348** (0.138-0.660)	0.000
other cancer	**1.074** (1.014-1.096)	0.024	1.083 (0.930-1.106)	0.151		**1.076** (1.003-1.099)	0.044
MV yes	1.000		1.000			1.000	
MV no	**0.494** (0.203-0.834)	0.001	**0.477** (0.148-0.889)	0.005		0.485 (0.076-1.012)	0.061
MV X	0.982 (0.652-1.107)	0.865	0.922 (0.331-1.125)	0.676		1.035 (0.613-1.132)	0.768
symptomatic	1.000		1.000			1.000	
incidental	**0.811** (0.713-0.896)	0.000	**0.885** (0.742-0.995)	0.040		**0.753** (0.614-0.874)	0.000
screen detected	0.999 (0.915-1.060)	0.988	1.006 (0.823-1.108)	0.924		1.010 (0.911-1.075)	0.811
presentation X	1.027 (0.982-1.063)	0.218	0.987 (0.889-1.058)	0.757		**1.055** (1.006-1.091)	0.029
non-smoker	1.000		1.000			1.000	
ex-smoker	0.974 (0.933-1.008)	0.157	0.947 (0.874-1.005)	0.080		0.994 (0.945-1.032)	0.814
smoker	0.979 (0.949-1.005)	0.123	0.977 (0.930-1.016)	0.286		0.982 (0.941-1.015)	0.318
smoking status X	**0.908** (0.874-0.939)	0.000	**0.925** (0.874-0.969)	0.000		**0.894** (0.844-0.936)	0.000
ever married	1.000		1.000			1.000	
never married	**0.951** (0.920-0.979)	0.000	**0.920** (0.870-0.965)	0.000		0.978 (0.937-1.012)	0.234
marital status X	**0.896** (0.826-0.955)	0.000	**0.880** (0.778-0.962)	0.002		**0.895** (0.786-0.979)	0.011

[a,b]See *Table 3.6.1*.
*Significant difference in RR between diagnosis periods.

Table 3.6.3 Risk ratios for radiotherapy of female breast cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.960 (0.903-1.018)	0.182	**0.870** (0.793-0.949)	0.001	*	1.046 (0.961-1.130)	0.284
age 55-64	0.989 (0.931-1.048)	0.729	**0.914** (0.835-0.995)	0.037	*	1.067 (0.981-1.152)	0.125
age 65-74	**0.868** (0.808-0.928)	0.000	**0.698** (0.622-0.778)	0.000	*	1.048 (0.958-1.138)	0.294
age 75+	**0.472** (0.423-0.526)	0.000	**0.370** (0.310-0.438)	0.000	*	**0.580** (0.502-0.666)	0.000
T1	1.000		1.000			1.000	
T2	**0.914** (0.871-0.957)	0.000	0.931 (0.862-1.003)	0.061		**0.908** (0.853-0.963)	0.001
T3	**0.918** (0.851-0.986)	0.019	0.939 (0.837-1.044)	0.255		0.916 (0.825-1.008)	0.076
T4	0.991 (0.914-1.069)	0.834	**1.156** (1.029-1.282)	0.016	*	**0.881** (0.782-0.982)	0.022
T X	**0.701** (0.622-0.784)	0.000	**0.815** (0.696-0.941)	0.004	*	**0.573** (0.468-0.690)	0.000
N negative	1.000		1.000			1.000	
N positive	1.018 (0.973-1.062)	0.425	**1.149** (1.074-1.225)	0.000	*	**0.937** (0.882-0.992)	0.027
N X	**0.869** (0.804-0.936)	0.000	0.991 (0.885-1.101)	0.883	*	**0.804** (0.718-0.893)	0.000
M negative	1.000		1.000			1.000	
M positive	0.914 (0.828-1.002)	0.056	0.888 (0.762-1.021)	0.098		0.916 (0.801-1.036)	0.170
M X	**1.059** (1.016-1.101)	0.006	1.001 (0.936-1.066)	0.973		**1.079** (1.023-1.135)	0.006
grade 1	1.000		1.000			1.000	
grade 2	**0.918** (0.847-0.990)	0.026	0.942 (0.814-1.076)	0.395		**0.909** (0.824-0.994)	0.036
grade 3+	**0.912** (0.841-0.984)	0.017	0.969 (0.844-1.100)	0.647		**0.895** (0.809-0.981)	0.017
grade X	**0.856** (0.788-0.926)	0.000	0.965 (0.844-1.091)	0.588	*	**0.804** (0.719-0.890)	0.000
ductal/lobular	1.000		1.000			1.000	
other adenocarc	1.005 (0.928-1.083)	0.890	1.015 (0.899-1.135)	0.792		1.020 (0.916-1.126)	0.696
other carcinoma	1.176 (0.988-1.361)	0.066	0.998 (0.709-1.311)	0.991		**1.248** (1.011-1.469)	0.040
carcinoma NOS	0.928 (0.846-1.013)	0.097	1.053 (0.936-1.172)	0.378	*	**0.782** (0.665-0.907)	0.001
cancer NOS	0.715 (0.448-1.048)	0.092	**0.447** (0.172-0.966)	0.039		0.914 (0.530-1.347)	0.700
other cancer	**0.501** (0.300-0.783)	0.001	**0.393** (0.149-0.878)	0.019		**0.581** (0.315-0.956)	0.030
MV yes	1.000		1.000			1.000	
MV no	0.656 (0.376-1.033)	0.072	1.000 (0.439-1.667)	0.999		**0.399** (0.154-0.868)	0.016
MV X	1.307 (0.821-1.741)	0.222	1.739 (0.977-2.181)	0.057		0.987 (0.404-1.648)	0.973
symptomatic	1.000		1.000			1.000	
incidental	**0.748** (0.615-0.895)	0.001	**0.621** (0.441-0.844)	0.001		0.834 (0.653-1.035)	0.104
screen detected	**1.185** (1.078-1.291)	0.001	**1.230** (1.006-1.454)	0.044		**1.144** (1.023-1.265)	0.019
presentation X	1.039 (0.948-1.131)	0.402	1.029 (0.837-1.231)	0.770		1.031 (0.927-1.136)	0.557
non-smoker	1.000		1.000			1.000	
ex-smoker	1.010 (0.933-1.090)	0.785	1.020 (0.893-1.151)	0.759		0.996 (0.899-1.095)	0.939
smoker	1.015 (0.961-1.070)	0.573	1.018 (0.935-1.103)	0.665		1.015 (0.943-1.088)	0.678
smoking status X	**1.084** (1.028-1.142)	0.003	**1.141** (1.050-1.233)	0.002		1.040 (0.967-1.114)	0.280
ever married	1.000		1.000			1.000	
never married	**0.934** (0.878-0.991)	0.025	0.928 (0.842-1.016)	0.110		0.937 (0.863-1.012)	0.104
marital status X	1.023 (0.908-1.142)	0.691	**1.211** (1.037-1.384)	0.017	*	**0.805** (0.653-0.971)	0.022

[a,b]See *Table 3.6.1*.
*Significant difference in RR between diagnosis periods.

Table 3.6.4 Risk ratios for chemotherapy of female breast cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1996-2001: multivariate model. Chemotherapy data were not available for the years 1994-95.

Variable value[b]	1996-2001		1996-1997 subtotal			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	**0.848** (0.798-0.896)	0.000	**0.799** (0.700-0.894)	0.000		**0.867** (0.808-0.922)	0.000
age 55-64	**0.598** (0.546-0.651)	0.000	**0.408** (0.330-0.496)	0.000	*	**0.672** (0.609-0.735)	0.000
age 65-74	**0.220** (0.189-0.255)	0.000	**0.096** (0.067-0.135)	0.000	*	**0.267** (0.224-0.316)	0.000
age 75+	**0.060** (0.047-0.077)	0.000	**0.043** (0.026-0.071)	0.000		**0.060** (0.044-0.081)	0.000
T1	1.000		1.000			1.000	
T2	**1.424** (1.339-1.509)	0.000	**1.437** (1.244-1.640)	0.000		**1.434** (1.339-1.528)	0.000
T3	**1.587** (1.442-1.729)	0.000	**1.521** (1.223-1.837)	0.000		**1.684** (1.517-1.842)	0.000
T4	**1.538** (1.378-1.696)	0.000	**1.669** (1.307-2.044)	0.000		**1.514** (1.334-1.689)	0.000
T X	0.882 (0.731-1.049)	0.163	1.040 (0.739-1.405)	0.810		0.805 (0.633-1.002)	0.052
N negative	1.000		1.000			1.000	
N positive	**2.143** (2.056-2.228)	0.000	**2.938** (2.678-3.186)	0.000	*	**1.992** (1.901-2.078)	0.000
N X	**1.221** (1.084-1.365)	0.001	**1.833** (1.473-2.222)	0.000	*	1.096 (0.945-1.256)	0.218
M negative	1.000		1.000			1.000	
M positive	0.920 (0.810-1.033)	0.168	0.853 (0.622-1.119)	0.269		0.914 (0.790-1.039)	0.181
M X	**0.843** (0.792-0.895)	0.000	0.958 (0.841-1.081)	0.505	*	**0.819** (0.761-0.877)	0.000
grade 1	1.000		1.000			1.000	
grade 2	**1.339** (1.173-1.515)	0.000	**1.391** (1.016-1.836)	0.040		**1.296** (1.115-1.488)	0.001
grade 3+	**1.852** (1.668-2.037)	0.000	**2.168** (1.704-2.647)	0.000		**1.788** (1.588-1.987)	0.000
grade X	**1.212** (1.055-1.381)	0.007	1.274 (0.934-1.682)	0.122		**1.243** (1.062-1.437)	0.007
ductal/lobular	1.000		1.000			1.000	
other adenocarc	**0.774** (0.671-0.883)	0.000	0.951 (0.720-1.212)	0.704		**0.709** (0.597-0.831)	0.000
other carcinoma	0.952 (0.721-1.198)	0.704	0.900 (0.427-1.546)	0.747		0.910 (0.662-1.173)	0.506
carcinoma NOS	1.013 (0.888-1.140)	0.840	0.886 (0.667-1.137)	0.360		1.075 (0.928-1.221)	0.314
cancer NOS	1.046 (0.618-1.495)	0.844	0.591 (0.129-1.656)	0.401		1.190 (0.677-1.633)	0.477
other cancer	**0.399** (0.202-0.719)	0.001	0.897 (0.231-1.969)	0.845		**0.283** (0.122-0.591)	0.000
MV yes	1.000		1.000			1.000	
MV no	**0.469** (0.192-0.965)	0.038	0.993 (0.200-2.254)	0.992		**0.396** (0.124-0.977)	0.043
MV X	0.744 (0.245-1.520)	0.505	1.681 (0.387-2.648)	0.386		0.278 (0.030-1.309)	0.140
symptomatic	1.000		1.000			1.000	
incidental	1.015 (0.803-1.239)	0.887	**0.526** (0.259-0.967)	0.038	*	1.149 (0.910-1.381)	0.223
screen detected	**0.817** (0.701-0.942)	0.005	1.016 (0.624-1.490)	0.943		**0.714** (0.602-0.835)	0.000
presentation X	0.960 (0.847-1.078)	0.508	0.675 (0.408-1.044)	0.081		0.895 (0.781-1.013)	0.081
non-smoker	1.000		1.000			1.000	
ex-smoker	1.088 (0.980-1.198)	0.108	0.968 (0.736-1.234)	0.807		1.112 (0.993-1.230)	0.065
smoker	1.013 (0.938-1.089)	0.731	1.064 (0.902-1.238)	0.446		0.994 (0.910-1.080)	0.901
smoking status X	0.924 (0.850-1.001)	0.056	1.049 (0.879-1.234)	0.581		**0.893** (0.809-0.979)	0.015
ever married	1.000		1.000			1.000	
never married	**0.861** (0.784-0.940)	0.001	0.995 (0.824-1.181)	0.960		**0.829** (0.743-0.918)	0.000
marital status X	**0.783** (0.641-0.940)	0.007	0.726 (0.501-1.008)	0.057		0.843 (0.657-1.045)	0.128

[a,b]See *Table 3.6.1*.
*Significant difference in RR between diagnosis periods.

Table 3.6.5 Risk ratios for hormonal treatment of female breast cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1996-2001: fuller multivariate model. Hormonal treatment data were not available for the years 1994-95.

Variable value[b]	1996-2001 [a]RR (95% CI)	P	1996-1997 subtotal RR (95% CI)	P		1998-2001 RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	**1.409** (1.282-1.542)	0.000	**1.453** (1.252-1.660)	0.000		**1.375** (1.215-1.546)	0.000
age 55-64	**1.865** (1.725-2.007)	0.000	**2.068** (1.865-2.258)	0.000	*	**1.744** (1.565-1.929)	0.000
age 65-74	**2.394** (2.250-2.533)	0.000	**2.461** (2.276-2.621)	0.000		**2.337** (2.142-2.527)	0.000
age 75+	**2.834** (2.698-2.959)	0.000	**2.659** (2.486-2.801)	0.000	*	**2.942** (2.755-3.114)	0.000
T1	1.000		1.000			1.000	
T2	0.951 (0.900-1.002)	0.061	0.984 (0.902-1.065)	0.718		**0.924** (0.861-0.989)	0.022
T3	**0.869** (0.789-0.951)	0.002	0.969 (0.843-1.090)	0.623	*	**0.777** (0.678-0.883)	0.000
T4	0.934 (0.847-1.022)	0.145	0.922 (0.780-1.062)	0.284		0.938 (0.828-1.051)	0.288
T X	**0.654** (0.566-0.749)	0.000	**0.674** (0.532-0.829)	0.000		**0.657** (0.546-0.779)	0.000
N negative	1.000		1.000			1.000	
N positive	**0.854** (0.809-0.899)	0.000	0.941 (0.868-1.012)	0.110	*	**0.807** (0.751-0.863)	0.000
N X	**0.808** (0.741-0.877)	0.000	**0.832** (0.727-0.936)	0.001		**0.778** (0.693-0.867)	0.000
M negative	1.000		1.000			1.000	
M positive	1.005 (0.908-1.105)	0.906	0.960 (0.808-1.105)	0.602		1.059 (0.932-1.190)	0.361
M X	1.025 (0.977-1.074)	0.302	**0.903** (0.831-0.975)	0.008	*	**1.078** (1.014-1.143)	0.016
grade 1	1.000		1.000			1.000	
grade 2	1.004 (0.922-1.084)	0.923	1.089 (0.946-1.221)	0.215		0.979 (0.881-1.078)	0.685
grade 3+	**0.881** (0.801-0.962)	0.004	0.973 (0.831-1.110)	0.712		**0.841** (0.745-0.939)	0.002
grade X	1.021 (0.941-1.101)	0.598	1.103 (0.968-1.227)	0.130		0.953 (0.855-1.053)	0.366
ductal/lobular	1.000		1.000			1.000	
other adenocarc	**1.128** (1.038-1.216)	0.005	1.099 (0.959-1.228)	0.161		**1.139** (1.023-1.255)	0.018
other carcinoma	0.883 (0.687-1.092)	0.271	1.166 (0.798-1.450)	0.361		0.805 (0.578-1.066)	0.140
carcinoma NOS	**0.860** (0.765-0.959)	0.006	0.862 (0.721-1.003)	0.057		**0.851** (0.727-0.982)	0.027
cancer NOS	1.039 (0.703-1.380)	0.823	0.570 (0.190-1.153)	0.151		1.259 (0.822-1.671)	0.253
other cancer	**0.429** (0.227-0.740)	0.001	0.471 (0.135-1.084)	0.090		**0.466** (0.220-0.874)	0.014
MV yes	1.000		1.000			1.000	
MV no	0.755 (0.455-1.118)	0.182	1.221 (0.617-1.597)	0.457	*	0.554 (0.277-0.975)	0.039
MV X	**0.291** (0.081-0.826)	0.015	-			**0.34**1 (0.088-0.994)	0.049
symptomatic	1.000		1.000			1.000	
incidental	1.034 (0.890-1.178)	0.637	1.025 (0.776-1.250)	0.840		1.068 (0.887-1.249)	0.463
screen detected	**0.887** (0.790-0.986)	0.026	1.192 (0.938-1.395)	0.132	*	0.901 (0.790-1.017)	0.096
presentation X	**0.332** (0.272-0.402)	0.000	**0.267** (0.133-0.494)	0.000		**0.356** (0.288-0.436)	0.000
ever married	1.000		1.000			1.000	
never married	1.044 (0.982-1.107)	0.162	1.009 (0.914-1.100)	0.850		1.048 (0.966-1.131)	0.250
marital status X	**0.736** (0.618-0.863)	0.000	**0.593** (0.437-0.771)	0.000	*	0.847 (0.681-1.028)	0.096
non-smoker	1.000		1.000			1.000	
ex-smoker	**0.843** (0.773-0.914)	0.000	0.932 (0.818-1.039)	0.223		**0.818** (0.731-0.908)	0.000
smoker	0.998 (0.947-1.049)	0.957	0.989 (0.915-1.058)	0.764		1.002 (0.934-1.070)	0.938
smoking status X	**0.671** (0.623-0.720)	0.000	**0.612** (0.538-0.689)	0.000		**0.702** (0.639-0.767)	0.000

[a,b]See *Table 3.6.1*.
*Significant difference in RR between diagnosis periods.

3.6.2 National and regional trends

Overall treatment

Both nationally and regionally, there were no significant trends in treatment during 1996-2001, based on an age-adjusted model (*Table 3.6.6*). However, after further adjustment for stage-related variables, a significant, but very small, annual reduction was apparent.

Table 3.6.6 Average annual changes in the proportion of breast cancer patients having any tumour-directed treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual [a]RR (95% CI)	P
basic model: age-adjusted		
total	0.999 (0.996-1.001)	0.622
E	1.002 (0.996-1.006)	0.426
M	0.993 (0.986-1.000)	0.053
MW	0.987 (0.972-1.000)	0.053
NE	1.001 (0.989-1.012)	0.757
NW	1.006 (0.992-1.016)	0.339
S	0.999 (0.992-1.004)	0.758
SE	0.998 (0.989-1.006)	0.816
W	0.998 (0.990-1.005)	0.701
fuller model: age-, stage-adjusted[b]		
total age, TNM-adj[b]	**0.996** (0.993-0.999)	0.026

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.

Surgical treatment

Age-adjusted trends during 1996-2001 showed a minor, albeit statistically significant, increase in surgery use nationally (averaging 0.5% annually in relative terms) (*Table 3.6.7*). Regionally, only patients from the Eastern region showed any significant trend, equivalent to a 1% annual increase in relative use of surgery.

Table 3.6.7 Average annual changes in the proportion of breast cancer patients having surgical treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	P
basic model: age-adjusted		
total	**1.005** (1.000-1.011)	0.047
E	**1.010** (1.000-1.020)	0.037
M	0.981 (0.958-1.002)	0.087
MW	1.009 (0.989-1.027)	0.361
NE	0.995 (0.976-1.013)	0.647
NW	0.999 (0.978-1.017)	0.928
S	1.010 (0.994-1.026)	0.191
SE	1.008 (0.992-1.022)	0.317
W	1.002 (0.983-1.019)	0.774
fuller model: age-, stage-adjusted		
total	0.997 (0.990-1.005)	0.555

Radiotherapy

There was no significant national trend in use of radiotherapy during 1996-2001, based on age-adjusted data (*Table 3.6.8*). However, significant trends were seen for patients from four regions: significant increases for patients from the Southern and Western regions, significant decreases for the North-Western and South-Eastern regions.

Table 3.6.8 Average annual changes in the proportion of breast cancer patients having radiotherapy (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	P
basic model: age-adjusted		
total	0.996 (0.983-1.010)	0.617
E	0.990 (0.969-1.011)	0.378
M	0.969 (0.926-1.011)	0.158
MW	0.985 (0.937-1.034)	0.565
NE	0.970 (0.925-1.016)	0.209
NW	**0.911** (0.847-0.977)	0.009
S	**1.099** (1.060-1.139)	0.000
SE	**0.928** (0.894-0.962)	0.000
W	**1.088** (1.020-1.159)	0.010
fuller model: age- & stage-adjusted		
total	0.990 (0.977-1.004)	0.179

Chemotherapy

Nationally, age-adjusted trends indicated a substantial and significant increase in chemotherapy use during 1996-2001, by about 13% annually in relative terms (*Table 3.6.9*). Patients from seven of the eight regions also showed significant increases, by between 10% and 20% annually. The exception was the Midland region, where no trend was seen.

Table 3.6.9 Average annual changes in the proportion of breast cancer patients having chemotherapy (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	P
basic model: age-adjusted		
total	**1.126** (1.107-1.145)	0.000
E	**1.099** (1.070-1.128)	0.000
M	0.989 (0.927-1.053)	0.754
MW	**1.176** (1.096-1.259)	0.000
NE	**1.150** (1.076-1.227)	0.000
NW	**1.109** (1.022-1.201)	0.013
S	**1.169** (1.116-1.224)	0.000
SE	**1.205** (1.138-1.274)	0.000
W	**1.184** (1.127-1.241)	0.000
fuller model: age- & stage-adjusted		
total	**1.155** (1.134-1.176)	0.000

Hormonal therapy

Nationally, there was a significant decline in hormonal use during 1996-2001 by about 9% annually in relative terms (*Table 3.6.10*). Significant declines were also seen for patients from all regions, by between 6% and 13% annually.

Table 3.6.10 Average annual changes in the proportion of breast cancer patients having hormonal treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual [a]RR (95% CI)	P
basic model: age-adjusted		
total	**0.912** (0.901-0.922)	0.000
E	**0.908** (0.886-0.930)	0.000
M	**0.930** (0.872-0.989)	0.021
MW	**0.939** (0.900-0.977)	0.002
NE	**0.885** (0.841-0.929)	0.000
NW	**0.915** (0.881-0.949)	0.000
S	**0.933** (0.915-0.951)	0.000
SE	**0.868** (0.835-0.900)	0.000
W	**0.916** (0.890-0.942)	0.000
fuller model: age- & stage-adjusted		
total	**0.902** (0.891-0.913)	0.000

3.6.3 Regional variation

Regional variations in treatment use (relative risks compared with the Eastern region) are summarized in *Figures 3.6.1-4* for the overall period 1994-2001 (1996-2001 for chemotherapy and hormone therapy) and for the most recent diagnosis period, 1998-2001.

Results of basic age-adjusted models and of fully adjusted models are presented for overall treatment, surgical treatment, radiotherapy, chemotherapy and hormonal therapy. More detailed summaries, overall and for the periods 1994-97 and 1998-2001, are presented in *Tables 3.6.11-15*.

Overall treatment

Regional variation in overall treatment was less marked than for individual treatment modalities. During 1994-2001 as a whole, age-adjusted analyses indicated that patients from two regions (North-Western and South-Eastern) were significantly more likely to receive treatment than those from the Eastern region (*Table 3.6.11*). However, the differences were very small. Patterns were broadly similar in 1994-97 and 1998-2001, but regional variation in the earlier period was not quite statistically significant. In the later period, patients from the Midland regions were significantly (albeit only slightly) less likely to receive treatment.

Further adjustment for stage or other variables modified the pattern of regional variation only slightly, and the magnitude of regional variation remained small. In the final multivariate model, patients from three regions (North-Western, South-Eastern and additionally Mid-Western) were significantly more likely to be treated than those from the Eastern region, while those from the Midland region were significantly less likely to be treated. As for the basic age-adjusted analyses, regional variation was slightly more marked in the most recent diagnosis period (1998-2001) but RRs did not differ significantly between periods.

Table 3.6.11 Risk ratios for overall treatment of female breast cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
basic model: age-adjusted[b]						
E	1.000		1.000		1.000	
M	0.989 (0.967-1.006)	0.264	1.008 (0.975-1.028)	0.531	**0.975** (0.940-0.998)	0.037
MW	1.003 (0.986-1.015)	0.681	1.010 (0.986-1.026)	0.333	0.996 (0.971-1.012)	0.714
NE	1.007 (0.991-1.019)	0.302	1.006 (0.979-1.023)	0.582	1.009 (0.986-1.023)	0.359
NW	**1.023** (1.010-1.032)	0.002	1.023 (0.999-1.036)	0.051	**1.025** (1.006-1.035)	0.016
S	1.009 (0.998-1.018)	0.089	1.012 (0.995-1.024)	0.139	1.006 (0.991-1.018)	0.344
SE	**1.022** (1.011-1.030)	0.000	1.019 (0.999-1.032)	0.052	**1.024** (1.010-1.033)	0.003
W	1.005 (0.990-1.016)	0.453	1.004 (0.979-1.020)	0.688	1.006 (0.985-1.020)	0.477
fuller model: age-, stage-adjusted[b,c]						
E	1.000		1.000		1.000	
M	0.982 (0.954-1.002)	0.093	1.003 (0.964-1.026)	0.824	**0.961** (0.913-0.993)	0.011
MW	1.008 (0.992-1.020)	0.249	1.014 (0.990-1.029)	0.207	1.005 (0.982-1.020)	0.592
NE	1.006 (0.987-1.019)	0.459	1.001 (0.970-1.021)	0.894	1.008 (0.983-1.023)	0.429
NW	**1.025** (1.011-1.034)	0.002	1.022 (0.997-1.037)	0.075	**1.028** (1.010-1.037)	0.008
S	1.009 (0.997-1.018)	0.124	1.010 (0.990-1.024)	0.252	1.009 (0.992-1.020)	0.240
SE	**1.015** (1.000-1.025)	0.048	1.014 (0.990-1.030)	0.194	1.013 (0.989-1.027)	0.206
W	1.004 (0.987-1.016)	0.559	1.008 (0.984-1.025)	0.416	0.997 (0.969-1.015)	0.840
final multivariate model[d]						
E	1.000		1.000		1.000	
M	**0.971** (0.937-0.995)	0.017	0.988 (0.936-1.018)	0.528	**0.959** (0.906-0.993)	0.013
MW	**1.015** (1.000-1.026)	0.038	**1.023** (1.003-1.036)	0.028	1.008 (0.983-1.023)	0.428
NE	1.005 (0.985-1.019)	0.527	1.000 (0.965-1.022)	0.979	1.010 (0.983-1.025)	0.367
NW	**1.025** (1.010-1.035)	0.004	1.019 (0.989-1.036)	0.164	**1.032** (1.015-1.040)	0.003
S	1.006 (0.991-1.017)	0.336	1.007 (0.983-1.023)	0.478	1.008 (0.987-1.021)	0.383
SE	**1.021** (1.007-1.031)	0.006	1.021 (0.998-1.035)	0.062	**1.022** (1.000-1.033)	0.043
W	1.002 (0.983-1.016)	0.768	1.004 (0.975-1.023)	0.721	0.995 (0.963-1.016)	0.746

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998). [b]Age-group 15-44, 45-54, 55-64, 65-74, or 75+.
[c]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[d]Adjusted for age-group; T, N and M categories; grade; tumour morphology; microscopic verification status; method of presentation; smoking status; marital status; individual year of diagnosis.

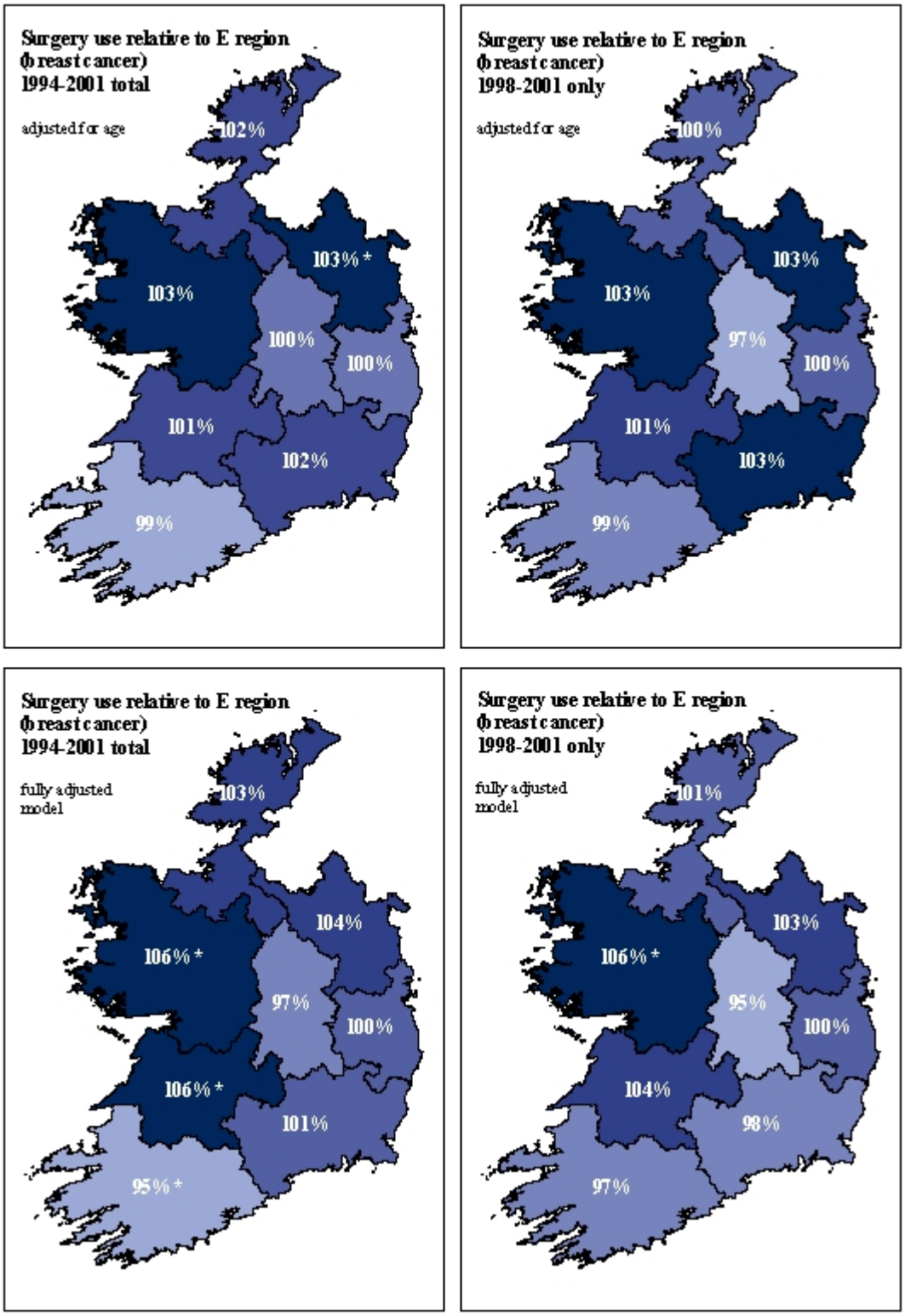


Figure 3.6.1 Regional variation in surgical treatment for breast cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 3.6.12* for further details. * = significantly high or low values (P<0.05).

Surgical treatment

The basic age-adjusted analyses indicated very little regional variation in the use of surgery. Overall, a slightly but significantly higher proportion of patients from the North-Eastern region had surgery, compared with the Eastern region (*Figure 3.6.1*, *Table 3.6.12*). No significant variation was evident within the earlier (1994-97) and later (1998-2001) diagnosis periods, and there were no significant differences in RRs between these periods.

Further adjustment for other variables appeared to accentuate regional variation somewhat. Based on a stage-adjusted model, two further regions (North-Western and Western, along with South-Eastern) had significantly high use of surgery compared with the Eastern region. Again, however, this variation was only significant for the period 1994-2001 as a whole. The results of the final multivariate model indicated significantly high use of surgery in patients from the Mid-Western and Western regions, but significantly low use in those from the Southern region. Patterns were broadly similar between earlier and later periods.

Table 3.6.12 Risk ratios for surgical treatment of female breast cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
basic model: age-adjusted[b]						
E	1.000		1.000		1.000	
M	0.995 (0.957-1.029)	0.824	1.024 (0.965-1.071)	0.379	0.972 (0.918-1.017)	0.252
MW	1.009 (0.977-1.036)	0.555	1.011 (0.962-1.051)	0.628	1.008 (0.965-1.043)	0.681
NE	**1.034** (1.004-1.059)	0.026	1.037 (0.989-1.075)	0.117	1.031 (0.990-1.064)	0.125
NW	1.016 (0.982-1.045)	0.330	1.033 (0.983-1.074)	0.176	1.001 (0.951-1.041)	0.949
S	0.988 (0.963-1.011)	0.351	0.990 (0.951-1.024)	0.596	0.988 (0.953-1.017)	0.455
SE	1.020 (0.992-1.044)	0.146	1.009 (0.964-1.047)	0.660	1.029 (0.993-1.058)	0.103
W	1.027 (0.999-1.051)	0.056	1.021 (0.977-1.058)	0.312	1.033 (0.995-1.063)	0.078
fuller model: age-, stage-adjusted[b,c]						
E	1.000		1.000		1.000	
M	0.978 (0.926-1.021)	0.354	1.001 (0.925-1.060)	0.961	0.952 (0.873-1.014)	0.149
MW	1.033 (0.998-1.062)	0.062	1.023 (0.968-1.068)	0.372	1.045 (0.999-1.081)	0.053
NE	**1.039** (1.004-1.069)	0.031	1.046 (0.992-1.087)	0.090	1.033 (0.982-1.073)	0.181
NW	**1.040** (1.000-1.073)	0.048	1.056 (0.997-1.100)	0.060	1.026 (0.964-1.071)	0.362
S	0.971 (0.936-1.002)	0.069	0.965 (0.911-1.011)	0.148	0.982 (0.936-1.021)	0.417
SE	0.996 (0.958-1.029)	0.849	0.989 (0.930-1.038)	0.709	0.992 (0.937-1.036)	0.769
W	**1.044** (1.012-1.070)	0.008	1.046 (0.996-1.085)	0.065	1.040 (0.994-1.075)	0.079
final multivariate model[d]						
E	1.000		1.000		1.000	
M	0.965 (0.907-1.013)	0.169	0.971 (0.883-1.038)	0.440	0.949 (0.862-1.016)	0.157
MW	**1.059** (1.025-1.087)	0.001	**1.088** (1.041-1.123)	0.001	1.035 (0.981-1.075)	0.179
NE	1.037 (0.996-1.070)	0.069	1.044 (0.980-1.092)	0.154	1.028 (0.968-1.073)	0.310
NW	1.031 (0.982-1.069)	0.191	1.047 (0.974-1.100)	0.182	1.009 (0.935-1.063)	0.776
S	**0.954** (0.913-0.991)	0.014	0.949 (0.884-1.003)	0.068	0.971 (0.915-1.017)	0.239
SE	1.006 (0.965-1.040)	0.736	1.021 (0.960-1.069)	0.456	0.977 (0.913-1.028)	0.429
W	**1.057** (1.024-1.084)	0.001	1.052 (0.997-1.094)	0.059	**1.059** (1.016-1.092)	0.010

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; T, N and M categories; grade; tumour morphology; microscopic verification; method of presentation; smoking status; marital status. [Year of diagnosis did not significantly improve model fit and was excluded from the final model.]

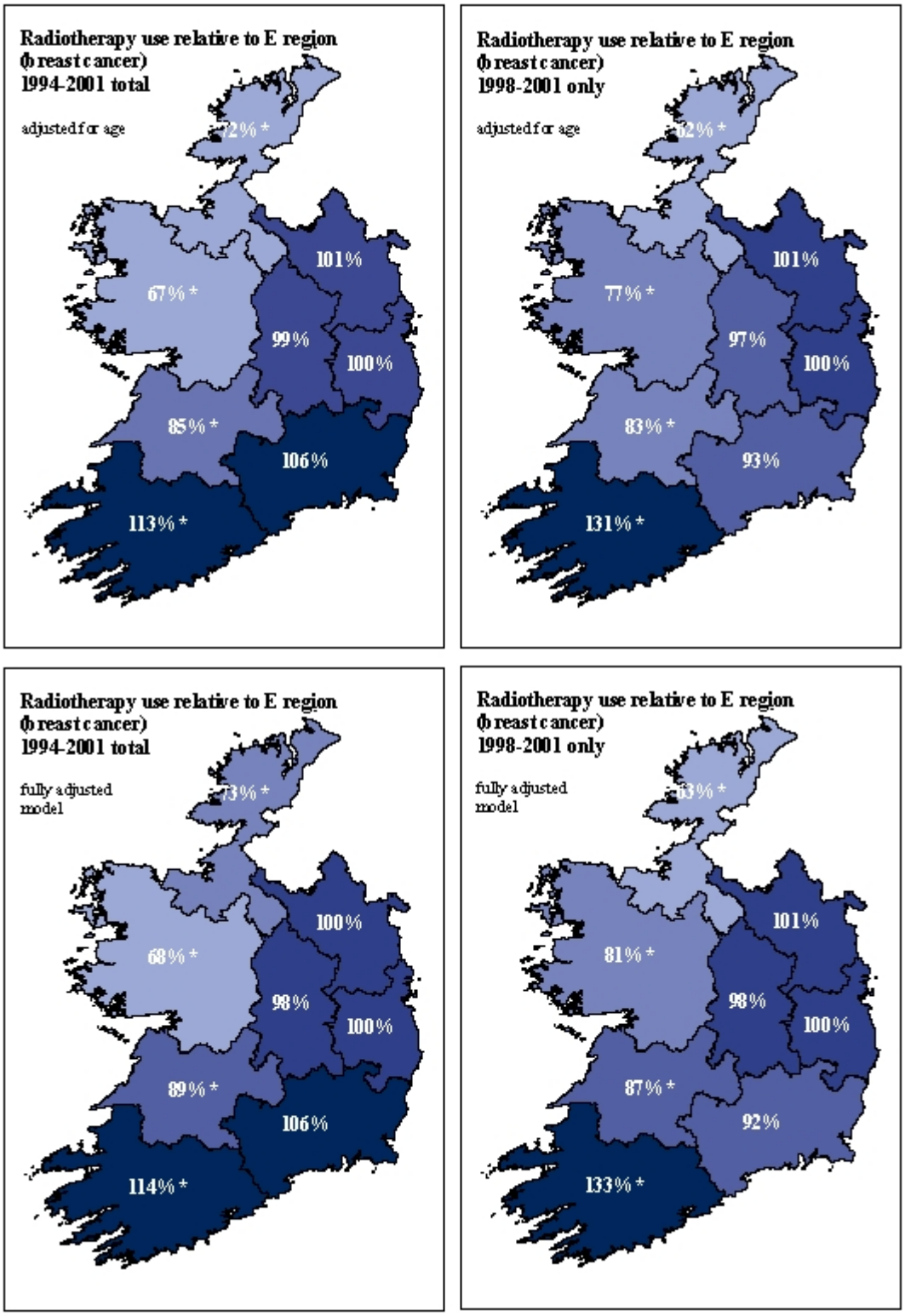


Figure 3.6.2 Regional variation in radiotherapy for breast cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 3.6.13* for further details. * = significantly high or low values (P<0.05).

Radiotherapy

For the period 1994-2001 as a whole, age-adjusted analyses indicate that breast cancer patients from Mid-Western, North-Western and Western regions were significantly less likely, but patients from Southern region were significantly more likely, to have radiotherapy than patients from the Eastern region (*Figure 3.6.2*, *Table 3.6.13*). These regional differences were quite substantial (up to 33% relative to Eastern region). For the first three regions, this pattern applied in both the 1994-97 and 1998-2001, but use of radiotherapy was significantly low for Southern region during 1994-97 and significantly high in 1998-2001. Radiotherapy use for patients from South-Eastern region was not significantly different from the Eastern region overall, but was significantly high during 1994-97 and significantly low during 1998-2001. For four regions (North-Western, Southern, South-Eastern and Western), either the magnitude or the direction of RRs (compared with Eastern region) differed significantly between periods.

These patterns of regional variation remained largely unchanged after further adjustment for stage-related and other patient and tumour variables, apart from minor changes in RRs or their statistical significance. This indicates that the variables examined did not account for, or 'explain', the marked regional variations in radiotherapy use. Across all the analyses, radiotherapy use was consistently similar among patients from the Eastern, Midland and North-Eastern regions. This suggests that geographic proximity to Dublin was a major factor.

Table 3.6.13 Risk ratios for radiotherapy of female breast cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.986 (0.901-1.074)	0.767	1.001 (0.871-1.135)	0.986		0.974 (0.862-1.090)	0.666
MW	**0.853** (0.781-0.928)	0.000	**0.882** (0.776-0.993)	0.039		**0.825** (0.728-0.927)	0.001
NE	1.007 (0.930-1.085)	0.852	0.997 (0.879-1.118)	0.964		1.012 (0.910-1.115)	0.811
NW	**0.724** (0.645-0.808)	0.000	**0.850** (0.728-0.980)	0.025	*	**0.620** (0.520-0.731)	0.000
S	**1.127** (1.068-1.186)	0.000	**0.908** (0.823-0.996)	0.042	*	**1.311** (1.233-1.387)	0.000
SE	1.057 (0.987-1.127)	0.107	**1.215** (1.109-1.321)	0.000	*	0.925 (0.834-1.018)	0.117
W	**0.667** (0.605-0.733)	0.000	**0.554** (0.471-0.646)	0.000	*	**0.768** (0.680-0.861)	0.000
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.980 (0.894-1.068)	0.656	0.985 (0.854-1.120)	0.828		0.971 (0.857-1.088)	0.633
MW	**0.859** (0.786-0.934)	0.000	**0.882** (0.775-0.994)	0.039		**0.836** (0.737-0.940)	0.002
NE	0.996 (0.918-1.075)	0.930	0.996 (0.877-1.118)	0.951		1.009 (0.905-1.115)	0.861
NW	**0.715** (0.636-0.799)	0.000	**0.835** (0.713-0.965)	0.014	*	**0.618** (0.517-0.730)	0.000
S	**1.103** (1.043-1.163)	0.001	**0.888** (0.803-0.976)	0.014	*	**1.306** (1.225-1.384)	0.000
SE	1.045 (0.975-1.116)	0.201	**1.208** (1.101-1.314)	0.000	*	**0.905** (0.813-0.999)	0.049
W	**0.663** (0.601-0.729)	0.000	**0.543** (0.461-0.635)	0.000	*	**0.769** (0.679-0.863)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.982 (0.895-1.071)	0.702	0.994 (0.862-1.131)	0.941		0.976 (0.860-1.096)	0.701
MW	**0.890** (0.815-0.967)	0.006	0.886 (0.776-1.002)	0.055		**0.874** (0.772-0.981)	0.022
NE	1.003 (0.923-1.083)	0.941	1.015 (0.894-1.140)	0.803		1.009 (0.904-1.117)	0.855
NW	**0.727** (0.647-0.813)	0.000	**0.857** (0.732-0.990)	0.036	*	**0.627** (0.524-0.741)	0.000
S	**1.136** (1.075-1.198)	0.000	0.926 (0.838-1.018)	0.116	*	**1.334** (1.251-1.415)	0.000
SE	1.063 (0.991-1.135)	0.083	**1.216** (1.107-1.325)	0.000	*	0.916 (0.823-1.013)	0.091
W	**0.684** (0.619-0.751)	0.000	**0.555** (0.470-0.649)	0.000	*	**0.814** (0.720-0.913)	0.000

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; T, N and M categories; grade; tumour morphology; microscopic verification status; method of presentation; marital status; individual year of diagnosis. [Smoking status did not significantly improve model fit and was excluded.]
*Significant difference in RR between diagnosis periods.

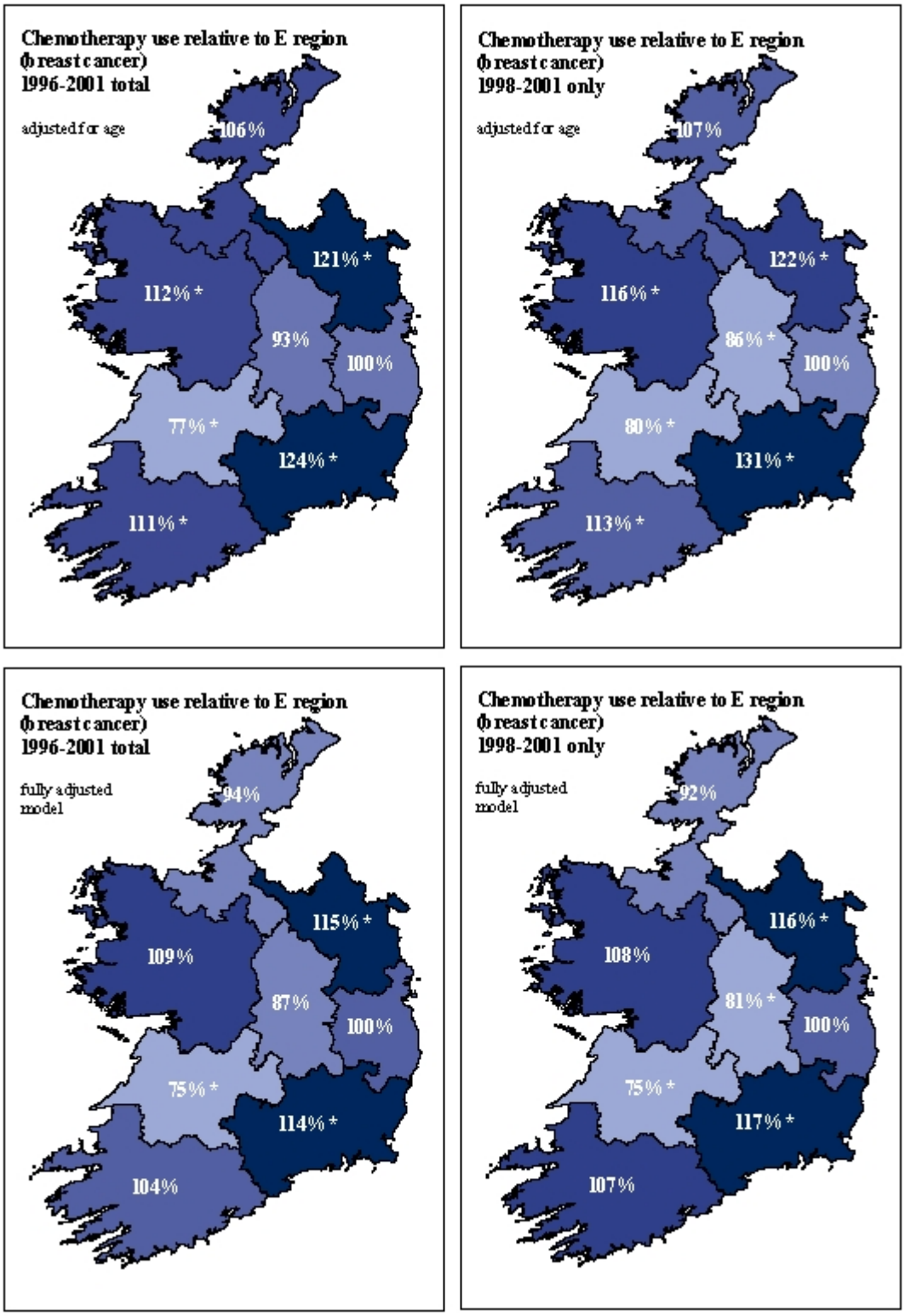


Figure 3.6.3 Regional variation in chemotherapy for breast cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1996-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 3.6.14* for further details. * = significantly high or low values (P<0.05).

Chemotherapy

As for radiotherapy, but to a lesser extent, there was substantial regional variation in the proportion of breast cancer patients receiving chemotherapy. Basic age-adjusted analyses indicated showed that patients from the North-Eastern, Southern, South-Eastern and Western regions were significantly more likely to receive chemotherapy than patients from the Eastern region, during 1996-2001 as a whole (*Figure 3.6.3*, *Table 3.6.14*). Patients from the Mid-Western region were significantly less likely to receive chemotherapy. The pattern of regional variation differed somewhat between earlier and later years, with only the finding for Mid-Western region significant for the earlier period (based on only two years' data however). Variation appeared to be more marked during 1998-2001, not only the extent of statistically significant variation (partly reflecting sample sizes) but also the apparent magnitude of variation. Chemotherapy use was significantly low among patients from a further region (Midland) during this period, compared with overall; but this was the only region showing a significant differences in RRs between periods.

The pattern of regional variation changed little after further adjustment for stage-related variables, but was modified somewhat when other patient and tumour variables were added to the model. Regional differences now involved significantly high use of chemotherapy in only two regions (North-Eastern and South-Eastern). However, significantly low use of chemotherapy was still apparent for the Mid-Western region and (during 1998-2001) Midland region.

Table 3.6.14 Risk ratios for chemotherapy of female breast cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1996-2001. Chemotherapy data were not available for the years 1994-95. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1996-2001		1996-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.932 (0.820-1.049)	0.257	1.155 (0.900-1.428)	0.242	*	**0.858** (0.736-0.986)	0.031
MW	**0.769** (0.679-0.866)	0.000	**0.723** (0.561-0.915)	0.006		**0.801** (0.694-0.915)	0.001
NE	**1.205** (1.099-1.312)	0.000	1.179 (0.956-1.415)	0.117		**1.222** (1.102-1.340)	0.000
NW	1.060 (0.939-1.184)	0.333	1.070 (0.821-1.345)	0.595		1.065 (0.927-1.205)	0.353
S	**1.105** (1.024-1.187)	0.011	1.019 (0.855-1.196)	0.818		**1.132** (1.041-1.224)	0.004
SE	**1.241** (1.143-1.338)	0.000	1.075 (0.882-1.282)	0.458		**1.314** (1.204-1.421)	0.000
W	**1.120** (1.022-1.220)	0.016	1.053 (0.858-1.264)	0.601		**1.155** (1.042-1.267)	0.007
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.888 (0.770-1.014)	0.081	1.102 (0.834-1.396)	0.473	*	**0.811** (0.683-0.950)	0.008
MW	**0.776** (0.678-0.881)	0.000	**0.681** (0.513-0.883)	0.003		**0.811** (0.694-0.936)	0.003
NE	**1.216** (1.098-1.333)	0.000	1.149 (0.903-1.414)	0.244		**1.223** (1.090-1.353)	0.001
NW	0.978 (0.851-1.110)	0.743	1.105 (0.832-1.406)	0.467		0.953 (0.808-1.103)	0.537
S	**1.109** (1.020-1.199)	0.016	1.021 (0.841-1.216)	0.825		**1.152** (1.049-1.254)	0.003
SE	**1.197** (1.091-1.303)	0.000	1.056 (0.846-1.285)	0.610		**1.256** (1.134-1.375)	0.000
W	**1.127** (1.021-1.235)	0.018	1.063 (0.845-1.300)	0.584		**1.130** (1.009-1.252)	0.034
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.871 (0.750-1.000)	0.052	1.090 (0.818-1.389)	0.535		**0.808** (0.675-0.951)	0.009
MW	**0.751** (0.651-0.858)	0.000	**0.710** (0.530-0.927)	0.011		**0.753** (0.637-0.879)	0.000
NE	**1.153** (1.031-1.275)	0.013	1.100 (0.853-1.371)	0.442		**1.163** (1.026-1.299)	0.019
NW	0.941 (0.811-1.078)	0.401	1.057 (0.784-1.362)	0.697		0.918 (0.770-1.073)	0.296
S	1.041 (0.947-1.136)	0.394	0.981 (0.796-1.184)	0.855		1.071 (0.963-1.180)	0.196
SE	**1.143** (1.033-1.255)	0.010	1.023 (0.809-1.259)	0.838		**1.168** (1.041-1.294)	0.009
W	1.089 (0.978-1.203)	0.115	1.040 (0.815-1.286)	0.739		1.076 (0.949-1.205)	0.238

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; T, N and M categories; grade; tumour morphology; method of presentation; smoking status; marital status; individual year of diagnosis. [Microscopic verification status did not significantly improve model-fit and was excluded.]
*Significant difference in RR between diagnosis periods.

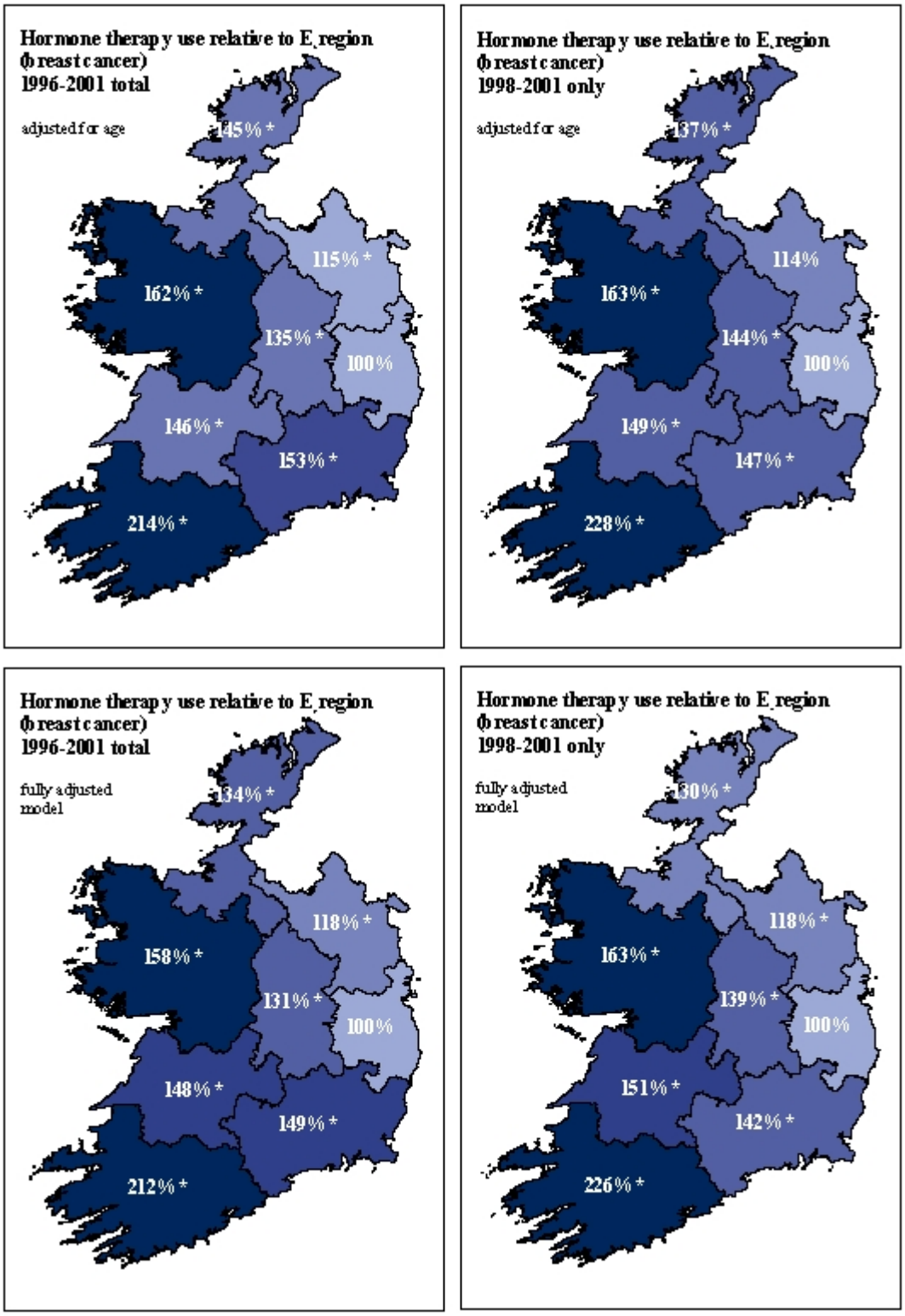


Figure 3.6.4 Regional variation in hormonal therapy for breast cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1996-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 3.6.15* for further details. * = significantly high or low values (P<0.05).

Hormonal therapy

Regional variation was again very marked, but involved significantly higher use of hormonal therapy in patients from other than the Eastern region. Overall, patients from the other regions were up to twice as likely to receive hormonal therapy, and generally 30-60% more likely (*Figure 3.6.4*, *Table 3.6.15*). This pattern was little modified by adjustment for patient and tumour variables, and was broadly the same in both earlier and later diagnosis periods. Only patients from the Southern region showed any significant differences in RRs between 1996-97 and 1998-2001: a further increase in the already high use of hormonal therapy, relative to patients from the Eastern region.

In general, regions closest to the Eastern region were most similar to the latter region in terms of hormonal use. This may support geographic or institutional factors, rather than variation in patient or tumour characteristics, having been a crucial determinant of the extent to which hormonal therapy was prescribed.

Data on oestrogen-receptor and progesterone-receptor status of patient were only available from about 2001 onwards, thus these variables could not be included in analyses.

Table 3.6.15 Risk ratios for hormonal treatment of female breast cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1996-2001. Hormonal treatment data were not available for the years 1994-95. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1996-2001 [a]RR (95% CI)	P	1996-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	**1.346** (1.215-1.478)	0.000	1.202 (0.998-1.405)	0.052		**1.441** (1.271-1.613)	0.000
MW	**1.463** (1.348-1.577)	0.000	**1.386** (1.219-1.544)	0.000		**1.487** (1.335-1.642)	0.000
NE	**1.148** (1.038-1.262)	0.008	1.158 (0.991-1.326)	0.062		1.135 (0.993-1.286)	0.062
NW	**1.453** (1.321-1.585)	0.000	**1.563** (1.372-1.735)	0.000		**1.373** (1.201-1.551)	0.000
S	**2.139** (2.063-2.212)	0.000	**1.903** (1.798-1.994)	0.000	*	**2.282** (2.176-2.381)	0.000
SE	**1.534** (1.430-1.638)	0.000	**1.624** (1.478-1.757)	0.000		1.466 (1.327-1.606)	0.000
W	**1.617** (1.509-1.723)	0.000	**1.578** (1.424-1.719)	0.000		1.629 (1.484-1.774)	0.000
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**1.345** (1.212-1.479)	0.000	1.181 (0.973-1.389)	0.088		1.446 (1.274-1.622)	0.000
MW	**1.506** (1.388-1.623)	0.000	**1.465** (1.294-1.625)	0.000		1.523 (1.366-1.681)	0.000
NE	**1.187** (1.072-1.305)	0.001	**1.261** (1.083-1.435)	0.004		1.171 (1.022-1.328)	0.023
NW	**1.439** (1.306-1.573)	0.000	**1.527** (1.329-1.706)	0.000		1.383 (1.209-1.564)	0.000
S	**2.157** (2.080-2.230)	0.000	**1.902** (1.794-1.994)	0.000	*	2.320 (2.213-2.420)	0.000
SE	**1.506** (1.399-1.612)	0.000	**1.620** (1.468-1.757)	0.000		1.436 (1.295-1.580)	0.000
W	**1.633** (1.523-1.740)	0.000	**1.659** (1.505-1.795)	0.000		1.635 (1.487-1.781)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**1.305** (1.167-1.446)	0.000	1.115 (0.904-1.330)	0.290		1.394 (1.215-1.577)	0.000
MW	**1.482** (1.357-1.606)	0.000	**1.435** (1.250-1.608)	0.000		1.505 (1.341-1.671)	0.000
NE	**1.184** (1.063-1.308)	0.003	1.183 (0.998-1.369)	0.052		1.178 (1.023-1.342)	0.023
NW	**1.344** (1.206-1.485)	0.000	**1.420** (1.209-1.616)	0.000		1.298 (1.121-1.483)	0.001
S	**2.120** (2.034-2.200)	0.000	**1.852** (1.729-1.957)	0.000	*	2.261 (2.142-2.371)	0.000
SE	**1.491** (1.378-1.604)	0.000	**1.626** (1.464-1.771)	0.000		1.418 (1.270-1.568)	0.000
W	**1.581** (1.464-1.697)	0.000	**1.527** (1.355-1.685)	0.000		1.625 (1.469-1.781)	0.000

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; T, N and M categories; grade; tumour morphology; microscopic verification status; method of presentation; smoking status; marital status; individual year of diagnosis.
*Significant difference in RR between diagnosis periods.

3.7 Discussion: breast cancer

The major findings here are:

- significant increases in relative survival of patients between the periods 1994-97 and 1998-2001, nationally and in some regions;
- significant regional variation in relative survival throughout 1994-2001, involving lower survival of patients in at least some regions outside of the Eastern region;
- significant increases in the use of chemotherapy between 1996 and 2001;
- significant decreases in the use of hormonal therapy;
- significant regional variation in treatments, most notably involving higher use of hormone therapy and lower use of radiotherapy for patients resident outside of the Eastern region.

Survival trends

Most of the improvements seen in breast cancer survival between the two periods considered seem likely to reflect improved treatment, as they seen even after adjustment for patient and tumour characteristics. This may involve greater or more appropriate use of specific treatments. Changes seen in the proportions of patients receiving particular treatments seem to support this.

Improvements in survival overall and in some individual regions (Eastern, North-Eastern and Southern) may also reflect, in part, improvements in early diagnosis. The introduction of the BreastCheck screening programme in eastern parts of the country during 2000-2001 is unlikely to have had a major effect on the figures presented here, although it may have influenced one-year and two-year survival sufficiently to have had some effect in relevant regions. Although population-based screening is expected to lead to substantial reductions in breast cancer mortality in the age range screened (currently 50-64), resultant improvements in survival rates may be exaggerated somewhat because of 'lead-time' bias. This results from some patients being diagnosed earlier than they otherwise would be, whether or not a true survival benefit is seen.

Regional variation in survival

For 1994-2001 as a whole, patients from all regions other than the Eastern region had significantly lower relative survival compared with the latter region, based on age-adjusted comparisons of 'relative excess risk'. After further adjustment for patient and tumour variables including stage, this variation reduced somewhat, but four regions still showed significantly high excess risks.

The patterns of regional variation differed somewhat between earlier (1994-97) and later (1998-2001) diagnosis periods. This reflected, in part, trends in relative survival. In particular, improvements in the Eastern, North-Eastern and Southern regions reduced differences in survival between those regions, but accentuated differences between the Eastern region and other regions. As for the interpretation of survival trends, the relative roles of treatment quality and early detection are difficult to quantify with certainty. However, a substantial proportion of the regional variation remained after adjustment for patient and tumour characteristics, suggesting that variations in treatment are likely to have been important.

Survival: international context

Average five-year relative survival for female breast cancer patients diagnosed in Ireland during 1994-97 was slightly lower than the European average for patients diagnosed during 1990-94 (EUROCARE-3 results summarized in *Table 3.7.1*). Note that figures tabulated here are age-standardized to the EUROCARE-3 patient population, thus the Irish figures differ slightly from those tabulated earlier in this chapter. More recent Europe-wide figures are not yet available.

Table 3.7.1 Comparison of five-year relative survival for female breast cancer patients, Ireland 1994-97 and 1998-2001, and Europe 1990-94, age-adjusted to the EUROCARE-3 standard patient population for this cancer.[a]

	Ireland 1994-97 5-yr survival (95% CI)		Ireland 1998-2001 survival (95% CI)		Europe 1990-94[b] survival (95% CI)		[range][c]
female	72.5%	(71.1%-74.0%)	77.5%	(75.9%-79.1%)	76.1%	(75.6%-76.6%)	[59.5%-82.6%]

[a]Capocaccia *et al*. (2003) and unpublished. [b]EUROCARE-3: Sant *et al*. (2003). [c]Range of national figures: highest Sweden.

Standard treatment modalities for breast cancer

Evidence-based summaries of standard treatment options, by stage or other prognostic grouping, are available as part of the US National Cancer Institute's PDQ Cancer Information Summaries: (2Hhttp://www.cancer.gov/cancertopics/pdq/cancerdatabase).

A brief summary is provided below, by broad modality (see also *Appendix 1*).

Clinical guidelines for treatment of Irish breast cancer patients have been prepared by the Clinical Guidelines Committee of the Royal College of Surgeons in Ireland (Walsh & O'Higgins 2000), which should be referred to (along with the NCI PDQ webpage) for further details.

Surgery: Curative intent (as single modality or in combination with adjuvant radiotherapy, chemotherapy or hormonal therapy) for stages I-IIIA and operable IIIC (TNM 6th edition); curative (in combination with adjuvant therapy) for stage IIIB, inoperable IIIC, and inflammatory carcinoma; palliative for stage IV.

Radiotherapy: Adjuvant for stages I-III; palliative for stage IV.

Chemotherapy and related treatments: Adjuvant for node-positive and intermediate- or high-risk node-negative cases in stages I-IIIA, and for stages IIIB, IIIC or inflammatory carcinoma; palliative for stage IV.

Hormone therapy: Adjuvant for hormone-receptive cancers in stages I-III; palliative for stage IV.

Treatment trends

No trend in overall treatment and little or no trend in surgical treatment were seen for breast cancer.

However, levels of treatment were already higher for this cancer than for the other major cancers (colorectal, lung and prostate) considered in this report. Analyses of surgical treatment here did not distinguish mastectomy (total breast-removal) from breast-conserving surgery (BCS), the use of which increased significantly in Ireland during the period 1994-99 (Walsh *et al*., 2006). Further analysis of trends and regional variation in BCS is planned.

No overall trend was seen in the use of radiotherapy, although increases were seen among patients from two regions (Southern and Western) and decreases for another two regions (North-Western and South-Eastern). Increased use of breast-conserving surgery might be expected to have led to increased use of adjuvant radiotherapy (required as part of breast-conserving therapy). However, radiotherapy is also administered to the site of breast-removal in many patients who have mastectomies, as well as to other sites in patients with more advanced disease. This may complicate interpretation of trends. Further analysis, looking at radiotherapy trends in relation to the detailed type of surgery undertaken, is planned.

The use of hormonal therapy for breast cancer appeared to decline significantly, nationally and in all regions. One possible interpretation is that this indicates more appropriate use, i.e. reduction in use of hormonal-therapy for patients who were negative for both oestrogen-receptor and progesterone-receptor status. However, data collected by NCR for the period covered here are not sufficient to examine directly trends in the proportions of cases tested for receptor status or in case-by-case appropriateness of hormonal therapy. We cannot exclude the possibility that hormonal therapy has been less completely recorded in hospital notes in more recent years, if there has been any substantial increase in outpatient (or non-hospital) prescribing of tamoxifen.

Significant increases in the use of chemotherapy (nationally and in almost all regions) do suggest, at least in part, improved targeting of therapies. This may include the appropriate use of chemotherapy for higher-risk patients, with more advanced or aggressive disease or with tumours not treatable hormonally.

Regional variation in treatment

For overall treatment and surgical treatment, regional variations were minor and likely to be of little practical consequence. This is not unexpected, as the vast majority of breast cancer patients will at least have surgery. For the other (largely adjuvant) modalities, however, there was marked regional variation, especially for radiotherapy and hormonal therapy.

Regional variation in the use of radiotherapy could not readily be accounted for by differences in patient or tumour characteristics between regions. However, it is noteworthy that radiotherapy use was highest (during 1994-2001 overall) for patients from the Eastern and Southern regions, the locations of the main radiotherapy centres in Ireland during those years. Also, patients from the Midland and North-Eastern regions were equally likely to receive radiotherapy as patients from the immediately adjacent Eastern region. Local availability of radiotherapy, and interplay between this and surgical treatment, may be the most important factors influencing regional variation in receipt of radiotherapy. In particular, breast cancer patients who opt for, or are recommended, breast-conserving surgery will generally require adjuvant radiotherapy, to a greater extent than patients who have a mastectomy (total breast-removal). Further planned analyses will examine regional variation in the breast-conserving surgery in relation to radiotherapy availability and other factors.

Patients from all regions other than the Eastern region were significantly more likely to receive hormonal therapy than those from the Eastern region. For one region (Southern), patients were twice as likely to receive hormonal therapy, particularly in the more recent diagnosis period (1998-2001). This variation could not be accounted for by available data on patient and tumour characteristics. This, combined with the geographic patterns seen, may suggest that institutional or other geographically-related healthcare factors were the main determinants of the extent to which hormonal therapy was used.

Treatment: international context

Comparisons are made here with first-course treatments reported for cancers in the USA as part of the National Cancer Data Base (http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm). Possible differences between the Irish and US data in the timing of treatment included should be borne in mind, but the data should be broadly comparable.

Patients in Ireland were significantly less likely to have surgery, or to a lesser extent radiotherapy, than in the USA (*Table 3.7.2*). The proportion of patients having chemotherapy or hormonal therapy appeared to be higher in Ireland, but the US figures do not explicitly show all cases that may have had these treatments. Of the specific single or multi-modal treatments reported, Irish patients were significantly less likely to have surgery only, surgery plus radiotherapy, or all four modalities, but significantly more likely to have surgery plus chemotherapy, surgery plus chemotherapy plus radiotherapy, or surgery plus hormonal therapy. Differences between Ireland and the USA were highest for cases having surgery only, with 10% of Irish cases but 25% of US cases having this treatment. This difference is seen across all age-groups, though perhaps greatest for older patients. The most likely explanation is that patients in the USA have, on average, less advanced disease and are thus less likely to be recommended systemic adjuvant treatment (chemotherapy or hormone therapy).

Further work is required to assess in more detail the extent to which treatment in Ireland reflects current national or international guidelines or best practice (e.g. *Appendix 1*; Walsh & O'Higgins, 2000).

Table 3.7.2 Comparison of main treatment modalities and combinations for female patients with invasive breast cancer, Ireland and USA, in diagnosis period 1998-2001. US data were not specified in detail for some treatments.

	Ireland 1998-2001		**USA[a©] 1998-2001**
any treatment	96.0%		-
no treatment	4.0%		-
any surgery	85.1%	***	94.2%
any chemotherapy	45.2%	-	[c]≥35.8%
any radiotherapy	44.1%	***	≥46.4%
any hormonal therapy	43.3%	-	≥33.4%
surgery + chemo	17.6%	***	10.5%
surge + chemo + radio	13.7%	*	12.8%
surge + hormo + radio	12.8%	ns	13.5%
surgery + hormone	12.5%	***	7.3%
surgery only	9.8%	***	24.8%
surgery + radio	8.3%	***	11.5%
sur + che + hor + rad	6.5%	***	8.6%
hormone only	5.7%	-	-
surge + chemo + horm	4.0%	ns	3.9%
chemotherapy only	1.8%	-	-
hormone + radio	0.9%	-	-
radiotherapy only	0.9%	-	-
others	1.5%	-	-

- = data not available or statistical comparison not possible.
[a]Source of US data: National Cancer Data Base of first-course treatments reported by hospitals approved by the American College of Surgeons Commission on Cancer; cases of stage 0 have been excluded but cases of unknown stage have been included and assumed to be invasive; see http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm.

[b]US surgical data are for surgery of primary site only.
[c]≥ indicates that overall use of these treatments among patients in the USA may be higher than shown, as figures for less frequent single modalities or combinations of modalities are not quoted on the NCDB website.

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Chapter 4. COLORECTAL CANCER

Summary

Trends in incidence, mortality and patient/tumour characteristics

Numbers of cases, but not deaths, showed a significant upward trend between 1994 and 2001. Age-standardized incidence rates appeared to be stable; increases in case-numbers largely reflected population increases and ageing. Age-standardized mortality rates declined significantly for females but not for males.

Overall, there was little evidence of any move towards earlier detection of colorectal cancers or improvements in the completeness or specificity of diagnostic and prognostic investigations.

Survival

1994-2001 average

Relative survival to five years after diagnosis was estimated as 49.2% (95% CI 48.1-50.3%) for 1994-2001 as a whole; 48.1% (46.6-49.5%) for males, 50.7% (49.1-52.2%) for females.

Survival trends

Five-year survival showed a clear improvement from 47.7% (95% CI 46.1-49.1%) for cases diagnosed during 1994-97 to 51.0% (49.3-52.6%) for 1998-2001. This improvement was also evident (and statistically significant) after adjustment for age, stage and other variables. It involved a 10% reduction in age-adjusted excess risk of death (i.e. the risk having allowed for expected background mortality), or a 22% reduction in excess risk after adjustment for other tumour or patient variables. Only the Western region showed a significant increase in relative survival between diagnosis-periods 1994-97 and 1998-2001, but the trends in most regions were consistent with the national improvement in survival.

Much of the improvement in survival seems likely to reflect improvements in the quality of treatment and in proportions of patients receiving appropriate treatment. Data indicating increased chemotherapy and radiotherapy use, in particular, may support this. Further improvements in survival can be expected once screening becomes more widespread.

Regional variation in survival

Taking account of a wide range of patient and tumour characteristics, three regions had a significantly high excess risk of death during 1994-2001: Mid-Western (15% higher than Eastern), Southern (24% higher) and South-Eastern (10% higher). Only the Southern region had significantly low survival (high excess risk) for 1994-97 cases, and the Southern and Mid-Western regions for 1998-2001 cases. Adjustment for patient and tumour characteristics appeared to moderate the extent and magnitude of regional variation in survival to some extent. The remaining variation may be accounted for by unmeasured variables, or regional variation in treatment, or both. Patients from the two regions with the highest excess mortality risk (Mid-Western and Southern) were the least likely to receive chemotherapy and radiotherapy.

International comparison of survival

Five-year relative survival estimates for Irish men and women diagnosed with colorectal cancer during 1994-97 were similar to or slightly lower than European averages based on cases diagnosed during 1990-94.

Treatment

Proportions of patients treated: main modalities and combinations

83% of cases diagnosed during 1994-2001 had some form of definitive or tumour-directed treatment within six months of diagnosis, 77% had surgical treatment, 28% had chemotherapy and 12% had radiotherapy. Equivalent figures for 1998-2001 were 84% treated, 77% surgery, 33% chemotherapy and 14% radiotherapy. The most frequent treatments or combinations were surgery only (51% of cases 1994-2001), surgery plus chemotherapy (18%), and surgery plus chemotherapy plus radiotherapy (6.1%).

Region of treatment versus region of residence

The majority of patients resident in each region had their main surgical treatment in the same region, ranging from 75% of surgical patients from the North-Eastern region to 99% of those from the Southern region.

Hospital caseloads

59 hospitals treated colorectal cancers surgically during 1994-2001. There was no strong evidence of any trend in numbers of hospitals providing surgical treatment. About one-fifth of hospitals in any given year treated fewer than 10 surgical cases

each; two-fifths treated fewer than 20, and over three-quarters treated fewer than 50 cases. There was a modest tendency for average hospital caseload to increase during the period 1994-2001. Significant declines were seen in the proportions of surgical cases treated in 'low volume' hospitals (if defined using thresholds of <10 and <50 cases annually, but not using <20 cases).

Surgical consultant caseloads

At least 293 individual consultants were responsible for surgical management of colorectal cancers during 1994-2001, 197 in 1994-97 and 241 during 1998-2001. About one-quarter of surgical consultants in any given year treated fewer than 10 surgical cases each, and over half treated fewer than 20 surgical cases. There was some evidence of a decline in the proportion of patients treated by consultants with low average caseloads.

Treatment trends

Use of surgery, nationally, fell significantly between 1996 and 2001, by about 1.5% annually after adjustment for age and stage. Significant age-adjusted declines were seen for the Midland (3.8% per year) and North-Eastern regions (2.4%).

Radiotherapy use increased between 1996 and 2001, by 11% annually overall and 16-43% annually in four of the eight regions (Midland, North-Eastern, Southern and South-Eastern) (adjusted for age and sex).

The proportion of patients having chemotherapy also increased (by 13% annually between 1996 and 2001) after adjustment for age, sex, and stage. Similar or more marked (age- and sex-adjusted) increases were seen for five regions (Eastern, North-Eastern, Southern, South-Eastern and Western), by 10-31% annually.

Regional variation in treatment

For 1994-2001, there was significantly low use of surgery in patients from the Midland and South-Eastern regions and significantly high use in those from the Mid-Western and Western regions. compared with the Eastern region, adjusted for age, stage and other variables. Regional variation was less marked for cases diagnosed during 1998-2001 than for 1994-97.

Patients from the Mid-Western, North-Eastern, Southern and Western regions were significantly (and substantially) less likely to have radiotherapy than those from the Eastern region during 1994-2001. Variation appeared to be more marked in the 1994-97 diagnosis period. During 1998-2001, patients from the Midland region were more likely to have radiotherapy than those from the Eastern region, a reversal of the pattern seen in the earlier period.

There was significantly low use of chemotherapy among patients from the Mid-Western and Southern regions (24-29% lower than patients from the Eastern region), and significantly high use among those from the North-Western and South-Eastern regions (26-31% higher)

Interpreting the variations seen in treatment, and the extent to which they can be accounted for by patient or tumour characteristics, is difficult. Some relevant variables may not have been measured or included. However, it seems likely that a substantial proportion of the variation in radiotherapy and chemotherapy use for colorectal cancer reflects regional or institutional differences in the extent to which given treatments were offered or provided.

International comparison of treatment

For both colon and rectal cancer, Irish patients were significantly less likely to receive overall treatment or surgical treatment than in the USA during 1998-2001. For rectal cancer, significantly smaller proportions of Irish patients had radiotherapy and chemotherapy but more had surgery. Surgery as was significantly less frequent for Irish colon cancer cases. Use of the main multimodal therapy for colon cancer (surgery plus adjuvant chemotherapy) was similar in Ireland and the US, but that for rectal cancer (surgery plus radiotherapy and chemotherapy) was less frequent in Ireland.

4.1 Incidence and mortality statistics

On average, there were 1821 cases of and 930 deaths from invasive colorectal cancer annually in Ireland during 1994-2001 (*Table 4.1.1*). Over this period, numbers of cases showed a significant upward trend, but numbers of deaths showed no significant trend. Age-standardized incidence rates appeared to be stable, thus increases in case-numbers largely reflected population increases and ageing. Age-standardized mortality rates declined significantly for females but showed no trend for males.

Table 4.1.1 Incidence of and mortality from invasive colorectal cancer, Republic of Ireland, 1994-2001.

	annual average numbers						age-standardized rate[a]			
1994-2001	**total**		**male**		**female**		**male**		**female**	
Incidence (cases)	1821		1029		792		65.0		40.3	
Incidence trend (per year)[b]	+1.5%	***	+1.8%	***	+1.1%	*	+0.1%	ns	-0.3%%	ns
Mortality (deaths)	930		526		404		33.2		19.1	
Mortality trend (per year)	-0.3%	ns	+0.7%	ns	-1.5%	ns	-0.8%	ns	-2.8%	*

[a]European age-standardized rate per 100,000 persons per year.
[b]Estimated annual percentage change (ns not significant, * P<0.05, **P<0.01, ***P<0.001).

4.2 Cases included for treatment and survival analyses; patient and tumour characteristics

Analyses cover invasive cancers of the colon (ICD-10 code C18), rectosigmoid junction (C19), rectum (C20) and anus (C21), diagnosed in 13,702 persons aged 15-99 years during 1994-2001. Full details of exclusion/inclusion criteria are shown in *Table 4.2.1*.

Table 4.2.1 Summary of inclusions and exclusions for colorectal cancer analyses.

Case definition	**total**
all registered tumours[a]	15 685
ages 15-99 only	15 656
excluding death-certificate-only & autopsy-only cases	15 206
invasive tumours only	14 318
first tumours only[b]	**13 702**

[a]Including in situ carcinomas, and tumours of unspecified behaviour, but excluding lymphomas (classified separately within ICD-10) [b]Or most serious tumour diagnosed same date.

A breakdown of basic patient and tumour characteristics is given in Table *4.2.2*, including comparisons between diagnosis periods 1994-97 and 1998-2001. The variables and category-values shown are those considered, later in this chapter, for inclusion in statistical models aimed at describing and if possible explaining regional variation and time-trends in survival and treatment.

Statistically significant changes between 1994-97 and 1998-2001 in proportions of patients or tumours with particular characteristics were:

- Decrease in stage I cancers, increase in stage III.
- Decrease in tumours in T2 and T3 categories, increase in T4.
- Increase in node-positive cancers.
- Decrease in cases with unknown metastatic status.
- Decrease in tumours sited in colon, increase in rectum/anus.
- Decrease in grade 1 tumours, increase in grade 2 and grade unknown.
- Increase in microscopically verified (MV) cases, decrease in non-MV cases.
- Decrease in symptomatic cases, increase in screen-detected cases and unknown method of presentation.
- Decrease in patients with marital status unknown.
- Decrease in smokers, increase in patients with unknown smoking status.

Overall, these changes provide little evidence of any move towards earlier detection of colorectal cancers or improvements in the completeness or specificity of diagnostic and prognostic investigations.

Variation in patient and tumour characteristics by region of residence is summarized in *Table 4.2.3*.

Table 4.2.2 Summary of patient and tumour characteristics for colorectal cancer patients included in survival and treatment analyses, 1994-2001.

	diagnosed 1994-2001		diagnosed 1994-1997		diagnosed 1998-2001	
	number	% of cases	number	% of cases	number	% of cases
total	13702		6708		6994	
age 15-44	486	3.5%	233	3.5%	253	3.6%
age 45-54	1297	9.5%	615	9.2%	682	9.8%
age 55-64	2734	20.0%	1351	20.1%	1383	19.8%
age 65-74	4491	32.8%	2234	33.3%	2257	32.3%
age 75+	4694	34.3%	2275	33.9%	2419	34.6%
male	7768	56.7%	3786	56.4%	3982	56.9%
female	5934	43.3%	2922	43.6%	3012	43.1%
stage I	1118	8.2%	605	9.0%	513	*7.3%
stage II	2205	16.1%	1107	16.5%	1098	15.7%
stage III	1826	13.3%	829	12.4%	997	*14.3%
stage IV	2908	21.2%	1397	20.8%	1511	21.6%
stage X[a]	5645	41.2%	2770	41.3%	2875	41.1%
T1	702	5.1%	356	5.3%	346	4.9%
T2	2043	14.9%	1056	15.7%	987	*14.1%
T3	6728	49.1%	3371	50.3%	3357	*48.0%
T4	1984	14.5%	858	12.8%	1126	*16.1%
T X	2245	16.4%	1067	15.9%	1178	16.8%
N negative	5751	42.0%	2861	42.7%	2890	41.3%
N positive	4316	31.5%	2038	30.4%	2278	*32.6%
N X	3635	26.5%	1809	27.0%	1826	26.1%
M negative	5827	42.5%	2817	42.0%	3010	43.0%
M positive[b]	2924	21.3%	1404	20.9%	1520	21.7%
M X	4951	36.1%	2487	37.1%	2464	*35.2%
grade 1	1396	10.2%	805	12.0%	591	*8.5%
grade 2	7340	53.6%	3503	52.2%	3837	*54.9%
grade 3+	1794	13.1%	906	13.5%	888	12.7%
grade X	3172	23.1%	1494	22.3%	1678	*24.0%
colon	8518	62.2%	4250	63.4%	4268	*61.0%
rectosigmoid	1072	7.8%	538	8.0%	534	7.6%
rectum/anus	4112	30.0%	1920	28.6%	2192	*31.3%
MV[c] yes	12558	91.7%	6138	91.5%	6420	91.8%
MV no	1045	7.6%	515	7.7%	530	7.6%
MV X	99	0.7%	55	0.8%	44	0.6%
symptomatic	13037	95.1%	6453	96.2%	6584	*94.1%
incidental	160	1.2%	80	1.2%	80	1.1%
screen detected	44	0.3%	14	0.2%	30	*0.4%
presentation X	461	3.4%	161	2.4%	300	*4.3%
non-smoker	5995	43.8%	2985	44.5%	3010	43.0%
ex-smoker	2217	16.2%	1057	15.8%	1160	16.6%
smoker	2740	20.0%	1404	20.9%	1336	*19.1%
smoking X	2750	20.1%	1262	18.8%	1488	*21.3%
ever married	10740	78.4%	5237	78.1%	5503	78.7%
never married	2503	18.3%	1234	18.4%	1269	18.1%
marital status X	459	3.3%	237	3.5%	222	3.2%

[a]Unknown values shown as "X" for stage and other variables. [b]Minor discrepancies between stage IV and M positive cases reflect morphologies for which TNM staging is not strictly applicable. [c]MV = microscopic verification (histology or cytology).
*Significant change in the proportion of cases in this category (χ^2 test, 1 df, $P<0.05$); but note that some further changes may be significant if cases in "unknown" categories are excluded.

Table 4.2.3 Summary of patient and tumour characteristics, by region of residence, for colorectal cancer patients included in survival and treatment analyses, 1994-2001. Account is taken of the potential confounding affect of these variables in statistical models of regional variation in survival (*section 4.4.4*) and treatment (*section 4.6.3*).

	Eastern	Mid-Western	Midland	North-Eastern	North-Western	Southern	South-Eastern	Western
total cases	4461	783	1057	1180	951	2315	1479	1476
age 15-44	3.5%	3.4%	3.9%	3.2%	2.5%	3.4%	4.6%	3.7%
age 45-54	9.7%	7.7%	10.8%	9.7%	10.0%	9.1%	8.8%	9.5%
age 55-64	21.3%	20.2%	21.2%	20.8%	*16.0%	19.5%	20.8%	*16.7%
age 65-74	33.1%	33.8%	33.0%	33.3%	30.4%	32.4%	32.4%	33.1%
age 75+	32.4%	34.9%	31.1%	33.0%	*41.1%	*35.6%	33.5%	*37.1%
male	54.3%	55.4%	*62.6%	*57.9%	54.4%	55.7%	*57.8%	*61.3%
female	45.7%	44.6%	*37.4%	*42.1%	45.6%	44.3%	*42.2%	*38.7%
stage I	8.1%	*12.9%	*10.8%	*4.4%	*10.7%	8.3%	9.4%	*3.9%
stage II	17.2%	20.2%	18.8%	*10.4%	16.7%	*13.5%	*20.1%	*12.7%
stage III	14.2%	13.5%	14.4%	*8.1%	13.7%	*10.5%	*17.3%	14.2%
stage IV	21.5%	*17.1%	20.2%	23.7%	20.1%	20.3%	*24.3%	20.3%
stage X	39.0%	36.3%	35.8%	*53.3%	38.8%	*47.4%	*28.8%	*49.0%
T1	4.5%	4.3%	4.4%	*7.3%	*6.2%	*7.3%	3.4%	3.9%
T2	14.5%	*19.5%	*18.4%	13.9%	14.5%	16.0%	13.9%	*11.7%
T3	51.3%	50.1%	48.3%	52.9%	49.0%	*42.3%	*46.7%	52.6%
T4	13.6%	*8.6%	13.0%	13.6%	16.0%	*17.4%	*18.3%	12.7%
T X	16.1%	17.5%	16.0%	*12.3%	14.3%	17.0%	17.8%	*19.0%
N negative	43.0%	43.0%	42.7%	42.8%	39.9%	43.5%	44.2%	*33.8%
N positive	31.8%	30.9%	*25.4%	32.6%	34.9%	*28.7%	33.9%	34.0%
N X	25.1%	26.1%	*31.9%	24.6%	25.2%	*27.9%	*21.8%	*32.2%
M negative	45.7%	*52.6%	*53.5%	*25.1%	45.2%	*35.1%	*52.1%	*34.1%
M positive	21.6%	*17.4%	20.5%	23.9%	20.2%	20.3%	*24.3%	20.5%
M X	32.7%	30.0%	*26.0%	*51.0%	34.6%	*44.5%	*23.6%	*45.5%
grade 1	3.5%	*39.8%	*35.4%	*10.8%	*5.3%	*5.4%	*6.9%	*10.2%
grade 2	66.4%	*24.3%	*29.3%	*50.5%	*54.0%	*58.1%	*56.7%	*39.6%
grade 3+	12.5%	11.9%	*9.7%	12.5%	*20.5%	13.2%	*9.0%	*17.6%
grade X	17.6%	*24.0%	*25.5%	*26.2%	20.2%	*23.3%	*27.5%	*32.5%
colon	61.3%	64.9%	60.5%	64.5%	*67.2%	63.2%	61.3%	58.6%
rectosigmoid	8.2%	6.6%	9.7%	7.3%	9.8%	*5.0%	7.8%	9.7%
rectum/anus	30.5%	28.5%	29.7%	28.2%	*23.0%	31.8%	31.0%	31.7%
MV yes	94.9%	*91.2%	*93.0%	*92.1%	*91.0%	*87.0%	*89.2%	*91.1%
MV no	4.3%	*8.0%	*6.1%	*7.4%	*8.6%	*12.8%	*9.3%	*8.1%
MV X	0.8%	0.8%	0.9%	0.5%	0.4%	*0.2%	*1.5%	0.8%
symptomatic	92.3%	*96.3%	93.8%	*96.9%	*98.3%	*97.7%	*95.5%	*96.2%
incidental	1.4%	0.9%	*0.5%	1.1%	*0.2%	1.8%	0.9%	0.9%
screen detected	0.6%	0.0%	0.3%	0.1%	0.4%	*0.1%	0.3%	0.2%
presentation X	5.7%	*2.8%	5.5%	*1.9%	*1.1%	*0.3%	*3.3%	*2.6%
non-smoker	35.7%	*45.8%	*43.6%	*39.9%	*44.4%	*54.9%	*48.0%	*48.1%
ex-smoker	18.4%	*13.7%	16.4%	18.8%	18.7%	*10.7%	*14.0%	17.9%
smoker	19.4%	19.8%	20.5%	19.5%	20.9%	20.1%	19.3%	*21.8%
smoking status X	26.6%	*20.7%	*19.5%	*21.8%	*16.0%	*14.3%	*18.7%	*12.2%
ever married	79.3%	77.0%	76.5%	79.7%	76.4%	78.3%	79.2%	77.2%
never married	16.4%	18.9%	18.4%	16.9%	*22.6%	*19.3%	17.8%	*20.6%
marital status X	4.3%	4.1%	5.1%	3.3%	*0.9%	*2.5%	*3.0%	*2.2%

*Significant difference in proportion of cases, compared with Eastern region (χ^2 test, 1 df, P<0.05)

4.3 Relative survival: descriptive analysis

Five-year relative survival estimates for national population, by period of diagnosis, age, sex and other patient or tumour characteristics, are shown in *Table 4.3.1*. Survival curves, to five years after diagnosis, are plotted for the same variables in *Figure 4.3.1*. Five-year survival estimates by treatment status are shown in *Table 4.3.2*; by sex and region in *Table 4.3.3*; and one-year, three-year and five-year estimates, nationally and regionally by diagnosis period, in *Table 4.3.4*.

Results and comparisons presented in this section are not adjusted for potential confounding variables, thus are potentially open to misinterpretation if taken at face value. More formal (multivariate) comparisons are made in *section 4.4*.

4.3.1 General summary

For colorectal cancer cases diagnosed in Ireland during 1994-2001 as a whole, relative survival to five years after diagnosis was estimated as 49.2% (95% CI 48.1-50.3%) (*Table 4.3.1*). Equivalent figures for males were 48.1% (46.6-49.5%), for females 50.7% (49.1-52.2%). Relative survival to one year averaged 70.2% (69.3-71.0%), and to three years 54.7% (53.7-55.6%) (*Table 4.3.4*).

4.3.2 Variation by patient and tumour characteristics

In general, relative survival (to five years) was highest for age-groups under 65 or 75 years or, for other specific variables, cases that were early stage; T category 1 or 2; node-negative; non-metastatic; grade 1 or 2; microscopically verified; screen-detected; or in non-smokers, ex-smokers or patients who were ever married (*Table 4.3.1* & *Figure 4.3.1*). Survival was lowest in the oldest age-group (75+), and, for other variables, cases that were stage IV; T category 4 or unknown; node-positive or nodal status unknown; metastatic; grade 3+ or unknown; lacking microscopic verification (or with MV status unknown); or in smokers, or patients with unknown smoking or marital status. Note however that patients in a given univariate category may differ with respect to other characteristics - see section *4.4.1* for multivariate comparisons.

4.3.3 Variation by treatment status

Patients who received any tumour-directed treatment, or surgery, within six months of diagnosis had substantially higher five-year survival than patients who did not receive these treatments: averaging 57% v 12% for treatment v no treatment, and 60% v 12% for surgery v no surgery for 1994-2001 as a whole (*Table 4.3.2*). In contrast, survival was slightly lower overall in patients who had radiotherapy compared with those did not, though this was mainly apparent for earlier diagnosis years (1994-97). No differences were apparent between patients who did and did not have chemotherapy. However, since patients given or not given particular treatments may have differed greatly in disease stage or other characteristics, these figures do not provide any measure of treatment effectiveness.

4.3.4 National and regional trends

National estimates of five-year survival showed a clear improvement from 47.7% (95% CI 46.1-49.1%) for cases diagnosed during 1994-97 to 51.0% (49.3-52.6%) for 1998-2001 (*Table 4.3.1, Figure 4.3.1*). Patients from most regions also showed evidence of improvements, but less clear-cut in terms of statistical significance (*Table 4.3.4*). See sections *4.4.2-3* for more formal comparisons, adjusted for age or other factors.

4.3.5 Regional variation

Five-year relative survival estimates during 1994-2001 ranged from 46.3% (95% CI 43.0-49.6%) for patients from the Western region to 52.4% (48.6-56.0%) for the North-Eastern region (*Table 4.3.4*). However, precise rankings varied between diagnosis periods, and these comparisons may be influenced by age or other factors (cf. *section 4.4.4*).

Table 4.3.1 National five-year relative survival for colorectal cancer patients, by patient and tumour characteristics, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population.

	1994-2001		1994-1997		1998-2001	
	5-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	49.2%	(48.1%-50.3%)	47.7%	(46.1%-49.1%)	*51.0%	(49.3%-52.6%)
age 15-44	53.2%	(48.4%-57.8%)	50.2%	(43.5%-56.4%)	58.1%	(51.1%-64.4%)
age 45-54	54.0%	(51.0%-56.9%)	49.9%	(45.8%-53.9%)	*59.6%	(55.3%-63.6%)
age 55-64	54.0%	(51.8%-56.0%)	50.6%	(47.6%-53.3%)	*57.8%	(54.4%-61.0%)
age 65-74	50.1%	(48.3%-51.9%)	48.4%	(45.9%-50.8%)	52.0%	(49.2%-54.7%)
age 75+	44.8%	(42.5%-47.1%)	45.9%	(42.7%-49.0%)	43.1%	(39.7%-46.5%)
male	48.1%	(46.6%-49.5%)	46.4%	(44.4%-48.4%)	50.1%	(47.9%-52.3%)
female	50.7%	(49.1%-52.2%)	49.1%	(46.9%-51.2%)	52.1%	(49.6%-54.5%)
stage I	88.1%	(84.4%-91.4%)	87.9%	(83.1%-92.2%)	87.7%	(81.5%-93.0%)
stage II	74.1%	(71.3%-76.8%)	72.7%	(68.9%-76.2%)	75.4%	(70.9%-79.5%)
stage III	51.6%	(48.5%-54.6%)	46.2%	(42.2%-50.2%)	*56.8%	(52.0%-61.4%)
stage IV	7.9%	(6.7%-9.1%)	7.5%	(6.1%-9.1%)	8.1%	(6.3%-10.0%)
stage X[a]	52.3%	(50.6%-54.0%)	49.8%	(47.4%-52.0%)	*55.5%	(52.9%-58.0%)
T1	80.7%	(76.0%-85.0%)	79.3%	(72.8%-85.1%)	80.5%	(72.6%-87.3%)
T2	77.0%	(74.1%-79.6%)	74.7%	(70.8%-78.2%)	80.3%	(75.9%-84.3%)
T3	55.4%	(53.7%-56.9%)	51.4%	(49.2%-53.4%)	*59.8%	(57.3%-62.2%)
T4	18.5%	(16.4%-20.6%)	16.9%	(14.2%-19.8%)	19.6%	(16.5%-22.8%)
T X	22.5%	(20.4%-24.6%)	23.2%	(20.2%-26.3%)	22.2%	(19.3%-25.2%)
N negative	72.8%	(71.0%-74.4%)	71.2%	(68.8%-73.4%)	74.7%	(72.0%-77.2%)
N positive	37.2%	(35.4%-39.0%)	33.6%	(31.2%-35.9%)	*40.8%	(37.9%-43.6%)
N X	26.0%	(24.3%-27.8%)	26.5%	(24.1%-29.0%)	25.7%	(23.2%-28.2%)
M negative	67.0%	(65.2%-68.6%)	65.9%	(63.5%-68.1%)	67.8%	(65.1%-70.3%)
M positive[b]	8.1%	(6.9%-9.2%)	7.8%	(6.3%-9.4%)	8.2%	(6.5%-10.1%)
M X	52.9%	(51.0%-54.6%)	49.7%	(47.2%-52.1%)	*56.9%	(54.1%-59.6%)
grade 1	59.2%	(55.7%-62.6%)	59.0%	(54.5%-63.2%)	59.4%	(53.1%-65.3%)
grade 2	56.4%	(54.9%-57.9%)	53.7%	(51.6%-55.7%)	*59.2%	(56.9%-61.4%)
grade 3+	40.0%	(37.2%-42.8%)	38.6%	(34.8%-42.3%)	41.5%	(37.1%-45.8%)
grade X	33.4%	(31.3%-35.4%)	32.7%	(29.8%-35.5%)	34.2%	(31.2%-37.1%)
colon	50.1%	(48.6%-51.4%)	49.1%	(47.2%-50.9%)	51.4%	(49.3%-53.4%)
rectosigmoid	47.8%	(43.9%-51.5%)	44.9%	(39.8%-49.9%)	50.1%	(43.9%-56.1%)
rectum/anus	47.9%	(45.9%-49.8%)	45.3%	(42.6%-47.8%)	50.4%	(47.4%-53.3%)
MV yes	52.9%	(51.7%-53.9%)	51.1%	(49.6%-52.6%)	*54.7%	(52.9%-56.4%)
MV no	7.7%	(5.7%-10.0%)	7.5%	(4.9%-10.8%)	8.2%	(5.4%-11.7%)
MV X	19.5%	(11.1%-30.0%)	24.9%	(12.8%-40.1%)	13.3%	(4.2%-28.7%)
symptomatic	48.9%	(47.8%-50.0%)	47.4%	(45.9%-48.9%)	*50.6%	(48.9%-52.2%)
incidental	49.5%	(39.5%-59.2%)	51.5%	(37.7%-65.0%)	45.6%	(30.6%-60.4%)
screen detected	86.0%	(64.9%-99.0%)	101.4%	(63.7%-113%)	80.9%	(55.7%-95.8%)
presentation X	54.7%	(48.4%-60.8%)	50.2%	(40.7%-59.4%)	59.4%	(51.1%-67.2%)
non-smoker	53.0%	(51.3%-54.6%)	51.7%	(49.4%-53.8%)	54.5%	(51.9%-56.9%)
ex-smoker	50.6%	(47.8%-53.3%)	48.2%	(44.3%-51.9%)	53.5%	(49.2%-57.7%)
smoker	44.3%	(42.0%-46.6%)	42.1%	(39.0%-45.1%)	47.2%	(43.5%-50.7%)
smoking X	45.0%	(42.6%-47.3%)	43.9%	(40.6%-47.2%)	45.6%	(42.1%-49.0%)
ever married	51.0%	(49.7%-52.2%)	49.7%	(47.9%-51.3%)	52.5%	(50.6%-54.3%)
never married	43.9%	(41.4%-46.4%)	40.9%	(37.6%-44.2%)	46.8%	(42.9%-50.5%)
marital status X	37.2%	(31.8%-42.6%)	38.2%	(31.0%-45.5%)	36.7%	(28.3%-45.4%)

[a]Unknown values shown as "X" for stage, T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status. [b]Minor discrepancies between Stage IV and M+ cases are because some M+ cases were of morphologies (e.g. carcinoid tumours) for which TNM staging is not strictly applicable for this site. *Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

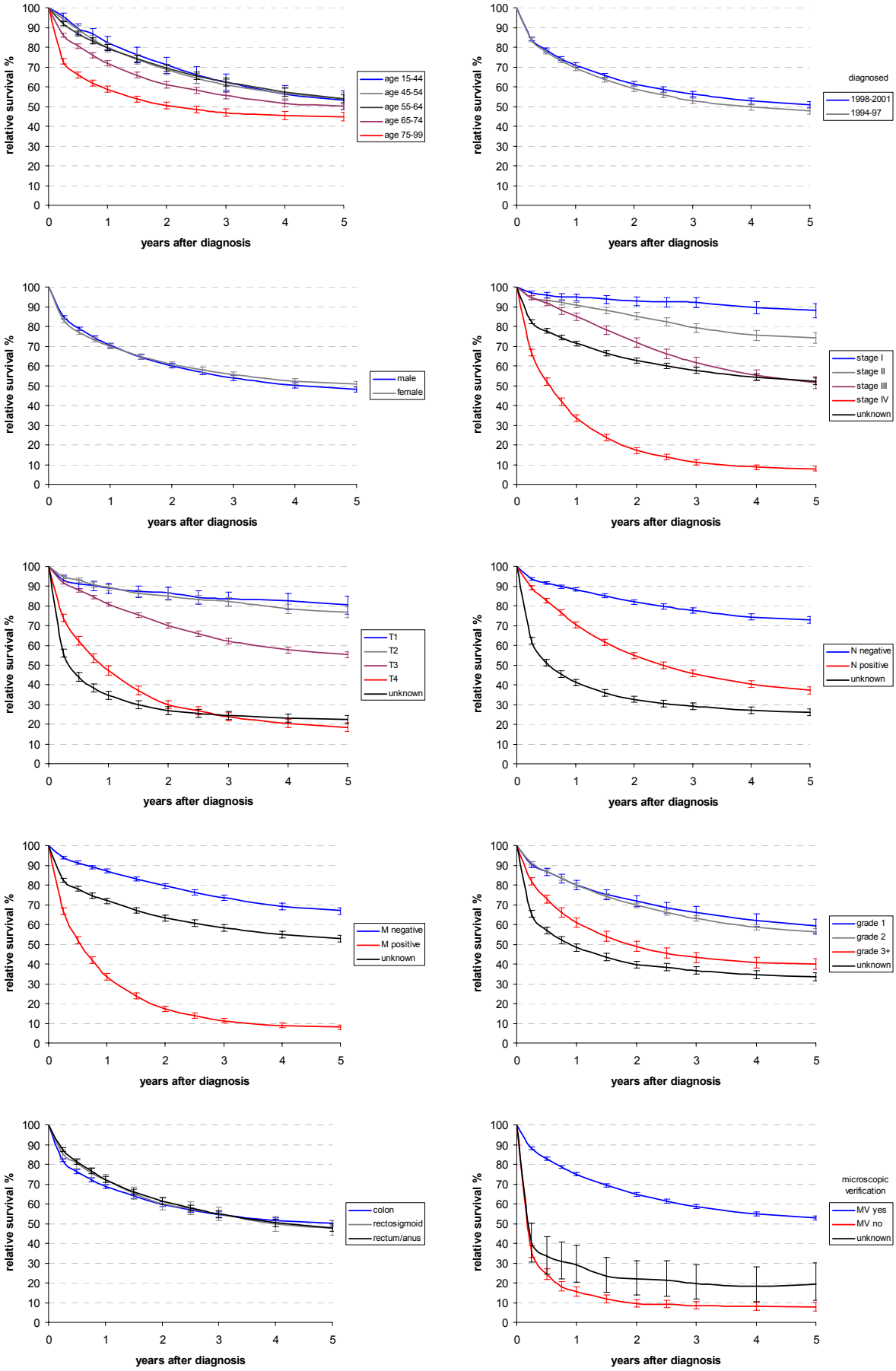
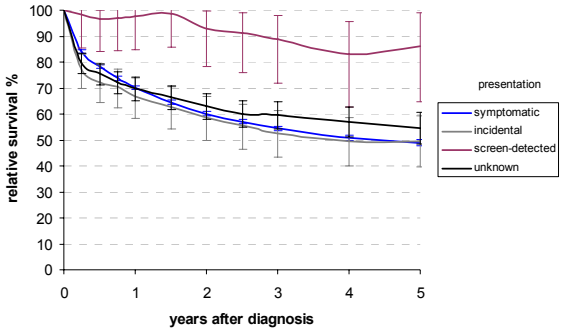
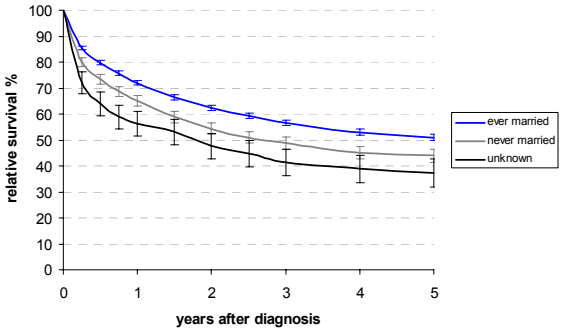


Figure 4.3.1 Relative survival up to five years after diagnosis for colorectal cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown.





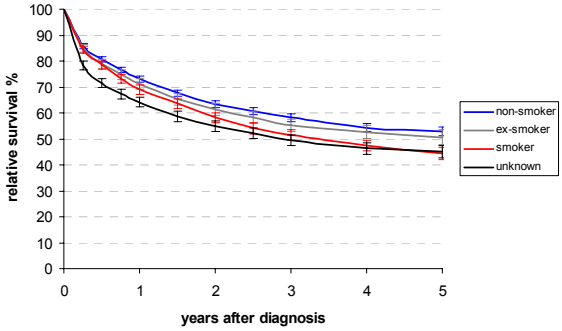


Figure 4.3.1 Relative survival up to five years after diagnosis for colorectal cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown. the general population (from the same region for regional estimates).

Figure 4.3.1 (continued)

Table 4.3.2 National five-year relative survival for colorectal cancer patients, by treatment status (within six months of diagnosis) and period of diagnosis, 1994-2001. Patients treated and not treated are likely to differ markedly in disease stage, age or other characteristics, thus *differences in survival between treated and untreated patients below should not be interpreted as reflecting the effect of treatment*.

	1994-2001		1994-1997		1998-2001	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	49.2%	(48.1%-50.3%)	47.7%	(46.1%-49.1%)	*51.0%	(49.3%-52.6%)
treatment	56.8%	(55.5%-57.9%)	55.4%	(53.7%-56.9%)	58.3%	(56.5%-60.1%)
no treatment	12.4%	(10.7%-14.1%)	12.4%	(10.2%-14.7%)	12.7%	(10.2%-15.3%)
surgery	59.8%	(58.5%-61.0%)	57.8%	(56.0%-59.4%)	*62.1%	(60.1%-63.9%)
no surgery	12.7%	(11.3%-14.1%)	11.7%	(9.8%-13.6%)	13.9%	(11.8%-16.1%)
radiotherapy	45.5%	(42.4%-48.5%)	39.8%	(35.4%-44.2%)	*49.1%	(44.8%-53.3%)
no radiotherapy	49.7%	(48.5%-50.8%)	48.5%	(46.9%-50.0%)	51.3%	(49.5%-53.0%)
chemotherapy	49.1%	(47.1%-50.9%)	45.2%	(42.4%-47.9%)	*52.4%	(49.6%-55.1%)
no chemotherapy	49.4%	(48.1%-50.7%)	48.7%	(46.9%-50.3%)	50.5%	(48.3%-52.5%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

Table 4.3.3 Five-year relative survival for colorectal cancer patients, unadjusted for age, by region of residence and sex, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population (from the same region for regional estimates).

Region	Total		Males		Females	
	5-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	49.2%	(48.1%-50.3%)	48.1%	(46.6%-49.5%)	50.7%	(49.1%-52.2%)
E	51.9%	(50.0%-53.8%)	50.8%	(48.1%-53.3%)	53.3%	(50.5%-55.9%)
M	48.8%	(44.2%-53.3%)	40.9%	(34.7%-47.1%)	57.6%	(50.8%-64.1%)
MW	49.7%	(45.7%-53.6%)	51.0%	(45.8%-56.0%)	47.7%	(41.5%-53.8%)
NE	52.4%	(48.6%-56.0%)	52.3%	(47.2%-57.3%)	52.4%	(46.8%-57.8%)
NW	49.3%	(45.1%-53.4%)	49.6%	(43.7%-55.3%)	49.0%	(43.1%-54.9%)
S	47.1%	(44.4%-49.7%)	45.8%	(42.2%-49.4%)	48.5%	(44.6%-52.3%)
SE	46.4%	(43.2%-49.6%)	46.4%	(42.1%-50.7%)	46.6%	(41.7%-51.3%)
W	46.3%	(43.0%-49.6%)	44.0%	(39.8%-48.2%)	49.9%	(44.5%-55.2%)

Table 4.3.4 One-year, three-year and five-year relative survival for colorectal cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001.

Region	1994-2001		1994-1997		1998-2001	
	1-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	70.2%	(69.3%-71.0%)	69.4%	(68.2%-70.5%)	71.0%	(69.8%-72.0%)
E	73.2%	(71.7%-74.5%)	73.4%	(71.3%-75.2%)	73.0%	(70.9%-74.8%)
M	70.7%	(67.1%-73.9%)	72.3%	(67.3%-76.8%)	69.0%	(63.7%-73.6%)
MW	71.5%	(68.4%-74.2%)	71.7%	(67.1%-75.8%)	71.2%	(67.1%-75.0%)
NE	72.4%	(69.5%-75.0%)	73.6%	(69.3%-77.4%)	71.3%	(67.4%-74.8%)
NW	66.9%	(63.5%-69.9%)	64.3%	(59.6%-68.7%)	69.6%	(64.9%-73.9%)
S	66.5%	(64.4%-68.5%)	65.3%	(62.2%-68.1%)	67.7%	(64.7%-70.4%)
SE	68.0%	(65.4%-70.4%)	65.8%	(62.0%-69.3%)	70.2%	(66.5%-73.5%)
W	69.0%	(66.3%-71.4%)	65.0%	(61.2%-68.6%)	*72.7%	(69.1%-75.9%)
	1994-2001		**1994-1997**		**1998-2001**	
	3-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	54.7%	(53.7%-55.6%)	53.0%	(51.5%-54.3%)	*56.4%	(55.0%-57.7%)
E	57.5%	(55.7%-59.1%)	56.2%	(53.8%-58.5%)	58.8%	(56.3%-61.0%)
M	55.5%	(51.3%-59.4%)	53.5%	(47.8%-59.0%)	57.6%	(51.6%-63.3%)
MW	55.0%	(51.4%-58.3%)	55.9%	(50.7%-60.8%)	54.2%	(49.4%-58.7%)
NE	58.0%	(54.7%-61.2%)	58.5%	(53.5%-63.1%)	57.7%	(53.1%-62.0%)
NW	53.2%	(49.4%-56.8%)	49.5%	(44.4%-54.5%)	57.3%	(51.9%-62.4%)
S	51.6%	(49.2%-53.9%)	50.0%	(46.6%-53.2%)	53.3%	(49.9%-56.4%)
SE	52.2%	(49.2%-55.0%)	50.4%	(46.3%-54.4%)	53.9%	(49.7%-57.9%)
W	52.1%	(49.1%-55.0%)	46.4%	(42.2%-50.5%)	57.6%	(53.4%-61.6%)
	1994-2001		**1994-1997**		**1998-2001**	
	5-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	49.2%	(48.1%-50.3%)	47.7%	(46.1%-49.1%)	*51.0%	(49.3%-52.6%)
E	51.9%	(50.0%-53.8%)	50.3%	(47.7%-52.8%)	54.3%	(51.4%-57.1%)
M	48.8%	(44.2%-53.3%)	47.8%	(41.8%-53.7%)	50.2%	(42.9%-57.2%)
MW	49.7%	(45.7%-53.6%)	51.0%	(45.4%-56.5%)	48.2%	(42.2%-54.0%)
NE	52.4%	(48.6%-56.0%)	53.1%	(47.8%-58.3%)	51.5%	(45.9%-56.9%)
NW	49.3%	(45.1%-53.4%)	45.7%	(40.2%-51.1%)	53.5%	(47.0%-59.9%)
S	47.1%	(44.4%-49.7%)	46.0%	(42.3%-49.5%)	47.9%	(43.9%-51.8%)
SE	46.4%	(43.2%-49.6%)	44.6%	(40.2%-48.8%)	48.4%	(43.3%-53.3%)
W	46.3%	(43.0%-49.6%)	41.0%	(36.7%-45.4%)	51.8%	(46.7%-56.8%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

4.4 Relative survival: modelling

4.4.1 Variation by patient and tumour characteristics

For assessment of regional variation in relative survival during 1994-2001, a full relative survival model was run, potentially incorporating and adjusting for available patient and tumour characteristics. These included year of follow-up (years 1 to 5 after diagnosis), age-group, stage-related variables (T, N and M categories), grade, interaction between those variables and year of follow-up, and additional patient and tumour variables without interaction terms (sex, tumour site, microscopic verification status, method of presentation, marital status, smoking status, year of diagnosis). Excluding region and year (covered later), and variables that did not contribute significantly to model-fit, statistically significant excess hazard ratios (EHRs) were recorded as follows:

- During year 1 of follow-up (for variables assessed using an interaction term for follow-up year):
  - Higher EHR (lower relative survival) for age-groups 55-64 years (1.348 [95% CI 1.073-1.694]), 65-74 (1.940 [1.557-2.417]) and 75+ (3.022 [2.427-3.763]), compared with age-group 15-44 years.
  - Higher EHR for T categories 3 (1.848 [1.409-2.422]), 4 (3.586 [2.739-4.696], and unknown or non-applicable (3.456 [2.645-4.517]), compared with T category 1.
  - Higher EHR for N positive (1.823 [1.638-2.030]) and N unknown cases (2.632 [2.332-2.971]), compared with N negative cases.
  - Higher EHR for M positive (4.133 [3.742-4.565]) and M unknown cases (1.487 [1.340-1.650], compared with M negative cases.
  - Higher EHR for grade 3+ (1.750 [1.500-2.042] and grade unknown cases (1.220 [1.047-1.422]), compared with grade 1.
- For age, stage-related and grade variables, EHRs varied significantly during subsequent follow-up and cannot readily be summarized beyond year 1.
- Overall (for variables assessed without an interaction term for follow-up year):
  - Lower EHR (higher relative survival) for female patients (0.936 [0.886-0.988)]), compared with males.
  - Higher EHR (lower relative survival) for cases lacking microscopic verification (1.991 [1.797-2.206]) or with unknown MV status (1.921 [1.487-2.480]).
  - Lower EHR for cases that were screen detected (0.382 [0.152-0.954]) or whose method of presentation was unknown (0.759 [0.643-0.897]), compared with cases presenting symptomatically.
  - Higher EHR for ex-smokers (1.121 [1.034-1.215]), current smokers (1.187 [1.105-1.274]) and patients of unknown smoking status (1.238 [1.150-1.332]), compared with non-smokers (never-smokers).
  - Higher EHR for patients who were never married (1.122 [1.050-1.199]), compared with those who were ever married.
- Tumour site did not significantly improve model fit, after adjustment for other variables, and was excluded from the full model.

These findings broadly confirmed the variations already noted for unadjusted relative survival (*Table 4.4.2*), for the overall period 1994-2001.

4.4.2 National and age-specific trends

Relative survival improved significantly (i.e. excess hazard ratios fell significantly) for Ireland as a whole between diagnosis periods 1994-97 and 1998-2001 (*Table 4.4.1*). The improvement represented a 10% reduction in age-adjusted excess risk of death, or a 22% reduction in excess risk after adjustment for other patient and tumour patient variables, including stage. Improvements in survival were also significant in age-groups 45-54, 55-64 and 65-74 years, equivalent to 10-20% reductions in excess risk of death, but not in younger or older patients (unadjusted models, *Table 4.4.1*).

4.4.3 Regional trends

Relative survival improved significantly for the Western region, between diagnosis periods 1994-97 and 1998-2001 (*Table 4.4.1*), equivalent to a 29% reduction in excess risk of death. Other regions showed no significant changes in relative survival, although the trends in most regions (sometimes approaching statistical significance) appeared to be consistent with the national improvement in survival.

4.4.4 Regional variation

This was moderately high over the period 1994-2001 as a whole. There was a significantly higher (by 12-24%) excess risk of death (lower relative survival) among patients from the North-Western, Southern, South-Eastern and Western regions, compared with the Eastern region, having adjusted for age and sex (*Figure 4.4.1*, *Table 4.4.2*). The pattern was similar for cases diagnosed during 1994-97, but excess risks were no longer significantly high for the North-Western and Western regions based on 1998-2001 cases. However, the Mid-Western region also showed significantly high excess risks among recent cases.

Adjustment for stage-related variables modified or reduced these differences somewhat. In the fully adjusted model, taking account of a wider range of patient and tumour characteristics, three regions had a significantly high excess risk of death during 1994-2001: Mid-Western (15% higher than Eastern), Southern (24% higher) and South-Eastern (10% higher). Only the Southern region had significantly low survival (high excess risk) for 1994-97 cases, and the Southern and Mid-Western regions for 1998-2001 cases.

While variations in patient and tumour characteristics appear to account for some of the regional variation in survival, cautious interpretation is needed. For example, patients from a region with a below-average proportion of cases microscopically verified – a factor associated with poor survival (*section 4.4.1*) - will tend to have below-average survival, other factors being equal. While this could reflect a higher proportion of patients from a given region being considered too unwell for full diagnostic investigation, it could also reflect poorer-quality investigation and care of patients from that region.

Table 4.4.1 Changes in relative survival between diagnosis-years 1994-97 and 1998-2001, stratified by age and region of residence, for patients diagnosed with colorectal cancer during 1994-2001. Excess hazard ratios in bold = significant difference from baseline (1994-1997). (EHR <1 = reduction in excess hazard thus improvement in relative survival, EHR >1 = increase in excess hazard thus reduction in relative survival). Only the basic model is shown for individual regions as regional sample sizes are generally too small too allow complex modelling.

	1998-2001 v 1994-97	
	[a]EHR (95% CI)	P
basic model: age-specific, sex-adjusted		
age 15-44	0.858 (0.654-1.126)	0.272
age 45-54	**0.795** (0.671-0.942)	0.008
age 55-64	**0.803** (0.712-0.907)	0.000
age 65-74	**0.905** (0.824-0.994)	0.038
age 75+	1.003 (0.916-1.099)	0.934
basic model: sex-, age-adjusted[b]		
total	**0.903** (0.856-0.952)	0.000
E	0.923 (0.838-1.017)	0.109
M	0.892 (0.711-1.119)	0.325
MW	1.080 (0.891-1.309)	0.431
NE	1.063 (0.878-1.285)	0.529
NW	0.827 (0.675-1.012)	0.066
S	0.903 (0.797-1.023)	0.112
SE	0.854 (0.730-1.000)	0.050
W	**0.710** (0.605-0.832)	0.000
fuller model: sex-, age-, stage-adjusted[b]		
total	**0.856** (0.812-0.902)	0.000
final multivariate model[b]		
total	**0.781** (0.703-0.867)	0.000

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.

[b]See *Table 4.4.2* but region and diagnosis year excluded here.

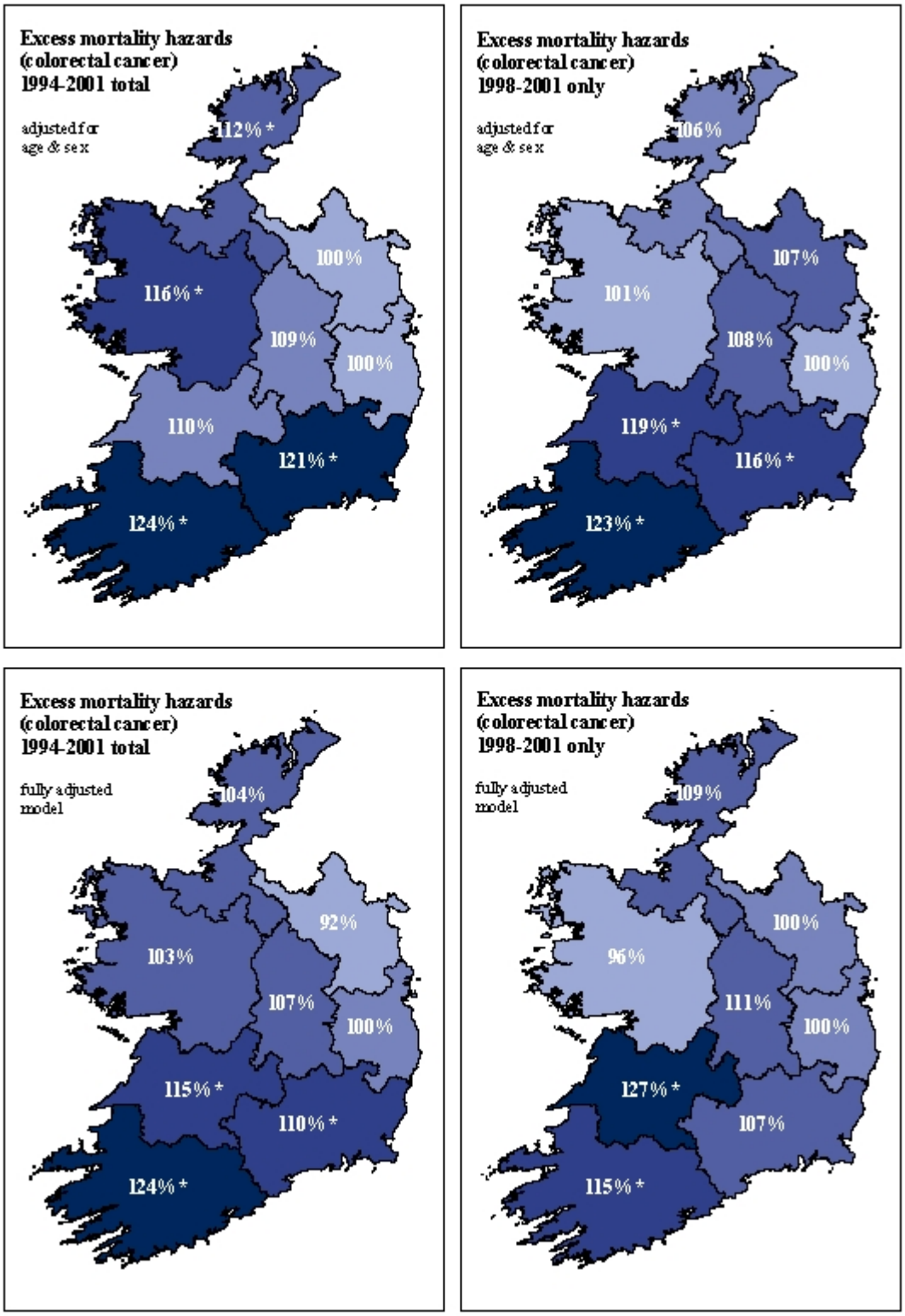


Figure 4.4.1 Regional variation in excess mortality hazards (based on relative survival) for colorectal cancer, expressed in comparison with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age- & sex-adjusted model (top), fully-adjusted model (bottom).
See *Table 4.4.2* for further details. * = significantly high or low excess risk (P<0.05).

Table 4.4.2 Variation in relative survival, by region of residence, for patients diagnosed with colorectal cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (EHR <1 = lower excess hazard thus higher relative survival than in Eastern region, EHR >1 = higher excess hazard thus lower relative survival).

	1994-2001		1994-1997		1998-2001	
	[a]EHR (95% CI)	P	EHR (95% CI)	P	EHR (95% CI)	P
basic model: sex-, age-adjusted[b,c]						
E	1.000		1.000		1.000	
M	1.087 (0.963-1.227)	0.176	1.090 (0.924-1.286)	0.304	1.079 (0.903-1.289)	0.401
MW	1.102 (0.990-1.227)	0.073	1.022 (0.873-1.195)	0.786	**1.194** (1.030-1.383)	0.018
NE	0.995 (0.895-1.106)	0.929	0.930 (0.796-1.086)	0.360	1.065 (0.921-1.231)	0.391
NW	**1.124** (1.006-1.256)	0.039	**1.188** (1.023-1.380)	0.023	1.058 (0.896-1.249)	0.504
S	**1.236** (1.143-1.337)	0.000	**1.248** (1.119-1.393)	0.000	**1.228** (1.097-1.375)	0.000
SE	**1.205** (1.100-1.321)	0.000	**1.249** (1.102-1.416)	0.000	**1.159** (1.015-1.324)	0.029
W	**1.158** (1.055-1.271)	0.002	**1.326** (1.170-1.503)	0.000	1.012 (0.882-1.163)	0.855
fuller model: sex-, age-, stage-adjusted[b,c,d]						
E	1.000		1.000		1.000	
M	1.119 (0.991-1.264)	0.068	0.987 (0.835-1.166)	0.880	**1.311** (1.098-1.567)	0.003
MW	**1.133** (1.018-1.260)	0.021	0.996 (0.852-1.165)	0.968	**1.311** (1.133-1.518)	0.000
NE	0.958 (0.863-1.064)	0.430	0.875 (0.751-1.021)	0.091	1.073 (0.929-1.240)	0.332
NW	1.088 (0.975-1.215)	0.129	1.071 (0.923-1.243)	0.362	1.109 (0.939-1.308)	0.220
S	**1.320** (1.221-1.426)	0.000	**1.386** (1.245-1.544)	0.000	**1.265** (1.132-1.414)	0.000
SE	**1.159** (1.058-1.269)	0.001	**1.162** (1.026-1.317)	0.018	**1.159** (1.015-1.324)	0.029
W	1.081 (0.986-1.185)	0.095	**1.169** (1.031-1.325)	0.015	1.014 (0.885-1.161)	0.837
final multivariate model[b,e]						
E	1.000		1.000		1.000	
M	1.066 (0.939-1.210)	0.317	1.036 (0.870-1.233)	0.690	1.111 (0.922-1.338)	0.267
MW	**1.152** (1.032-1.286)	0.012	1.069 (0.906-1.261)	0.426	**1.269** (1.092-1.474)	0.002
NE	0.917 (0.825-1.020)	0.112	0.873 (0.747-1.020)	0.088	0.995 (0.860-1.151)	0.949
NW	1.038 (0.929-1.160)	0.501	1.015 (0.873-1.179)	0.844	1.093 (0.926-1.291)	0.289
S	**1.240** (1.145-1.343)	0.000	**1.327** (1.188-1.483)	0.000	**1.145** (1.019-1.286)	0.023
SE	**1.100** (1.003-1.206)	0.042	1.125 (0.991-1.276)	0.068	1.071 (0.935-1.227)	0.319
W	1.027 (0.935-1.129)	0.565	1.114 (0.978-1.269)	0.103	0.955 (0.832-1.096)	0.517

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]Models included interaction terms between follow-up interval (years 1-5) and age (plus stage-related variables and grade), equivalent to stratification by these variables, to allow for non-proportional hazards across follow-up time.
[c]Age-categories: EUROCARE age-groups 15-44, 45-54, 55-64, 65-74, 75+.
[d]Stage-related variables: T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[e]Final (full) multivariate model, also including: grade 1, 2, 3+ or unknown; microscopic verification (yes, no, or unknown); method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever married, never married, unknown); individual year of diagnosis. [Tumour site – colon, rectosigmoid junction or rectum/anus – did not significantly improve model-fit and was excluded.]

4.5 Treatment: descriptive analysis

4.5.1 General comment

Analyses here are restricted to *treatments administered within six months after diagnosis*. Variations noted in treatment between patient groups may thus, to some extent, reflect variations in timing of treatment. However, the majority of first-line treatments for this cancer should be included.

4.5.2 General summary of treatment

Of the total 13,702 colorectal cancer cases included in analyses for the period 1994-2001, 83% had some form of definitive or tumour-directed treatment within six months of diagnosis, 77% had surgical treatment, 28% had chemotherapy and 12% had radiotherapy (*Table 4.5.1*). Equivalent figures for the most recent period, 1998-2001, were 6994 cases, of which 84% were treated, 77% had surgery, 33% had chemotherapy and 14% had radiotherapy (*Table 4.5.1*, *Figure 4.5.2*). A further breakdown by age is shown in *Table 4.5.1* and *Figure 4.5.1*.

The most frequent treatments or combinations were surgery only (51% of cases 1994-2001), surgery plus chemotherapy (18%), and surgery plus chemotherapy plus radiotherapy (6.1%). For the most recent period (1998-2001), equivalent figures were 46%, 20% and 8.0% (*Table 4.5.1*).

Table 4.5.1 Summary of main treatment modalities and combinations (within six months of diagnosis) for colorectal cancer patients, by age and diagnosis period, 1994-2001. Only treatments or combinations making up at least 1% of cases in any period are listed.

	1994-2001						1994-97	1998-2001	
	age 15-44	44-54	55-64	65-74	75+	total	subtotal	subtotal	
total cases	486	1297	2734	4491	4694	13 702	6708	6994	
any treatment	94.4%	92.8%	90.6%	85.8%	71.4%	82.8%	81.8%	83.7%	*
no treatment	5.6%	7.2%	9.4%	14.2%	28.6%	17.2%	18.2%	16.3%	*
any surgery[a]	86.6%	82.7%	84.3%	79.7%	68.5%	77.3%	77.8%	76.8%	
any chemotherapy[b]	61.7%	54.2%	44.4%	28.7%	7.1%	28.0%	22.3%	33.5%	*
any radiotherapy	19.5%	20.7%	16.3%	12.7%	4.5%	11.6%	8.8%	14.3%	*
surgery only	28.0%	33.9%	42.2%	52.2%	60.9%	50.6%	55.6%	45.8%	*
surge + chemo	42.2%	32.9%	28.3%	18.3%	4.9%	17.9%	15.4%	20.4%	*
surge + chemo + radio	12.6%	12.3%	10.8%	6.2%	0.9%	6.1%	4.1%	8.0%	*
surge + radio	3.9%	3.4%	2.8%	3.0%	1.7%	2.6%	2.6%	2.6%	
chemotherapy only	4.7%	5.1%	3.7%	2.5%	1.0%	2.5%	1.9%	3.1%	*
radiotherapy only	0.8%	1.2%	1.0%	1.8%	1.6%	1.5%	1.2%	1.8%	*
chemo + radio	2.3%	3.9%	1.6%	1.7%	0.3%	1.4%	1.0%	1.9%	*
others	0.0%	0.2%	0.2%	0.2%	0.1%	0.1%	0.1%	0.2%	

[a]Surgery and related treatments. [b]Chemotherapy and related treatments (excluding hormonal therapy).
*Significant difference between diagnosis periods in percentage having this treatment (χ^2 tests), unadjusted for age or other variables.

4.5.3 Region of surgical treatment v. region of residence

Based on surgical treatment within six months of diagnosis, the majority of colorectal cancer patients during 1994-2001 had their main surgical treatment within their region of residence (*Table 4.5.2*). The proportion was highest for the Eastern and Southern regions (98-99%), lowest for the North-Eastern, Midland and South-Eastern regions (75-79%). Patterns based on the most recent four years (1998-2001) were broadly similar to the longer-term average, with the proportion again highest for the Eastern and Southern regions (98-99%), lowest for the North-Eastern, Midland and Mid-Western regions (77-79%) (*Table 4.5.2*).

Table 4.5.2 Breakdown of colorectal cancer surgery, 1994-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases. Only surgical procedures within 6 months of diagnosis are included.

		Region of residence																	
Region where		**1994-2001 total**									**1998-2001 subtotal**								
treated		**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**	**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Eastern	%	**98.5**	13.8	4.9	24.6	10.8	0.9	10.0	3.8	**38.4**	**98.4**	13.0	5.7	21.7	10.7	0.8	8.2	3.7	**37.5**
Midland	%	0.5	**76.0**	0.7	0.2	0.7	0.0	0.5	0.1	4.5	0.4	**78.5**	0.9	0.4	0.8	0.0	0.7	0.2	4.3
Mid-Western	%	0.0	0.3	**82.7**	0.0	0.0	0.2	1.0	0.1	6.9	0.0	0.4	**79.3**	0.0	0.0	0.2	0.7	0.0	6.9
North-Eastern	%	0.5	1.0	0.0	**74.6**	3.3	0.0	0.0	0.0	7.1	0.6	1.1	0.0	**77.0**	4.0	0.0	0.0	0.0	7.6
North-Western	%	0.0	0.0	0.0	0.3	**84.2**	0.0	0.1	1.3	6.0	0.1	0.0	0.0	0.4	**83.5**	0.0	0.2	2.1	6.1
Southern	%	0.1	0.0	5.1	0.0	0.0	**98.8**	9.5	0.0	17.5	0.2	0.0	5.5	0.0	0.0	**98.7**	4.1	0.0	17.1
South-Eastern	%	0.2	0.3	3.3	0.1	0.0	0.1	**79.0**	0.0	8.6	0.3	0.4	4.6	0.2	0.0	0.2	**86.0**	0.0	9.5
Western	%	0.1	8.4	3.4	0.1	0.6	0.0	0.0	**94.7**	11.0	0.2	6.7	4.1	0.2	0.5	0.0	0.0	**94.1**	10.9
Northern Ireland	%	0.0	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5	0.0	0.0	0.0	0.0

4.5.4 Hospital caseloads (surgical cases)

Colorectal cancer cases were surgically treated (within six months of diagnosis) in a total of 59 hospitals in the Republic of Ireland during 1994-2001 (*Table 4.5.3*). There was no strong evidence of any trend in numbers of hospitals providing surgical treatment, although slightly fewer hospitals were involved for cases diagnosed during 1998-2001 (54) than during 1994-97 (57).

About one-fifth (8-11 annually) of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each, accounting for between 2.5% and 6.3% of annual totals. About two-fifths (19-25) of the hospitals treated fewer than 20 surgical cases each in a given year (12% to 18% of annual totals), and over three-quarters (38-45) treated fewer than 50 cases (53% to 72% of annual totals).

There was a modest tendency for average hospital caseload to increase during the period 1994-2001. Significant declines were seen in the proportions of surgical cases treated in 'low volume' hospitals (using thresholds of <10 and <50 cases annually). However, no trend was apparent based on a threshold of <20 cases annually. Based on surgical caseloads averaged over four-year periods, there was an increase from 23 annual cases per hospital during 1994-97 to 26 cases per hospital during 1998-2001. The proportion of surgical cases treated in hospitals treating 50 or more cases per year increased significantly from 30% during 1994-97 to 36% during 1998-2001.

4.5.5 Consultant caseloads (surgical cases)

At least 293 individual consultants were coded as responsible for surgical managements of colorectal cancers during 1994-2001. Of these, there were more during 1998-2001 (241) than 1994-97 (197) (*Table 4.5.4*).

About one-quarter of surgical consultants in any given year treated fewer than 10 surgical cases each, accounting for 19%-27% of annual totals. More than half of the consultants treated fewer than 20 surgical cases each in a given year (54%-67% of annual totals), and almost all treated fewer than 50 cases (99-100% of annual totals).

There was limited (and somewhat conflicting) evidence that average annual caseloads increased over time. Significant declines during 1994-2001 were seen in the proportions of surgical patients treated by 'low volume' consultants if defined using caseloads of less than 20 (or less than 50) cases annually, but a significant increase if defined using caseloads of less than 10 cases annually (*Table 4.5.4*). These trends and their interpretation could be further complicated, however, if recording of multiple surgical treatments has been more complete in recent years. This might increase recorded caseloads, and the apparent proportion of patients treated by higher-volume surgeons.

Table 4.5.3 Summary of surgical caseloads by year of diagnosis and hospital, based on colorectal cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* hospital where surgical treatment received, excluding unidentified hospitals and those outside the Republic of Ireland.

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
hospitals (1+ case)	48	52	50	51	50	49	50	49		57	54	
case average	28	24	26	28	28	28	28	29		23	26	
<10 cases/year[a]	13	11	9	10	8	9	8	9		17	13	
% of cases	*6.3*	*3.6*	*2.7*	*2.7*	*2.5*	*3.0*	*2.6*	*2.8*	***	*3.8*	*3.1*	*
<20 cases/year	19	25	23	20	19	21	22	20		30	26	
% of cases	*13.2*	*17.9*	*16.6*	*11.6*	*13.4*	*14.9*	*17.3*	*12.1*		*17.7*	*16.1*	*
<50 cases/year	40	45	43	44	44	41	44	38		51	46	
% of cases	*60.6*	*66.1*	*65.2*	*65.7*	*70.6*	*60.0*	*71.8*	*52.8*	*	*69.9*	*63.7*	***
50+ cases/year	8	7	7	7	6	8	6	11		6	8	
% of cases	*39.4*	*33.9*	*34.8*	*34.3*	*29.4*	*40.0*	*28.2*	*47.2*	*	*30.1*	*36.3*	***

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated in hospitals of a given caseload

Table 4.5.4 Summary of surgical caseloads by year of diagnosis and surgical consultant, based on colorectal cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* surgical consultant involved, excluding unknown consultants and those based outside the Republic of Ireland

caseload category	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**	**2000**	**2001**		**94-97**	**98-01**	
consultants (1+ case)	133	129	136	132	150	138	157	171		197	241	
case average	10	10	10	11	9	10	9	8		7	6	
<10 cases/year[a]	81	76	80	73	98	87	102	119		148	195	
% of cases	*23.0*	*22.6*	*21.8*	*18.6*	*25.2*	*23.6*	*25.1*	*27.2*	***	*28.6*	*33.1*	***
<20 cases/year	118	110	122	114	130	118	140	149		181	224	
% of cases	*64.9*	*57.5*	*66.7*	*59.7*	*56.2*	*54.0*	*63.0*	*53.5*	***	*64.4*	*62.2*	*
<50 cases/year	133	129	135	131	148	136	155	170		196	239	
% of cases	*100*	*100*	*99.3*	*99.2*	*98.7*	*98.6*	*98.7*	*99.4*	***	*99.5*	*99.2*	***
50+ cases/year	0	0	1	1	2	2	2	1		1	2	
% of cases	*0.0*	*0.0*	*4.4*	*4.7*	*8.4*	*9.2*	*7.9*	*3.7*	***	*3.8*	*7.9*	***

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated by surgical consultants of a given caseload.

4.5.6 Variation by patient and tumour characteristics

More detailed comparisons are made under the section covering logistic regression analysis (*section 4.6.1*). Basic tabulations of treatment for each category of patient or tumour are shown in *Table 4.5.5*. Note that cases lacking information on a given characteristic tend to be less likely to receive a given treatment. It should also be noted that these tabulations are based on unadjusted data – thus patients or tumours compared under a given variable may also differ in other characteristics, some of which may be more important determinants of treatment.

See also *Table 4.5.1* and *Figure 4.5.1* for further summaries of treatments in relation to age.

Table 4.5.5 Summary of treatment of colorectal cancer cases, 1998-2001, by patient and tumour characteristics: unadjusted percentages receiving treatment within six months of diagnosis. See *Table 4.2.2* for sample sizes.

	Overall treatment	Surgery	Radiotherapy	Chemotherapy
total cases	83.7%	76.8%	14.3%	33.5%
age 15-44[a]	92.9%	83.0%	21.3%	64.4%
age 45-54	93.3%	81.5%	24.3%	59.7%
age 55-64	91.6%	84.0%	19.6%	52.0%
age 65-74	87.4%	79.5%	16.3%	36.6%
age 75+	72.1%	68.2%	5.9%	9.4%
male	85.1%	77.6%	17.0%	36.4%
female	81.9%	75.8%	10.8%	29.6%
stage I	98.1%	96.9%	7.6%	10.5%
stage II	97.7%	95.1%	14.2%	34.3%
stage III	98.1%	94.2%	22.2%	60.8%
stage IV	66.8%	50.4%	9.7%	39.0%
stage X	79.7%	74.2%	15.3%	24.8%
T1	93.1%	90.8%	4.9%	8.4%
T2	96.9%	93.9%	12.7%	22.2%
T3	96.8%	94.1%	14.9%	42.5%
T4	79.7%	66.7%	18.4%	40.1%
T X	36.7%	18.9%	13.1%	18.1%
N negative	96.2%	93.7%	11.7%	25.5%
N positive	95.7%	90.2%	18.3%	55.4%
N X	49.0%	33.5%	13.6%	18.8%
M negative	94.4%	90.4%	17.2%	37.4%
M positive	66.8%	50.4%	9.7%	38.8%
M X	81.1%	76.6%	13.7%	25.4%
grade 1	92.2%	85.6%	12.9%	28.8%
grade 2	93.4%	88.7%	14.8%	37.3%
grade 3+	90.0%	81.5%	18.4%	41.0%
grade X	55.3%	44.0%	11.7%	22.5%
colon	82.8%	78.4%	3.8%	31.5%
rectosigmoid	85.4%	79.8%	16.1%	36.1%
rectum/anus	85.1%	73.1%	34.4%	36.7%
MV yes	90.1%	83.3%	15.2%	36.0%
MV no	11.7%	3.8%	4.3%	4.9%
MV X	13.6%	6.8%	4.5%	6.8%
symptomatic	84.1%	77.1%	14.4%	33.8%
incidental	80.0%	76.3%	6.3%	21.3%
screen detected	90.0%	90.0%	10.0%	26.7%
presentation X	76.0%	69.3%	15.0%	30.3%
non-smoker	85.2%	79.0%	13.1%	35.7%
ex-smoker	86.0%	79.6%	14.0%	32.6%
smoker	85.5%	77.9%	19.1%	35.8%
smoking status X	77.4%	69.4%	12.8%	27.5%
ever married	85.3%	78.4%	14.4%	35.3%
never married	80.9%	73.4%	15.3%	28.4%
marital status X	60.4%	57.2%	5.9%	18.5%

[a]See *Table 4.5.1* for a further breakdown by age, for the overall period 1994-2001.

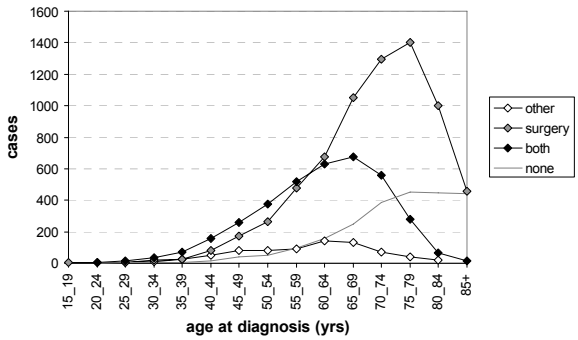


Figure 4.5.1 Age-profiles for tumour-directed treatments within six months of diagnosis for colorectal cancer cases diagnosed 1994-2001: numbers of cases having surgery (only), other treatments (radiotherapy, chemotherapy or hormone therapy but not surgery), both surgery and other treatments, or no treatment.

4.5.7 National trends

See *section 4.5.2*.

4.5.8 Regional variation

Regional variations in treatment, unadjusted for patients or tumour characteristics, are summarized for the period 1998-2001 in *Figure 4.5.2*. Overall treatment varied little between regions (range 80-86% of regional cases), use of surgery to a slightly greater extent (70-82%). More substantial variation was apparent for chemotherapy (ranging from 26% of cases in the Mid-Western to 46% in the South-Eastern region) and radiotherapy (from 9% in the Mid-Western to 20% in the Midland region). The degree of variation was broadly similar during earlier years (not presented) although precise patterns differed somewhat. More rigorous comparisons of treatments between regions, taking account of age and where possible other patient and tumour characteristics, are presented in *section 4.6.3*.

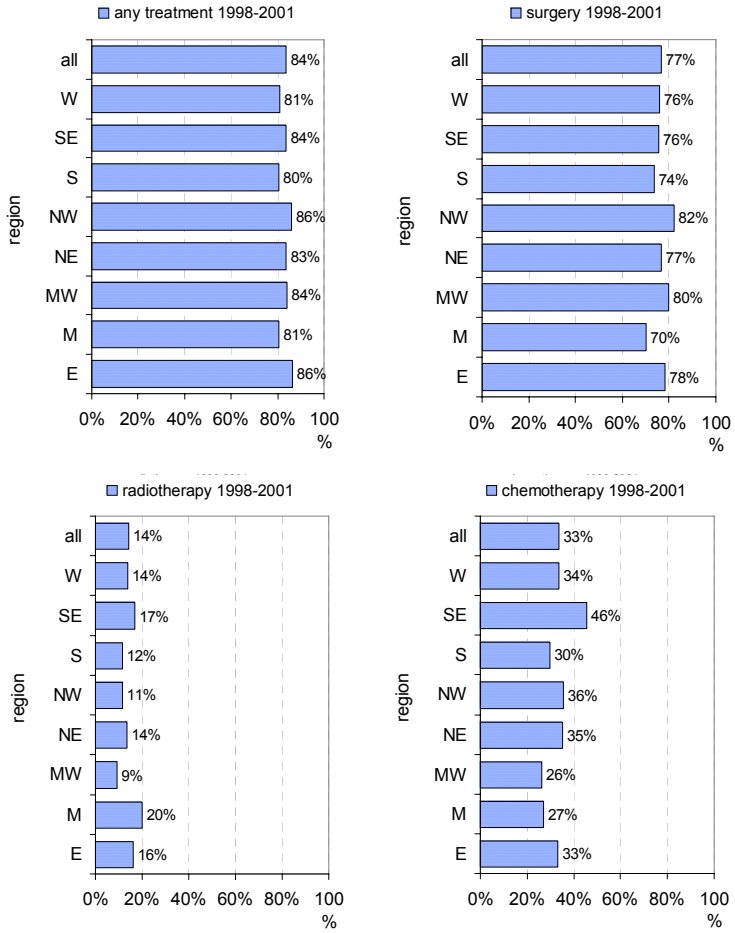


Figure 4.5.2 Percentage of colorectal cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence, 1998-2001.

4.6 Treatment: logistic regression analysis

4.6.1 Variation by patient and tumour characteristics

Preliminary multivariate logistic regression models were used to assess variation in treatments in relation to patient and tumour characteristics other than region of residence and year of diagnosis (before examining those). Comparisons here are with baseline groups for relevant variables – diagnosis age 15-44, male, T category 1 (smallest size/local extension), N negative (no nodal involvement), M negative (no distant metastasis), colon (colorectal site), tumour grade 1, microscopically verified (MV), symptomatic method of presentation, non-smoker and ever married – having adjusted for all variables shown in the relevant table (*Tables 4.6.1-4*). The main comparisons are based on data for 1994-2001 as a whole. However, attention is drawn to any significant differences in patterns between the diagnosis periods 1994-97 and 1998-2001 (details also tabulated).

Overall treatment

For 1994-2001 as a whole, treatment was significantly less likely, compared with baseline groups, for patients aged 55 or above; T category 4 or unknown; N category unknown; M category positive or unknown; grade unknown; cases lacking microscopic verification (MV) or with MV status unknown; and for patients who were never married (*Table 4.6.1*). Cases in T category 2 or 3 were significantly more likely to be treated. Patterns in general were similar for the diagnosis periods 1994-97 and 1998-2001, although the magnitude or significance of relative risk values (RRs) showed some changes. The only significant differences between these periods were for cases in the T 3, M positive or M unknown categories, incidentally detected cases and patients of unknown marital status.

Surgical treatment

Surgical treatment was significantly less likely for age-groups 45 or over and cases that were T category 4 or unknown; N category unknown; metastatic; grade 3+ or unknown; sited in the rectum or anus; lacking MV or with MV status unknown; and for patients who were never married or whose smoking status was unknown (*Table 4.6.2*). Patterns varied between diagnosis periods to a greater extent than for overall treatment, with significant differences in RRs for T categories 2, 3, and unknown; M category unknown; grade 2 and 3+; rectal/anal site; incidentally detected cases; smokers; and marital status unknown.

Radiotherapy

Variation was greater than for surgical treatment. Radiotherapy use was significantly lower for patients aged 55 or over, and for women; metastatic cases or M category unknown; cases lacking MV; and marital status unknown (*Table 4.6.3*). Its use was significantly higher, relative to baseline groups, for cases that were T category 2-4 or unknown; N positive or N unknown; grade 3+; and sited in the rectosigmoid junction or, especially, the rectum or anus. These patterns were broadly similar for 1994-97 and 1998-2001, and RRs differed significantly only for rectal/anal cancers (higher RR latterly) and metastatic cases.

Chemotherapy

Chemotherapy use was significantly less likely among patients aged 45 or over (*Table 4.6.4*), and age-related variation was greater than for other treatment modalities. Its use was also less for female patients, and cases that with M category unknown, lacking MV or with MV status unknown, and for patients who were smokers, never married or of unknown smoking or marital status. Chemotherapy use was significantly more likely for cases coded as T 2-4 or unknown; N positive or unknown; grade 2 or 3+; or rectal/anal. RR estimates differed significantly between diagnosis periods for age-group 65-74, cases of unknown nodal status and rectal/anal tumours, otherwise patterns were broadly similar.

Table 4.6.1 Risk ratios for overall treatment of colorectal cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.979 (0.932-1.009)	0.208	0.962 (0.875-1.005)	0.108		0.992 (0.926-1.030)	0.755
age 55-64	**0.939** (0.880-0.981)	0.001	**0.903** (0.779-0.973)	0.001		0.971 (0.899-1.016)	0.262
age 65-74	**0.887** (0.811-0.943)	0.000	**0.841** (0.687-0.938)	0.000		**0.926** (0.835-0.986)	0.010
age 75+	**0.771** (0.668-0.856)	0.000	**0.743** (0.556-0.878)	0.000		**0.787** (0.652-0.891)	0.000
male	1.000		1.000			1.000	
female	0.991 (0.967-1.012)	0.434	0.992 (0.957-1.024)	0.674		0.994 (0.962-1.022)	0.730
T1	1.000		1.000			1.000	
T2	**1.036** (1.009-1.055)	0.012	**1.060** (1.021-1.085)	0.006		1.015 (0.972-1.040)	0.412
T3	**1.035** (1.012-1.052)	0.004	**1.062** (1.030-1.084)	0.001	*	1.013 (0.976-1.036)	0.420
T4	**0.909** (0.853-0.954)	0.000	**0.928** (0.850-0.989)	0.017		**0.883** (0.794-0.948)	0.000
T X	**0.779** (0.706-0.843)	0.000	**0.796** (0.695-0.883)	0.000		**0.746** (0.630-0.843)	0.000
N negative	1.000		1.000			1.000	
N positive	0.999 (0.990-1.007)	0.955	0.992 (0.976-1.005)	0.297		1.006 (0.994-1.014)	0.269
N X	**0.887** (0.860-0.911)	0.000	**0.898** (0.860-0.929)	0.000		**0.876** (0.835-0.911)	0.000
M negative	1.000		1.000			1.000	
M positive	**0.882** (0.854-0.907)	0.000	**0.843** (0.795-0.883)	0.000	*	**0.920** (0.885-0.948)	0.000
M X	**0.980** (0.967-0.992)	0.000	**0.967** (0.946-0.985)	0.000	*	0.994 (0.977-1.008)	0.479
grade 1	1.000		1.000			1.000	
grade 2	0.992 (0.969-1.010)	0.443	0.971 (0.934-1.000)	0.057		1.009 (0.977-1.031)	0.518
grade 3+	0.979 (0.949-1.003)	0.105	**0.953** (0.903-0.991)	0.012		1.001 (0.961-1.029)	0.915
grade X	**0.964** (0.934-0.989)	0.004	**0.957** (0.912-0.992)	0.013		0.967 (0.919-1.002)	0.077
colon	1.000		1.000			1.000	
rectosigmoid	0.998 (0.951-1.039)	0.960	0.999 (0.932-1.053)	0.978		0.995 (0.923-1.052)	0.901
rectum/anus	1.003 (0.976-1.027)	0.810	1.002 (0.963-1.037)	0.874		1.002 (0.964-1.036)	0.883
MV yes	1.000		1.000			1.000	
MV no	**0.541** (0.472-0.611)	0.000	**0.498** (0.400-0.600)	0.000		**0.584** (0.486-0.679)	0.000
MV X	**0.718** (0.548-0.862)	0.000	**0.719** (0.491-0.903)	0.000		**0.761** (0.499-0.947)	0.004
symptomatic	1.000		1.000			1.000	
incidental	0.942 (0.809-1.039)	0.284	**0.786** (0.573-0.960)	0.011	*	1.059 (0.919-1.131)	0.329
screen detected	0.995 (0.702-1.132)	0.964	1.099 (0.638-1.197)	0.511		0.831 (0.388-1.090)	0.303
presentation X	0.943 (0.869-1.005)	0.075	**0.847** (0.700-0.966)	0.009		0.977 (0.886-1.045)	0.556
non-smoker	1.000		1.000			1.000	
ex-smoker	1.012 (0.982-1.039)	0.386	1.021 (0.977-1.057)	0.318		1.010 (0.965-1.046)	0.631
smoker	0.985 (0.955-1.013)	0.326	0.976 (0.931-1.015)	0.256		0.999 (0.955-1.035)	0.968
smoking status X	0.980 (0.949-1.007)	0.160	0.961 (0.913-1.003)	0.076		0.993 (0.951-1.028)	0.743
ever married	1.000		1.000			1.000	
never married	**0.965** (0.935-0.992)	0.011	**0.954** (0.909-0.994)	0.024		0.980 (0.939-1.015)	0.283
marital status X	0.982 (0.920-1.032)	0.522	**1.071** (1.008-1.115)	0.029	*	**0.839** (0.711-0.943)	0.001

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant difference in RR between diagnosis periods.

Table 4.6.2 Risk ratios for surgical treatment of colorectal cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	**0.910** (0.826-0.977)	0.006	**0.909** (0.788-0.991)	0.026		0.903 (0.773-1.005)	0.066
age 55-64	**0.926** (0.850-0.986)	0.014	**0.899** (0.782-0.981)	0.010		0.946 (0.832-1.032)	0.251
age 65-74	**0.869** (0.785-0.938)	0.000	**0.846** (0.716-0.943)	0.000		**0.883** (0.760-0.981)	0.017
age 75+	**0.823** (0.732-0.900)	0.000	**0.800** (0.659-0.910)	0.000		**0.840** (0.710-0.947)	0.002
male	1.000		1.000			1.000	
female	1.003 (0.974-1.030)	0.788	1.018 (0.978-1.055)	0.343		0.991 (0.948-1.030)	0.692
T1	1.000		1.000			1.000	
T2	1.013 (0.975-1.042)	0.458	**1.049** (1.003-1.081)	0.039	*	0.971 (0.902-1.019)	0.285
T3	1.004 (0.969-1.032)	0.761	1.040 (0.996-1.071)	0.067	*	0.967 (0.904-1.012)	0.177
T4	**0.775** (0.699-0.842)	0.000	**0.829** (0.728-0.912)	0.000		**0.707** (0.589-0.812)	0.000
T X	**0.555** (0.474-0.636)	0.000	**0.647** (0.533-0.754)	0.000	*	**0.454** (0.342-0.573)	0.000
N negative	1.000		1.000			1.000	
N positive	0.990 (0.984-1.006)	0.522	0.994 (0.977-1.008)	0.496		0.998 (0.981-1.012)	0.874
N X	**0.809** (0.775-0.841)	0.000	**0.827** (0.778-0.870)	0.000		**0.785** (0.733-0.832)	0.000
M negative	1.000		1.000			1.000	
M positive	**0.770** (0.733-0.805)	0.000	**0.752** (0.695-0.803)	0.000		**0.787** (0.734-0.835)	0.000
M X	1.001 (0.987-1.013)	0.865	0.983 (0.962-1.001)	0.069	*	1.016 (0.995-1.033)	0.114
grade 1	1.000		1.000			1.000	
grade 2	0.994 (0.964-1.019)	0.662	**0.947** (0.899-0.986)	0.006	*	1.048 (1.009-1.079)	0.018
grade 3+	**0.955** (0.913-0.990)	0.010	**0.904** (0.838-0.958)	0.000	*	1.013 (0.956-1.057)	0.599
grade X	**0.929** (0.886-0.967)	0.000	**0.922** (0.863-0.969)	0.000		0.950 (0.882-1.004)	0.078
colon	1.000		1.000			1.000	
rectosigmoid	0.977 (0.921-1.027)	0.394	0.981 (0.904-1.046)	0.600		0.963 (0.875-1.037)	0.356
rectum/anus	**0.847** (0.809-0.884)	0.000	**0.903** (0.852-0.951)	0.000	*	**0.788** (0.730-0.844)	0.000
MV yes	1.000		1.000			1.000	
MV no	**0.294** (0.224-0.377)	0.000	**0.309** (0.215-0.427)	0.000		**0.270** (0.177-0.394)	0.000
MV X	**0.646** (0.439-0.841)	0.000	**0.711** (0.459-0.924)	0.004		**0.543** (0.225-0.897)	0.006
symptomatic	1.000		1.000			1.000	
incidental	0.990 (0.837-1.102)	0.887	0.824 (0.592-1.013)	0.072	*	1.138 (0.962-1.228)	0.104
screen detected	1.152 (0.899-1.246)	0.176	1.209 (0.860-1.267)	0.145		1.014 (0.533-1.230)	0.940
presentation X	0.946 (0.858-1.022)	0.183	**0.847** (0.684-0.984)	0.026		1.005 (0.895-1.091)	0.919
non-smoker	1.000		1.000			1.000	
ex-smoker	1.001 (0.962-1.036)	0.932	1.007 (0.953-1.053)	0.760		1.007 (0.949-1.056)	0.794
smoker	0.972 (0.935-1.006)	0.113	**0.938** (0.883-0.986)	0.011	*	1.013 (0.961-1.058)	0.590
smoking status X	**0.949** (0.910-0.986)	0.006	**0.937** (0.879-0.988)	0.014		0.963 (0.905-1.013)	0.162
ever married	1.000		1.000			1.000	
never married	**0.957** (0.920-0.991)	0.013	**0.934** (0.880-0.982)	0.007		0.978 (0.925-1.025)	0.395
marital status X	1.053 (0.985-1.106)	0.114	**1.113** (1.042-1.162)	0.004	*	0.931 (0.792-1.041)	0.248

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant difference in RR between diagnosis periods.

Table 4.6.3 Risk ratios for radiotherapy of colorectal cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.989 (0.772-1.251)	0.935	0.889 (0.606-1.273)	0.535		1.081 (0.775-1.464)	0.633
age 55-64	**0.772** (0.604-0.976)	0.031	**0.660** (0.454-0.942)	0.022		0.890 (0.640-1.208)	0.468
age 65-74	**0.591** (0.461-0.752)	0.000	**0.452** (0.309-0.653)	0.000		0.736 (0.528-1.005)	0.055
age 75+	**0.204** (0.153-0.271)	0.000	**0.157** (0.100-0.243)	0.000		**0.238** (0.161-0.348)	0.000
male	1.000		1.000			1.000	
female	**0.844** (0.754-0.943)	0.003	0.885 (0.738-1.059)	0.185		**0.819** (0.707-0.945)	0.006
T1	1.000		1.000			1.000	
T2	**2.945** (2.008-4.239)	0.000	**2.733** (1.456-4.950)	0.002		**3.081** (1.894-4.819)	0.000
T3	**5.213** (3.730-7.089)	0.000	**4.821** (2.731-8.075)	0.000		**5.577** (3.697-7.956)	0.000
T4	**8.103** (5.982-10.55)	0.000	**7.985** (4.662-12.59)	0.000		**7.921** (5.473-10.67)	0.000
T X	**5.055** (3.537-7.012)	0.000	**3.944** (2.114-6.994)	0.000		**5.704** (3.711-8.238)	0.000
N negative	1.000		1.000			1.000	
N positive	**1.630** (1.441-1.839)	0.000	**1.608** (1.309-1.966)	0.000		**1.640** (1.404-1.905)	0.000
N X	**1.430** (1.204-1.691)	0.000	**1.607** (1.216-2.104)	0.001		**1.358** (1.089-1.679)	0.007
M negative	1.000		1.000			1.000	
M positive	**0.465** (0.393-0.548)	0.000	**0.591** (0.456-0.764)	0.000	*	**0.401** (0.321-0.499)	0.000
M X	**0.879** (0.779-0.991)	0.036	1.009 (0.826-1.227)	0.926		**0.842** (0.721-0.980)	0.026
grade 1	1.000		1.000			1.000	
grade 2	1.115 (0.919-1.346)	0.265	1.203 (0.897-1.601)	0.214		0.965 (0.740-1.246)	0.790
grade 3+	**1.381** (1.108-1.710)	0.004	1.390 (0.992-1.926)	0.056		1.326 (0.985-1.753)	0.062
grade X	1.190 (0.949-1.482)	0.129	1.233 (0.864-1.740)	0.245		1.050 (0.775-1.402)	0.748
colon	1.000		1.000			1.000	
rectosigmoid	**4.063** (3.370-4.871)	0.000	**3.762** (2.819-4.964)	0.000		**4.397** (3.431-5.568)	0.000
rectum/anus	**8.708** (7.870-9.595)	0.000	**6.831** (5.751-8.048)	0.000	*	**10.20** (9.023-11.44)	0.000
MV yes	1.000		1.000			1.000	
MV no	**0.526** (0.366-0.749)	0.000	**0.508** (0.285-0.892)	0.018		**0.568** (0.355-0.892)	0.013
MV X	0.852 (0.334-1.967)	0.725	1.177 (0.349-3.334)	0.783		0.659 (0.141-2.374)	0.566
symptomatic	1.000		1.000			1.000	
incidental	0.461 (0.201-1.015)	0.055	0.216 (0.029-1.415)	0.115		0.593 (0.228-1.417)	0.254
screen detected	0.603 (0.169-1.903)	0.412	-	-		0.898 (0.237-2.667)	0.865
presentation X	1.292 (0.976-1.689)	0.073	1.402 (0.811-2.329)	0.221		1.122 (0.801-1.539)	0.492
non-smoker	1.000		1.000			1.000	
ex-smoker	1.090 (0.932-1.271)	0.278	1.120 (0.871-1.432)	0.372		1.045 (0.851-1.274)	0.669
smoker	1.066 (0.930-1.219)	0.353	0.967 (0.776-1.200)	0.767		1.168 (0.979-1.386)	0.083
smoking status X	1.019 (0.873-1.186)	0.807	0.868 (0.667-1.123)	0.285		1.099 (0.905-1.326)	0.333
ever married	1.000		1.000			1.000	
never married	0.929 (0.809-1.065)	0.295	0.813 (0.644-1.020)	0.075		1.025 (0.860-1.215)	0.776
marital status X	**0.539** (0.358-0.801)	0.002	0.706 (0.400-1.216)	0.215		**0.472** (0.258-0.842)	0.010

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant difference in RR between diagnosis periods.

Table 4.6.4 Risk ratios for chemotherapy of colorectal cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001 [a]RR (95% CI)	P	1994-97 RR (95% CI)	P		1998-2001 RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	**0.864** (0.769-0.958)	0.004	**0.823** (0.683-0.963)	0.013		0.900 (0.771-1.023)	0.115
age 55-64	**0.704** (0.618-0.792)	0.000	**0.618** (0.502-0.744)	0.000		**0.785** (0.664-0.905)	0.000
age 65-74	**0.431** (0.367-0.502)	0.000	**0.346** (0.269-0.438)	0.000	*	**0.504** (0.406-0.613)	0.000
age 75+	**0.109** (0.087-0.135)	0.000	**0.083** (0.060-0.116)	0.000		**0.121** (0.089-0.163)	0.000
male	1.000		1.000			1.000	
female	**0.896** (0.838-0.957)	0.001	0.945 (0.847-1.051)	0.304		**0.880** (0.807-0.957)	0.003
T1	1.000		1.000			1.000	
T2	**2.625** (1.994-3.402)	0.000	**2.696** (1.729-4.068)	0.000		**2.528** (1.770-3.498)	0.000
T3	**5.040** (4.071-6.101)	0.000	**4.852** (3.340-6.730)	0.000		**5.203** (4.039-6.430)	0.000
T4	**5.109** (4.095-6.222)	0.000	**4.826** (3.258-6.795)	0.000		**4.967** (3.783-6.237)	0.000
T X	**3.734** (2.869-4.751)	0.000	**2.858** (1.785-4.400)	0.000		**4.084** (2.980-5.353)	0.000
N negative	1.000		1.000			1.000	
N positive	**2.184** (2.063-2.306)	0.000	**2.185** (1.972-2.408)	0.000		**2.169** (2.032-2.304)	0.000
N X	**1.149** (1.020-1.289)	0.023	**1.367** (1.134-1.632)	0.001	*	1.049 (0.896-1.216)	0.541
M negative	1.000		1.000			1.000	
M positive	0.987 (0.905-1.072)	0.764	1.056 (0.918-1.207)	0.434		0.975 (0.873-1.082)	0.654
M X	**0.776** (0.716-0.839)	0.000	**0.791** (0.693-0.899)	0.000		**0.789** (0.713-0.869)	0.000
grade 1	1.000		1.000			1.000	
grade 2	**1.162** (1.042-1.289)	0.007	1.046 (0.889-1.222)	0.575		1.164 (0.999-1.343)	0.051
grade 3+	**1.219** (1.073-1.377)	0.003	1.171 (0.967-1.400)	0.102		**1.219** (1.018-1.436)	0.031
grade X	1.116 (0.974-1.269)	0.110	0.952 (0.765-1.170)	0.649		1.135 (0.944-1.343)	0.171
colon	1.000		1.000			1.000	
rectosigmoid	1.063 (0.944-1.190)	0.307	1.062 (0.880-1.268)	0.520		1.071 (0.916-1.238)	0.376
rectum/anus	**1.157** (1.080-1.238)	0.000	0.975 (0.864-1.097)	0.689	*	**1.263** (1.162-1.367)	0.000
MV yes	1.000		1.000			1.000	
MV no	**0.355** (0.259-0.479)	0.000	**0.388** (0.236-0.624)	0.000		**0.361** (0.240-0.528)	0.000
MV X	**0.371** (0.138-0.885)	0.023	0.248 (0.033-1.376)	0.125		0.593 (0.196-1.367)	0.262
symptomatic	1.000		1.000			1.000	
incidental	0.742 (0.509-1.044)	0.090	0.769 (0.424-1.303)	0.349		0.729 (0.444-1.117)	0.159
screen detected	1.014 (0.566-1.623)	0.958	1.447 (0.525-2.816)	0.436		0.803 (0.379-1.437)	0.507
presentation X	1.080 (0.892-1.289)	0.416	0.820 (0.512-1.254)	0.378		1.029 (0.829-1.248)	0.785
non-smoker	1.000		1.000			1.000	
ex-smoker	0.989 (0.901-1.081)	0.818	0.971 (0.832-1.127)	0.712		0.986 (0.877-1.100)	0.809
smoker	**0.886** (0.812-0.964)	0.005	0.903 (0.787-1.032)	0.137		**0.892** (0.796-0.993)	0.038
smoking status X	**0.835** (0.758-0.918)	0.000	**0.806** (0.684-0.945)	0.008		**0.832** (0.737-0.934)	0.002
ever married	1.000		1.000			1.000	
never married	**0.746** (0.679-0.817)	0.000	**0.702** (0.601-0.816)	0.000		**0.779** (0.692-0.874)	0.000
marital status X	**0.799** (0.634-0.992)	0.042	0.971 (0.688-1.325)	0.862		**0.723** (0.522-0.968)	0.029

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant difference in RR between diagnosis periods.

4.6.2 National and regional trends

Overall treatment

Over the period 1996-2001, nationally there was a small but significant average annual increase in overall treatment within six months of diagnosis, by *c.*0.6% per year in relative terms, having adjusted for age and sex, or *c.*0.9% per year after further adjustment for stage-related variables (*Table 4.6.5*). At regional scales, significant increases were also seen for patients resident in the Eastern and South-Eastern regions (+1.0% and +3.4% per year, respectively). Other regions showed no significant trends.

Table 4.6.5 Average annual changes in the proportion of colorectal cancer patients having any tumour-directed treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual [a]RR (95% CI)	P
age- & sex-adjusted		
total	**1.006** (1.000-1.012)	0.021
E	**1.010** (1.001-1.018)	0.023
M	0.985 (0.962-1.006)	0.172
MW	0.994 (0.977-1.009)	0.478
NE	0.992 (0.973-1.009)	0.413
NW	1.022 (0.998-1.044)	0.067
S	1.008 (0.994-1.022)	0.224
SE	**1.034** (1.008-1.058)	0.010
W	1.002 (0.984-1.019)	0.791
age-, sex-, stage-adjusted[b]		
total	**1.009** (1.002-1.017)	0.012

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.

Surgical treatment

Nationally, the use of surgery fell slightly but significantly between 1996 and 2001, by *c.*0.7% per year in relative terms, adjusted for age and sex, or *c.*1.5% after further adjustment for stage (*Table 4.6.6.*). Most regions showed no trends, but significant age-adjusted declines were seen for the Midland and North-Eastern regions (by about 3.8% and 2.4% per year, respectively).

Table 4.6.6 Average annual changes in the proportion of colorectal cancer patients having surgical treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	P
age- & sex-adjusted		
total	**0.993** (0.986-0.999)	0.027
E	0.998 (0.988-1.008)	0.789
M	**0.962** (0.938-0.984)	0.001
MW	0.985 (0.967-1.002)	0.090
NE	**0.976** (0.958-0.993)	0.008
NW	1.012 (0.986-1.037)	0.332
S	0.999 (0.983-1.014)	0.954
SE	0.997 (0.972-1.021)	0.847
W	0.998 (0.977-1.017)	0.849
age-, sex-, stage-adjusted		
total	**0.985** (0.976-0.994)	0.002

Radiotherapy

Radiotherapy use increased significantly, at national scale, by *c.*11% annually in relative terms between 1996 and 2001 (*Table 4.6.7*). Patients from four of the eight regions (Midland, North-Eastern, Southern and South-Eastern) also showed significant increases, by 16-43% annually (adjusted for age and sex), but no clear trends for evident for other regions.

Table 4.6.7 Average annual changes in the proportion of colorectal cancer patients having radiotherapy (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	P
age- & sex-adjusted		
total	**1.108** (1.074-1.142)	0.000
E	1.041 (0.993-1.092)	0.092
M	**1.427** (1.243-1.637)	0.000
MW	1.076 (0.943-1.227)	0.273
NE	**1.156** (1.028-1.299)	0.015
NW	0.945 (0.837-1.064)	0.355
S	**1.213** (1.107-1.327)	0.000
SE	**1.273** (1.157-1.399)	0.000
W	1.068 (0.966-1.179)	0.195
age-, sex-, stage-adjusted		
total	**1.106** (1.071-1.141)	0.000

Chemotherapy

As for radiotherapy, a marked increase was seen the proportion of patients nationally having chemotherapy within six months of diagnosis: by *c*.12% annually in relative terms between 1996 and 2001 after adjustment for age and sex, or *c*.13% annually after further adjustment for stage (*Table 4.6.8).* Similar or more marked increases were seen for five regions (Eastern, North-Eastern, Southern, South-Eastern and Western), by 10-31% annually in relative terms (age- and sex-adjusted). No significant trends were evident in the Midland, Mid-Western or North-Western regions.

Table 4.6.8 Average annual changes in the proportion of colorectal cancer patients having chemotherapy (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual RR (95% CI)	**P**
age- & sex-adjusted		
total	**1.123** (1.101-1.146)	0.000
E	**1.100** (1.066-1.135)	0.000
M	1.019 (0.939-1.102)	0.638
MW	1.020 (0.948-1.095)	0.591
NE	**1.137** (1.059-1.219)	0.000
NW	0.979 (0.914-1.047)	0.555
S	**1.309** (1.227-1.395)	0.000
SE	**1.249** (1.176-1.325)	0.000
W	**1.184** (1.109-1.263)	0.000
age-, sex-, stage-adjusted		
total	**1.133** (1.109-1.158)	0.000

4.6.3 Regional variation

Regional variations in treatment use (relative risks compared with the Eastern region) are summarized in *Figures 4.6.1-3* for the overall period 1994-2001 and for the most recent diagnosis period, 1998-2001. Results of basic age- and sex-adjusted models and of fully adjusted models are presented for overall treatment, surgical treatment, radiotherapy and chemotherapy. More detailed summaries, overall and for periods 1994-97 and 1998-2001, are presented in *Tables 4.6.9-12*.

Overall treatment

Regional variation in overall treatment was less marked than for individual treatment modalities (especially radiotherapy and chemotherapy). During 1994-2001 as a whole, patients from three regions (Midland, Southern and South-Eastern) were slightly but significantly less likely to be treated than those from the Eastern region, after adjustment for patients' age and sex (*Table 4.6.9*). This applied to two of these regions during 1994-97, and to four regions (additionally including North-Eastern and Western regions) in 1998-2001. Relative risk estimates (RRs) differed significantly between diagnosis periods for the North-Eastern and Western regions.

Regional patterns during 1994-2001 changed only slightly after further adjustment for stage-related variables, but this adjustment further accentuated regional differences specific to 1994-97 or 1998-2001. Fuller adjustment for patient and tumour variables reduced the amount of regional variation overall and for 1998-2001. In this final model, only the Midland and South-Eastern region has significant overall RRs (lower proportions treated) compared with the Eastern region, and only Midland and North-Eastern regions for 1998-2001. However, RRs differed significantly between diagnosis periods for three regions (Mid-Western, North-Eastern and Western).

Table 4.6.9 Risk ratios for overall treatment of colorectal cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.950** (0.911-0.984)	0.003	0.959 (0.902-1.007)	0.103		**0.940** (0.884-0.986)	0.010
MW	0.989 (0.957-1.017)	0.471	1.018 (0.972-1.056)	0.407		0.962 (0.916-1.001)	0.061
NE	0.991 (0.961-1.018)	0.554	1.023 (0.980-1.059)	0.259	*	**0.962** (0.918-0.999)	0.044
NW	0.982 (0.949-1.011)	0.242	0.962 (0.912-1.005)	0.091		1.006 (0.962-1.041)	0.758
S	**0.936** (0.910-0.961)	0.000	**0.940** (0.901-0.975)	0.001		**0.932** (0.895-0.965)	0.000
SE	**0.937** (0.906-0.965)	0.000	**0.907** (0.859-0.950)	0.000		0.966 (0.926-1.001)	0.059
W	0.977 (0.949-1.002)	0.076	1.012 (0.973-1.045)	0.493	*	**0.942** (0.900-0.979)	0.001
fuller model: sex-, age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**0.894** (0.832-0.948)	0.000	0.944 (0.862-1.009)	0.102		**0.843** (0.743-0.927)	0.000
MW	1.006 (0.967-1.039)	0.727	**1.070** (1.023-1.104)	0.005	*	**0.928** (0.856-0.986)	0.013
NE	0.962 (0.918-1.000)	0.052	1.030 (0.975-1.073)	0.257	*	**0.876** (0.801-0.940)	0.000
NW	0.963 (0.916-1.004)	0.082	0.982 (0.918-1.033)	0.532		0.954 (0.877-1.013)	0.143
S	**0.941** (0.905-0.973)	0.000	**0.945** (0.893-0.991)	0.018		**0.932** (0.879-0.976)	0.002
SE	**0.896** (0.849-0.938)	0.000	**0.877** (0.808-0.938)	0.000		**0.922** (0.857-0.975)	0.003
W	1.009 (0.976-1.037)	0.555	**1.065** (1.026-1.096)	0.002	*	**0.942** (0.883-0.991)	0.018
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.916** (0.852-0.971)	0.002	0.948 (0.860-1.017)	0.158		**0.894** (0.795-0.972)	0.005
MW	1.013 (0.971-1.047)	0.516	**1.070** (1.017-1.108)	0.012	*	0.945 (0.871-1.002)	0.064
NE	0.992 (0.951-1.027)	0.700	**1.052** (1.000-1.092)	0.048	*	**0.920** (0.848-0.979)	0.006
NW	0.992 (0.946-1.030)	0.715	1.026 (0.967-1.072)	0.340		0.950 (0.870-1.012)	0.130
S	0.989 (0.955-1.018)	0.480	0.993 (0.944-1.034)	0.772		0.983 (0.934-1.023)	0.446
SE	**0.944** (0.900-0.982)	0.003	**0.925** (0.858-0.982)	0.008		0.968 (0.908-1.016)	0.220
W	1.030 (0.999-1.057)	0.054	**1.088** (1.052-1.115)	0.000	*	0.966 (0.908-1.012)	0.165

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998). [b]Age-group 15-44, 45-54, 55-64, 65-74, or 75+,
[c]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[d]Adjusted for age-group; T, N and M categories; grade; colon, rectosigmoid junction, or rectum/anus; microscopic verification status; marital status; individual year of diagnosis. [Sex, method of presentation and smoking status did not significantly improve model-fit and were excluded from the final model.]
*Significant difference in RR between diagnosis periods.

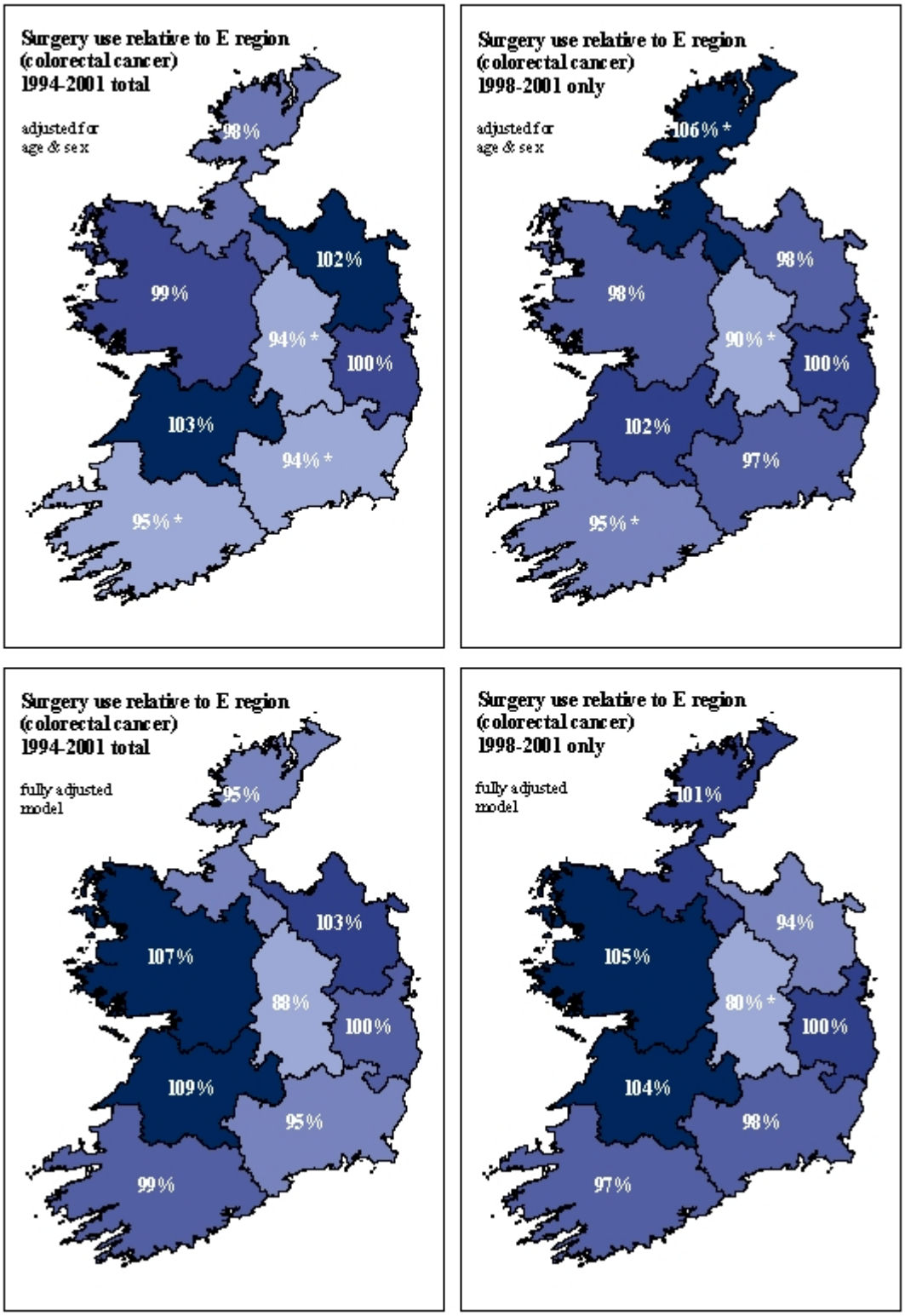


Figure 4.6.1 Regional variation in surgical treatment for colorectal cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age- and sex- adjusted model (top), fully-adjusted model (bottom). See *Table 4.6.10* for further details. * = significantly high or low values (P<0.05).

Surgical treatment

Patients from the Midland, Southern and South-Eastern regions, diagnosed during 1994-2001, were significantly less likely to receive surgical treatment than patients from the Eastern region (*Figure 4.6.1*, *Table 4.6.10*), allowing for regional variation in age or sex of patients. Regional patterns for 1994-97 and 1998-2001 differed in some details, but mainly involved lower use of surgery for patients from some regions. Relative risk estimates (RRs) differed significantly between periods for patients from the North-Eastern and North-Western regions.

Further adjustment for stage-related variables appeared to accentuate regional variations, and also the differences between diagnosis periods. But somewhat less complex patterns were evident after fuller adjustment for a range of patient and tumour variables. For 1994-2001, there significantly low use of surgery in patients from the Midland and South-Eastern regions and significantly high use in those from the Mid-Western and Western regions. compared with the Eastern region. Based on variables included in the final models, regional variation appeared to be much less marked for cases diagnosed during 1998-2001 (significantly low use of surgery in the Midland region) than for 1994-97 (low use in two regions, high use in three regions). RRs for three regions (Midland, Mid-Western and North-Eastern) differed significantly between periods, although this involved an increase in RR for the Midland region.

Table 4.6.10 Risk ratios for surgical treatment of colorectal cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.943** (0.898-0.984)	0.006	0.980 (0.919-1.032)	0.478		**0.902** (0.834-0.963)	0.001
MW	1.029 (0.993-1.060)	0.102	1.045 (0.995-1.088)	0.073		1.016 (0.965-1.061)	0.500
NE	1.016 (0.981-1.047)	0.344	**1.060** (1.013-1.099)	0.013	*	0.978 (0.927-1.024)	0.374
NW	0.979 (0.940-1.015)	0.278	**0.908** (0.849-0.962)	0.000	*	**1.058** (1.006-1.101)	0.029
S	**0.948** (0.919-0.976)	0.000	**0.952** (0.910-0.990)	0.013		**0.946** (0.904-0.985)	0.006
SE	**0.942** (0.907-0.974)	0.000	**0.916** (0.865-0.962)	0.000		0.967 (0.918-1.011)	0.154
W	0.992 (0.960-1.022)	0.638	1.007 (0.962-1.047)	0.732		0.978 (0.931-1.021)	0.341
fuller model: sex-, age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**0.846** (0.771-0.915)	0.000	0.977 (0.888-1.050)	0.577	*	**0.687** (0.572-0.798)	0.000
MW	**1.083** (1.042-1.118)	0.000	**1.134** (1.087-1.169)	0.000	*	1.013 (0.936-1.076)	0.719
NE	0.992 (0.941-1.038)	0.773	**1.088** (1.030-1.134)	0.005	*	**0.881** (0.795-0.958)	0.002
NW	**0.938** (0.876-0.993)	0.028	**0.880** (0.791-0.959)	0.002	*	1.019 (0.931-1.089)	0.645
S	**0.945** (0.901-0.985)	0.007	0.964 (0.904-1.016)	0.195		**0.918** (0.849-0.979)	0.008
SE	**0.907** (0.854-0.956)	0.000	**0.892** (0.816-0.960)	0.001		**0.925** (0.848-0.993)	0.031
W	**1.041** (1.000-1.077)	0.046	**1.075** (1.024-1.117)	0.006		1.003 (0.934-1.061)	0.913
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.880** (0.801-0.951)	0.000	0.974 (0.875-1.053)	0.558	*	**0.796** (0.674-0.907)	0.000
MW	**1.091** (1.047-1.127)	0.000	**1.129** (1.074-1.169)	0.000	*	1.039 (0.964-1.100)	0.277
NE	1.032 (0.983-1.075)	0.180	**1.108** (1.051-1.151)	0.001	*	0.942 (0.857-1.016)	0.133
NW	0.950 (0.885-1.006)	0.088	**0.904** (0.810-0.984)	0.017		1.009 (0.915-1.083)	0.833
S	0.988 (0.944-1.028)	0.599	1.004 (0.944-1.056)	0.863		0.970 (0.900-1.030)	0.357
SE	**0.952** (0.900-0.999)	0.049	**0.930** (0.854-0.996)	0.039		0.982 (0.907-1.046)	0.611
W	**1.069** (1.029-1.104)	0.001	**1.094** (1.042-1.135)	0.001		1.047 (0.981-1.101)	0.146

[a,b,c]See *Table 3.6.11*.
[d]Age-group; T, N and M categories; grade; colon, rectosigmoid junction, or rectum/anus; microscopic verification status; method of presentation; smoking status; marital status; individual year of diagnosis. [Sex did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

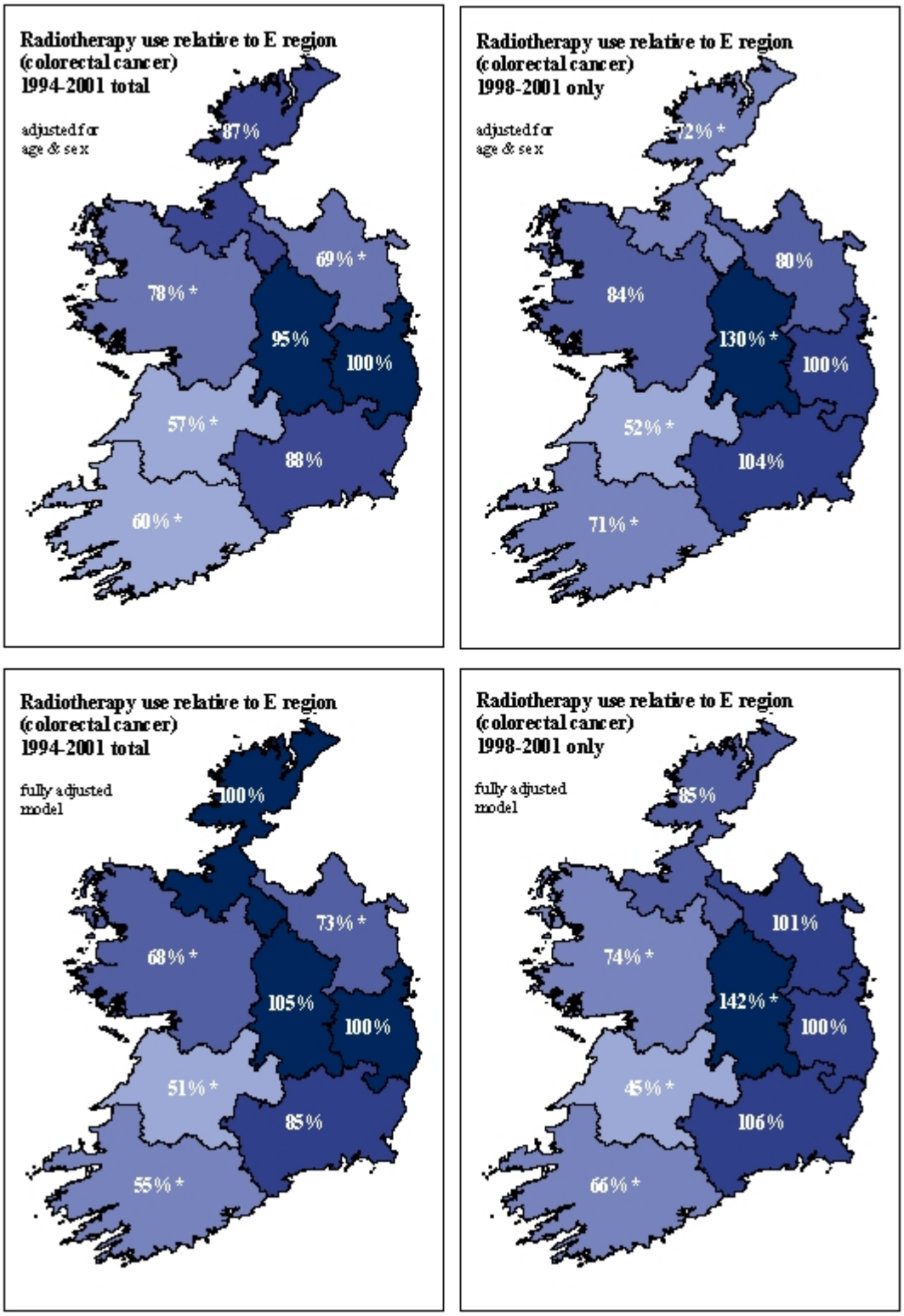


Figure 4.6.2 Regional variation in radiotherapy for colorectal cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age- and sex- adjusted model (top), fully-adjusted model (bottom). See *Table 4.6.11* for further details. * = significantly high or low values (P<0.05).

Radiotherapy

Patients from four regions (Mid-Western, North-Eastern, Southern and Western) were significantly, and substantially (by 22-43%), less likely to have radiotherapy than patients from the Eastern region, based on an age- and sex-adjusted model for 1994-2001 as a whole (*Figure 4.6.2*, *Table 4.6.11*). Variation appeared to be most marked (and involved two further regions) in the 1994-97 diagnosis period, and relative risk estimates (RRs) differed significantly between 1994-97 and 1998-2001 for five regions. In the latter period, patients from the Midland region were actually more likely to have radiotherapy than those from the Eastern region, a reversal of the pattern seen in the earlier period.

These patterns of regional variation were little changed, and RRs modified only slightly, after further adjustment for stage-related variables. Fuller adjustment for a range of variables had little effect for 1994-2001 as a whole, but perhaps accentuated regional differences for the (same) four regions with significantly low RRs (now 27-49% lower than for the Eastern region). In one or other four-year period, patients from six regions were significantly less likely, and only those from the Midland region (in 1998-2001) more likely, to receive radiotherapy (compared with the Eastern region).

Table 4.6.11 Risk ratios for radiotherapy of colorectal cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.952 (0.778-1.157)	0.628	**0.522** (0.347-0.777)	0.001	*	**1.302** (1.036-1.615)	0.024
MW	**0.565** (0.454-0.700)	0.000	**0.623** (0.443-0.869)	0.005		**0.518** (0.389-0.684)	0.000
NE	**0.692** (0.570-0.836)	0.000	**0.478** (0.330-0.687)	0.000	*	0.804 (0.640-1.002)	0.053
NW	0.865 (0.710-1.048)	0.142	1.076 (0.814-1.406)	0.600	*	**0.720** (0.542-0.947)	0.018
S	**0.600** (0.512-0.702)	0.000	**0.429** (0.322-0.569)	0.000	*	**0.712** (0.588-0.859)	0.000
SE	0.882 (0.753-1.029)	0.112	**0.674** (0.512-0.882)	0.004	*	1.042 (0.859-1.255)	0.668
W	**0.783** (0.661-0.923)	0.003	**0.683** (0.515-0.900)	0.007		0.843 (0.683-1.033)	0.102
fuller model: sex-, age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.958 (0.781-1.167)	0.676	**0.511** (0.339-0.763)	0.001	*	**1.324** (1.049-1.647)	0.019
MW	**0.550** (0.440-0.684)	0.000	**0.625** (0.443-0.876)	0.006		**0.499** (0.373-0.663)	0.000
NE	**0.734** (0.603-0.888)	0.001	**0.479** (0.329-0.691)	0.000	*	0.893 (0.708-1.117)	0.328
NW	0.849 (0.694-1.032)	0.102	1.040 (0.783-1.367)	0.781		**0.703** (0.525-0.931)	0.013
S	**0.610** (0.519-0.714)	0.000	**0.427** (0.319-0.567)	0.000	*	**0.744** (0.611-0.901)	0.002
SE	0.861 (0.733-1.009)	0.066	**0.650** (0.491-0.855)	0.002	*	1.028 (0.843-1.245)	0.778
W	**0.746** (0.628-0.883)	0.001	**0.632** (0.472-0.839)	0.001		**0.803** (0.647-0.991)	0.041
final multivariate model[d]							
E	1.000		1.000			1.000	
M	1.046 (0.826-1.313)	0.701	**0.595** (0.380-0.917)	0.018	*	**1.423** (1.073-1.844)	0.015
MW	**0.508** (0.395-0.651)	0.000	**0.635** (0.432-0.921)	0.016		**0.448** (0.320-0.623)	0.000
NE	**0.729** (0.587-0.899)	0.003	**0.441** (0.296-0.652)	0.000	*	1.010 (0.781-1.291)	0.934
NW	0.997 (0.801-1.231)	0.980	1.188 (0.875-1.590)	0.264		0.854 (0.621-1.157)	0.318
S	**0.552** (0.461-0.660)	0.000	**0.424** (0.312-0.573)	0.000	*	**0.656** (0.522-0.819)	0.000
SE	0.852 (0.712-1.017)	0.077	**0.615** (0.456-0.826)	0.001	*	1.064 (0.846-1.323)	0.587
W	**0.681** (0.561-0.822)	0.000	**0.600** (0.436-0.818)	0.001		**0.742** (0.580-0.941)	0.014

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; sex; T, N and M categories; grade; colon, rectosigmoid junction, or rectum/anus; microscopic verification status; marital status; individual year of diagnosis. [Method of presentation and smoking status did not significantly improve model-fit and were excluded from the final model.]
*Significant difference in RR between diagnosis periods.

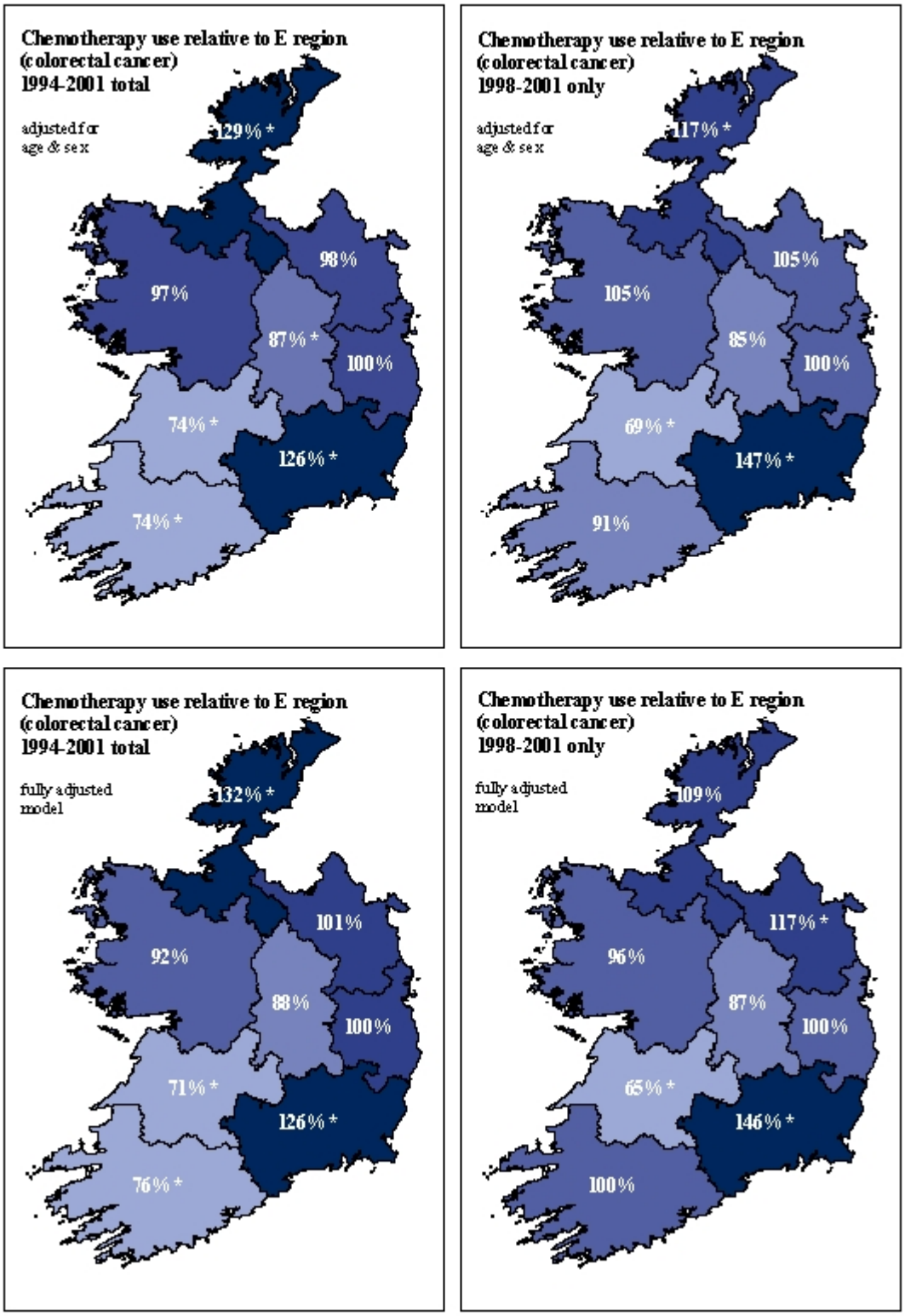


Figure 4.6.3 Regional variation in chemotherapy for colorectal cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age- and sex- adjusted model (top), fully-adjusted model (bottom). See *Table 4.6.12* for further details. * = significantly high or low values (P<0.05).

Chemotherapy

For three regions during 1994-2001 as a whole (Midland, Mid-Western and Southern), patients were significantly less likely (by 18-26% in relative terms) to receive chemotherapy than those from the Eastern region, after adjustment for patients' age and sex (*Figure 4.6.3*, *Table 4.6.12*). Patients from the North-Western and South-Eastern regions were significantly more likely (by 25-28%) to receive chemotherapy than those from Eastern region. The detailed patterns differed somewhat between the 1994-97 and 1998-2001 diagnosis periods, including significant differences in relative risk estimates (RRs) for four regions (North-Western, Southern, South-Eastern and Western).

In contrast to the other treatment modalities considered, the patterns of variation simplified slightly (rather than became more complex) after further adjustment for stage. However, changes were minor. Adjustment for a wider range of patient and tumour variables had little further effect. The overall pattern, based on this final model, involved significantly low use of chemotherapy among patients from the Mid-Western and Southern regions (24-29% lower than patients from the Eastern region), and significantly high use among those from the North-Western and South-Eastern regions (26-31% higher).

Table 4.6.12 Risk ratios for chemotherapy of colorectal cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.867** (0.751-0.994)	0.041	0.892 (0.716-1.095)	0.283		0.846 (0.696-1.014)	0.072
MW	**0.738** (0.646-0.839)	0.000	**0.782** (0.633-0.958)	0.017		**0.694** (0.583-0.820)	0.000
NE	0.982 (0.878-1.092)	0.746	0.842 (0.691-1.017)	0.076		1.047 (0.914-1.189)	0.491
NW	**1.285** (1.154-1.420)	0.000	**1.476** (1.261-1.704)	0.000	*	**1.165** (1.002-1.337)	0.046
S	**0.735** (0.665-0.811)	0.000	**0.495** (0.411-0.594)	0.000	*	0.909 (0.807-1.017)	0.099
SE	**1.255** (1.148-1.365)	0.000	1.005 (0.857-1.169)	0.944	*	**1.466** (1.325-1.609)	0.000
W	0.972 (0.876-1.075)	0.596	0.846 (0.707-1.005)	0.057	*	1.053 (0.926-1.188)	0.417
fuller model: sex-, age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.866 (0.743-1.002)	0.054	0.892 (0.708-1.108)	0.313		0.845 (0.684-1.027)	0.094
MW	**0.756** (0.656-0.866)	0.000	0.874 (0.702-1.074)	0.207	*	**0.646** (0.533-0.776)	0.000
NE	1.032 (0.917-1.155)	0.591	0.860 (0.697-1.049)	0.142	*	1.121 (0.970-1.281)	0.117
NW	**1.282** (1.143-1.427)	0.000	**1.571** (1.338-1.816)	0.000	*	1.067 (0.897-1.250)	0.450
S	**0.776** (0.698-0.861)	0.000	**0.508** (0.418-0.614)	0.000	*	0.998 (0.880-1.123)	0.982
SE	**1.221** (1.108-1.338)	0.000	0.988 (0.833-1.161)	0.894	*	**1.425** (1.270-1.581)	0.000
W	0.949 (0.848-1.058)	0.359	0.875 (0.724-1.048)	0.151		0.970 (0.838-1.112)	0.676
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.883 (0.751-1.030)	0.118	0.900 (0.703-1.133)	0.382		0.865 (0.693-1.059)	0.168
MW	**0.714** (0.612-0.827)	0.000	0.870 (0.687-1.086)	0.227		**0.648** (0.530-0.784)	0.000
NE	1.014 (0.897-1.140)	0.808	0.844 (0.681-1.034)	0.105	*	**1.166** (1.009-1.332)	0.037
NW	**1.315** (1.169-1.467)	0.000	**1.586** (1.346-1.838)	0.000	*	1.089 (0.915-1.275)	0.325
S	**0.762** (0.682-0.849)	0.000	**0.491** (0.402-0.598)	0.000	*	1.000 (0.878-1.129)	0.999
SE	**1.257** (1.139-1.380)	0.000	1.010 (0.849-1.189)	0.905	*	**1.458** (1.299-1.617)	0.000
W	0.920 (0.816-1.032)	0.160	0.862 (0.708-1.039)	0.123		0.957 (0.822-1.102)	0.557

[a,b,c]See *Table 3.6.11*.
[d]Adjusted for age-group; sex; T, N and M categories; grade; colon, rectosigmoid junction, or rectum/anus; microscopic verification status; smoking status; marital status; individual year of diagnosis. [Method of presentation did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

4.7 Discussion: colorectal cancer

The major findings here are:

- significant increases in relative survival of patients between the periods 1994-97 and 1998-2001, nationally and in the Western region;
- significant regional variation in relative survival throughout 1994-2001, involving lower survival of patients in some regions outside of the Eastern region;
- significant increases in the use of radiotherapy and chemotherapy between 1996 and 2001;
- significant regional variation in treatments, most notably involving lower use of radiotherapy therapy, and either lower or higher use of chemotherapy, for patients from four of the seven regions outside of the Eastern region.

Survival trends

Improvements seen in relative survival at national scale (representing about a 10% reduction in relative excess mortality risk) were also seen to a greater or less or extent among patients from most individual regions. Adjustment for stage and other tumour or patient characteristics did not reduce (in fact increased) the apparent improvement. Much of the improvement in survival thus seems likely to reflect improvements in the quality of treatment and in proportions of patients receiving appropriate treatment. Data indicating increased chemotherapy and radiotherapy use, in particular, may support this. Population-based screening for colorectal cancer is not yet available in Ireland, thus there is currently only limited potential for earlier detection, but further improvements in survival can be expected once screening becomes more widespread.

Regional variation in survival

This was quite substantial, with significantly poorer relative survival in up to four regions, compared with the Eastern region, depending on the period considered or the extent of adjustment for patient and tumour characteristics. Overall during 1994-2001, excess mortality risks associated with a colorectal cancer diagnosis were 12-20% higher in four regions (after basic adjustment for age and sex), or 10-24% higher in three regions (after fuller adjustment).

Regional variations in relative survival were not fully consistent between diagnosis periods 1994-97 and 1998-2001. Most notably, for the Mid-Western region lower survival compared with the Eastern region was largely confined to the more recent period. Overall, and within each period, fuller adjustment for patient and tumour characteristics appeared to moderate the extent and magnitude of regional variation in survival to some extent. The remaining variation may be accounted for by unmeasured variables, or regional variation in treatment, or both. It may relevant that patients from the two regions with the highest excess mortality risk (Mid-Western and Southern), in the final survival model, were the least likely to receive chemotherapy and radiotherapy.

Survival: international context

Five-year relative survival estimates for Irish men and women diagnosed with colorectal cancer during 1994-97 were similar to or slightly lower than European averages based on cases diagnosed during 1990-94 (EUROCARE-3 results summarized in *Table 4.7.1*). More recent Europe-wide figures are not yet available. Note that figures tabulated here are age-standardized to the EUROCARE-3 patient population, thus the Irish figures differ slightly from those tabulated earlier in this chapter.

Table 4.7.1 Comparison of five-year relative survival for colorectal cancer patients, Ireland 1994-97 and 1998-2001, and Europe 1990-94, age-adjusted to the EUROCARE-3 standard patient population for this cancer.[a]

	Ireland 1994-97 5-yr survival (95% CI)		Ireland 1998-2001 survival (95% CI)		Europe 1990-94[b] survival (95% CI)		[range][c]
male	47.2%	(44.9%-49.4%)	49.4%	(46.9%-51.9%)	47.6%	(46.7%-48.4%)	[26.8%-55.2%]
female	49.5%	(47.2%-51.7%)	52.1%	(49.7%-54.6%)	50.5%	(49.7%-51.3%)	[28.6%-60.0%]

[a]Capocaccia *et al*. (2003) and unpublished. [b]EUROCARE-3: Sant *et al*. (2003).
[c]Range of national figures: highest Switzerland (male), France (female).

Treatment trends

The major trends seen were significant and substantial increases (by 11-12% annually in relative terms) in the proportion of patients receiving radiotherapy and chemotherapy, between 1996 and 2001. Significant increases were also seen for radiotherapy in four of the eight regions and for chemotherapy in five regions. Trends for surgical treatment involved a small but significant annual decline nationally, although at regional scale this was significant for two regions only.

Standard treatment modalities for colorectal cancer

Evidence-based summaries of standard treatment options, by stage or other prognostic grouping, are available as part of the US National Cancer Institute's PDQ Cancer Information Summaries: (http://www.cancer.gov/cancertopics/pdq/cancerdatabase).

A brief summary is provided below, by broad modality (see also *Appendix 1*).

Colon cancer

Surgery: Curative intent (as single modality) for stages I and II; curative in combination with adjuvant chemotherapy for stage III; palliative or curative for some stage IV cases.

Radiotherapy: Palliative for some stage IV cases.

Chemotherapy: Adjuvant for stage III, palliative for stage IV.

Rectal cancer

Surgery: Curative (as single modality or in combination with adjuvant radiotherapy and chemotherapy) for stage I; curative (in combination with adjuvant radiotherapy and chemotherapy) for stages II-III; mainly palliative for stage IV.

Radiotherapy: Adjuvant (sometimes curative) for stage I; adjuvant for stage II; adjuvant or palliative for stage III; palliative for stage IV.

Chemotherapy: Adjuvant for stages I-II, adjuvant or palliative for stages III-IV.

Regional variation in treatment

Marked regional variation was seen in the proportions of patients receiving treatment, particularly radiotherapy and chemotherapy. For radiotherapy, this involved significantly lower use (by *c*.20-50%) in four regions, compared with the Eastern region, during 1994-2001 as a whole. For chemotherapy over the same period, there was significantly lower use (by *c*.15-30%) in two or three regions but significantly higher use (by *c*.25-30%) in two regions (North-Western and South-Eastern). Patterns were broadly the same whether basic or fuller adjustments were made for patient and tumour characteristics. However, for both these modalities the regional patterns differed substantially between diagnosis periods 1994-97 and 1998-2001. Regional variation in surgical treatment was less marked, i.e. of lower magnitude and including a mix of lower and higher use of surgery compared with the Eastern region.

As for other cancers, interpreting the variations seen in treatment, and the extent to which they can be accounted for by patient or tumour characteristics, is difficult. Some relevant variables may not have been measured or included in the statistical models (e.g. comorbidity or general patient condition). However, it seems likely that a substantial proportion of the 'unexplained' variation in radiotherapy and chemotherapy use for colorectal cancer reflects regional or institutional differences in the extent to which given treatments were offered or provided.

Treatment: international context

Comparisons are made here with first-course treatments reported for colon and rectal cancers in the USA as part of the National Cancer Data Base (http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm). NCDB data have been extracted for cases other than stage 0, diagnosed during 1998-2001, to provide nearest-equivalent data on treatments of invasive colorectal cancers. Possible minor differences between the Irish and US data in the timing of treatment included should be borne in mind, but the data should be broadly comparable.

For both colon and rectal cancer, Irish patients were significantly less likely to receive overall treatment or surgical treatment than in the USA (*Table 4.7.2*). For rectal cancer, significantly smaller proportions of Irish patients had radiotherapy and chemotherapy. Surgery as the only treatment was significantly less frequent for Irish colon cancer cases, but more frequent for Irish rectal cancer cases. Use of the main multi-modal treatment for colon cancer (surgery plus chemotherapy) was similar in Ireland and the US. However, a significantly smaller proportion of Irish cases received the main multi-modal treatment for rectal cancer (surgery plus chemotherapy plus radiotherapy).

Further work is required to assess in more detail the extent to which treatment in Ireland reflects current international guidelines or best practice (cf. *Appendix 1* for a brief summary).

Table 4.7.2 Comparison of main treatment modalities and combinations for patients with invasive colon and rectal cancer, Ireland and USA, in diagnosis period 1998-2001. US data were not specified in detail for some treatments. Irish data here exclude rectosigmoid junction and anus, to facilitate comparisons with the US data.

	colon			rectum		
	Ireland 1998-2001		**USA[a©] 1998-2001**	**Ireland 1998-2001**		**USA[a©] 1998-2001**
any treatment	82.8%	***	92.6%	84.7%	***	91.4%
no treatment	17.2%	***	7.4%	15.3%	***	8.6%
any surgery[b]	78.4%	***	90.5%	74.1%	***	80.0%
any chemotherapy	31.5%	-	≥24.3%	36.3%	***	[c]≥46.1%
any radiotherapy	3.8%	-	-	32.7%	***	≥45.6%
surgery only	49.6%	***	62.5%	39.4%	***	35.8%
surge + chemo	25.5%	ns	24.3%	10.2%	***	5.1%
surge + chemo + radio	2.0%	-	-	18.9%	***	33.6%
surge + radio	1.1%	-	-	5.3%	ns	4.6%
chemotherapy only	3.7%	-	-	2.3%	-	-
radiotherapy only	0.4%	-	-	3.7%	-	-
chemo + radio	0.2%	-	-	4.6%	***	7.4%
others	0.2%	-	5.8%	0.2%	-	4.9%

- = data not available or statistical comparison not possible.
[a]Source of US data: National Cancer Data Base of first-course treatments reported by hospitals approved by the American College of Surgeons Commission on Cancer; cases of stage 0 have been excluded but cases of unknown stage have been included and assumed to be invasive; see http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm.

[b]US surgical data are for surgery of primary site only.
* (P<0.05), ** (P<0.01), *** (P<0.001): significant differences between Ireland and USA in proportion of patients treated (χ^2 tests, 1.d.f.).
[c]≥ indicates that overall use of these treatments among patients in the USA may be higher than shown, as figures for less frrequent single modalities are not quoted on the NCDB website.

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Chapter 5. LUNG CANCER

Summary

Trends in incidence, mortality and patient/tumour characteristics

Numbers of cases and age-standardized incidence rates showed a significant upward trend in females, while incidence rates fell significantly for males. Numbers of deaths showed no significant trends, while mortality rates among males declined significantly.

Overall, some improvements in completeness of staging were seen, but no tendency towards earlier detection. The proportion of patients aged 65-74 decreased, while the proportion aged 75+ increased. The proportion of stage III and IV cancers increased; those with unknown stage decreased.

Survival

1994-2001 average

Relative survival to five years after diagnosis was estimated as 8.6% (95% CI 8.0-9.2%) overall, 7.9% (7.1-8.5%) for males and 10.0% (8.9-11.0%) for females.

Survival trends

Five-year relative survival showed some indication of improvement (not statistically significant) from 8.2% (95% CI 7.4-9.0%) for 1994-97 to 9.0% (8.1-9.9%) for 1998-2001. Having adjusted for age, sex and cell-type the change in relative survival was again not significant. Patients aged 55-64 or resident in the North-Eastern region showed a significant reduction in relative survival between 1994-97 and 1998-2001; other regions and age-groups showed no significant change.

The lack of any notable or general improvement in relative survival for this cancer, within the period examined, is not unexpected. Lung cancer is, on average, far more fatal and far less treatable than other cancers considered in this report. The scope for improvements in treatment and survival is also, currently, less, in the absence of effective approaches to population-based screening.

Regional variation in survival

Taking account of a range of patient and tumour characteristics, three regions (Mid-Western, North-Western and Western) had a significantly low excess risk of death i.e. high survival (compared with the Eastern region) during 1994-2001, and also during both 1994-97 and 1998-2001. The North-Eastern region also showed a significantly low excess risk, during 1994-97. Only one region (South-Eastern in 1998-2001) showed a significantly high excess risk of death (lower survival) compared with the Eastern region.

Regional variation in risk was less marked than for the other cancers considered in this report and, by contrast, largely involved higher relative survival for patients from a number of regions compared with the Eastern region. However, the low average survival of lung cancer patients should be borne in mind. Statistically significant differences between regions may involve only small absolute differences in survival.

International comparison of survival

For males, the average five-year relative survival for Irish patients diagnosed with lung cancer during 1994-97 was lower than the European average for patients diagnosed during 1990-94. For female patients, Irish and average European survival figures were similar.

Treatment

Proportions of patients treated: main modalities and combinations

Overall during 1994-2001, 53% of patients had some form of definitive or tumour-directed treatment within six months of diagnosis, 32% had radiotherapy, 15% had chemotherapy and 14% had surgery. For 1998-2001, 54% were treated, 34% had radiotherapy, 16% had chemotherapy and 13% had surgery. For non-small-cell lung cancers, radiotherapy was the main treatment (40% of cases); for small-cell lung cancers, chemotherapy (56%). A substantial proportion of small-cell cancers cases received multimodal treatment, in particular chemotherapy plus radiotherapy (17%).

Region of treatment versus region of residence

The majority of surgical patients from six of the eight regions had their main surgical treatment in the Eastern region. Only in the Eastern, Southern and Western regions did most have their surgical treatments locally (100%, 97% and 55% of 1994-2001 cases, respectively).

Hospital caseloads

Lung cancers were surgically treated in a total of

29 hospitals during 1994-2001. In contrast to other major cancers (breast, colorectal and lung), there were indications that the number of hospitals where lung cancer patients had surgical treatment increased, and average surgical caseloads by hospital fell, during this period. About half of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each, and about two-thirds treated fewer than 20 surgical cases. Apparent declines in average surgical caseloads per hospital were supported by significant increases in the proportion of surgical cases treated in hospitals averaging <20 or <50 surgical cases annually.

Surgical consultant caseloads

99 individual consultants were coded as responsible for surgical managements of lung cancers diagnosed during 1994-2001. There were more during 1998-2001 (68) than 1994-1997 (51). Most treated fewer than 10 surgical cases, and almost all treated fewer than 20 surgical cases, annually. There was some evidence that average surgical caseloads, by consultant, decreased over time. Reflecting this, significant increases were seen in the proportions of surgical patients treated by 'low volume' consultants treating <10 or, especially, <20 surgical cases annually.

Treatment trends

The use of surgery fell significantly, by *c*.5.0% annually in relative terms after adjustment for age and stage, between 1996 and 2001. Regional trends were not statistically significant. The trends largely involved surgery of non-small-cell lung cancers.

Radiotherapy use increased significantly by *c*.2.2% annually between 1996 and 2001, although the basic trend was not significant after adjustment for stage. Significant increases were also seen among patients from the Mid-Western and North-Eastern regions.

Chemotherapy use increased significantly, by *c*.6.4% annually (age-adjusted), or *c*.4.6% (age- and stage-adjusted), and also among patients from the Eastern region. These trends largely reflected increased use of chemotherapy for non-small-cell cancers.

Regional variation in treatment

There was a general tendency for higher proportions of patients from the Eastern region to be treated than those from other regions, overall and based on specific modalities. This tendency was strongest for chemotherapy, especially in the most recent period.

Approximately two-fold regional variation in proportions of patients treated was apparent for surgery (e.g. range 8-16% of regional cases during 1998-2001), radiotherapy (range 20-37%) and chemotherapy (range 10-22%). There was apparently little in common between patterns for different modalities, except that use of all three modalities was high among patients from the Eastern region.

During 1994-2001 as a whole, significantly low use of surgical treatment, after full adjustment for patient and tumour characteristics, was seen in the Mid-Western, North-Western and Western and South-Eastern regions, compared with the Eastern region. This was also seen in the North-Western and Western regions for 1994-97, and the Southern and South-Eastern for 1998-2001. These patterns were essentially the same for non-small-cell cancers as for lung cancers as a whole. Case numbers were too small to examine regional patterns in surgery for small-cell cancers.

Patients from the Mid-Western, South-Eastern and Western regions during 1994-97, but only the Western region during 1998-2001, had significantly low use of radiotherapy compared with the Eastern region. Similar regional patterns were evident for non-small-cell lung cancers.

Regional variation in chemotherapy use was very marked, although there were substantial differences between diagnosis periods. Overall, patients from five regions (Midland, Mid-Western, North-Eastern, North-Western and South-Eastern) were significantly less likely, and patients from the Western region significantly more likely, to receive chemotherapy than those from the Eastern region. However, regional variation (except for the Western region) was largely confined to 1998-2001.

International comparison of treatment

For both non-small-cell and small-cell lung cancer, Irish patients were significantly less likely to receive treatment, whether overall, radiotherapy, chemotherapy or surgery, than in the USA during 1998-2001. For both cell-types, Irish cases were less likely to have a combination of radiotherapy and chemotherapy and more likely to have radiotherapy only.

5.1 Incidence and mortality statistics

On average, there were 1576 cases of and 1497 deaths from invasive lung cancer annually in Ireland during 1994-2001 (*Table 5.1.1*). Over this period, total numbers of cases showed a significant upward trend, but this was confined to females.

Age-standardized incidence rates fell significantly for males but increased for females. Numbers of deaths showed no significant trends, while mortality rates among males (but not females) declined significantly.

Table 5.1.1 Incidence of and mortality from invasive lung cancer, Republic of Ireland, 1994-2001.

	Annual average numbers						age-standardized rate[a]			
1994-2001	**total**		**male**		**female**		**male**		**female**	
Incidence (cases)	1576		1014		562		63.9		28.6	
Incidence trend (per year)[b]	+1.1%	**	+0.1%	ns	+3.1%	***	-1.4%	**	+1.8%	**
Mortality (deaths)	1497		963		534		60.5		26.6	
Mortality trend (per year)	-0.4%	ns	-1.2%	ns	+1.2%	ns	-2.6%	***	-0.4%	ns

[a]European age-standardized rate per 100,000 persons per year.
[b]Estimated annual percentage change (ns not significant, * P<0.05, **P<0.01, ***P<0.001).

5.2 Cases included for treatment and survival analyses; patient and tumour characteristics

Analyses cover invasive cancers of the bronchus and lung (ICD-10 code C34) diagnosed in 11,663 persons aged 15-99 years during 1994-2001 (*Table 5.2.1*).

Table 5.2.1 Summary of inclusions and exclusions for lung cancer analyses.

Case definition	**total**
all registered tumours[a]	12 686
ages 15-99 only	12 682
excluding death-certificate-only & autopsy-only cases	12 045
invasive tumours only	12 002
first tumours only[b]	**11 663**

[a] Including in situ carcinomas, and tumours of unspecified behaviour, but excluding lymphomas and any other cancer morphologies that are classified separately within ICD-10.
[b] Or most serious tumour diagnosed same date.

A breakdown of basic patient and tumour characteristics is given in *Table 5.2.2*, including comparisons between diagnosis periods 1994-97 and 1998-2001. The variables and category-values shown are those considered, later in this chapter, for inclusion in statistical models aimed at describing and if possible explaining regional variation and time-trends in survival and treatment.

For this cancer, overall numbers of cases increased only slightly between 1994-97 and 1998-2001, thus proportional changes match changes in absolute numbers of cases. Statistically significant changes between 1994-97 and 1998-2001 in proportions of patients or tumours with particular characteristics were as follows:

- Decrease in male, increase in female patients.
- Decrease in patients aged 65-74, increase in those aged 75+ at diagnosis.
- Increase in stage III and stage IV cancers, decrease in unknown stage.
- Decrease in tumours in T4 category, decrease in T unknown.
- Increase in node-positive cancers, decrease in unknown nodal status.
- Increase in cases with and without metastases, decrease in unknown metastatic status.
- Decrease in grade 2 and grade 3+ tumours, increase in grade unknown.
- Decrease in microscopically verified (MV) cases, increase in non-MV cases.
- Decrease in symptomatic cases, increase in incidental presentation and unknown method of presentation.
- Decrease in patients with marital status unknown.
- Decrease in patients recorded as smokers, increase in patients with unknown smoking status.

Overall, these changes indicate improvements in completeness of staging but no tendency towards earlier detection.

Variation in patient and tumour characteristics by region of residence is summarized in *Table 5.2.3*.

Table 5.2.2 Summary of patient and tumour characteristics for lung cancer patients included in survival and treatment analyses, 1994-2001.

	diagnosed 1994-2001		diagnosed 1994-1997		diagnosed 1998-2001	
	number	% of cases	number	% of cases	number	% of cases
total	11663		5734		5929	
age 15-44	234	2.0%	104	1.8%	130	2.2%
age 45-54	898	7.7%	422	7.4%	476	8.0%
age 55-64	2235	19.2%	1122	19.6%	1113	18.8%
age 65-74	4494	38.5%	2280	39.8%	2214	*37.3%
age 75+	3802	32.6%	1806	31.5%	1996	*33.7%
male	7508	64.4%	3772	65.8%	3736	*63.0%
female	4155	35.6%	1962	34.2%	2193	*37.0%
non-small-cell	6953	59.6%	3456	60.3%	3497	59.0%
small-cell	1623	13.9%	799	13.9%	824	13.9%
other/NOS	3087	26.5%	1479	25.8%	1608	27.1%
stage I	496	4.3%	258	4.5%	238	4.0%
stage II	192	1.6%	103	1.8%	89	1.5%
stage III	849	7.3%	296	5.2%	553	*9.3%
stage IV	3258	27.9%	1403	24.5%	1855	*31.3%
stage X[a]	6868	58.9%	3674	64.1%	3194	*53.9%
T1	935	8.0%	444	7.7%	491	8.3%
T2	2838	24.3%	1391	24.3%	1447	24.4%
T3	1057	9.1%	508	8.9%	549	9.3%
T4	2067	17.7%	817	14.2%	1250	*21.1%
T X	4766	40.9%	2574	44.9%	2192	*37.0%
N negative	1775	15.2%	838	14.6%	937	15.8%
N positive	3438	29.5%	1463	25.5%	1975	*33.3%
N X	6450	55.3%	3433	59.9%	3017	*50.9%
M negative	2190	18.8%	971	16.9%	1219	*20.6%
M positive[b]	3267	28.0%	1408	24.6%	1859	*31.4%
M X	6206	53.2%	3355	58.5%	2851	*48.1%
grade 1	288	2.5%	156	2.7%	132	2.2%
grade 2	1358	11.6%	750	13.1%	608	*10.3%
grade 3+	3086	26.5%	1663	29.0%	1423	*24.0%
grade X	6931	59.4%	3165	55.2%	3766	*63.5%
MV[c] yes	8709	74.7%	4336	75.6%	4373	*73.8%
MV no	2797	24.0%	1316	23.0%	1481	*25.0%
MV X	157	1.3%	82	1.4%	75	1.3%
symptomatic	10777	92.4%	5371	93.7%	5406	*91.2%
incidental	432	3.7%	174	3.0%	258	*4.4%
screen detected	32	0.3%	13	0.2%	19	0.3%
presentation X	422	3.6%	176	3.1%	246	*4.1%
non-smoker	1056	9.1%	503	8.8%	553	9.3%
ex-smoker	2774	23.8%	1301	22.7%	1473	*24.8%
smoker	6403	54.9%	3237	56.5%	3166	*53.4%
smoking X	1430	12.3%	693	12.1%	737	12.4%
ever married	9239	79.2%	4510	78.7%	4729	79.8%
never married	2039	17.5%	1014	17.7%	1025	17.3%
marital status X	385	3.3%	210	3.7%	175	*3.0%

[a]Unknown values shown as "X" for stage and other variables. [b]Minor discrepancies between stage IV and M positive cases reflect morphologies for which TNM staging is not strictly applicable. [c]MV = microscopic verification (histology or cytology).
*Significant change in the proportion of cases in this category (χ^2 test, 1 df, $P<0.05$); but note that some further changes may be significant if cases in "unknown" categories are excluded.

Table 5.2.3 Summary of patient and tumour characteristics, by region of residence, for lung cancer patients included in survival and treatment analyses, 1994-2001. Account is taken of the potential confounding affect of these variables in statistical models of regional variation in survival (*section 5.4.4*) and treatment (*section 5.6.3*).

	Eastern	Mid-Western	Midland	North-Eastern	North-Western	Southern	South-Eastern	Western
total cases	4686	587	875	905	753	1678	1189	990
age 15-44	2.3%	3.1%	1.6%	2.4%	1.7%	*1.4%	1.7%	1.6%
age 45-54	8.2%	*4.6%	7.8%	7.8%	7.6%	8.5%	6.9%	6.9%
age 55-64	19.7%	16.2%	*24.0%	19.4%	*16.3%	19.3%	17.8%	17.6%
age 65-74	39.3%	42.8%	37.1%	36.2%	37.8%	*36.1%	41.1%	37.1%
age 75+	30.6%	33.4%	29.5%	*34.0%	*36.5%	*34.7%	32.5%	*36.9%
male	60.7%	*69.2%	*66.3%	*65.5%	*69.1%	*64.7%	*67.0%	*68.7%
female	39.3%	*30.8%	*33.7%	*34.5%	*30.9%	*35.3%	*33.0%	*31.3%
non-small-cell	65.1%	61.3%	*47.8%	*57.8%	*53.4%	*61.0%	*53.5%	*54.4%
small-cell	15.1%	13.5%	*11.1%	13.3%	13.0%	14.9%	*12.8%	*12.0%
other/NOS	19.8%	*25.2%	*41.1%	*29.0%	*33.6%	*24.1%	*33.7%	*33.5%
stage I	5.3%	4.3%	5.4%	*2.8%	*3.1%	*3.2%	*3.6%	*3.3%
stage II	2.0%	0.9%	1.5%	1.2%	2.1%	*0.8%	1.4%	2.0%
stage III	8.3%	8.7%	7.2%	*5.6%	*5.7%	*4.4%	8.4%	8.0%
stage IV	29.7%	*25.0%	*23.9%	*25.0%	*22.8%	29.5%	27.8%	28.9%
stage X	54.7%	*61.2%	*62.1%	*65.4%	*66.3%	*62.2%	*58.8%	57.8%
T1	9.3%	8.2%	*6.4%	*13.4%	*3.7%	*6.7%	*6.2%	*6.3%
T2	24.6%	*28.8%	22.3%	24.6%	21.5%	23.9%	27.2%	*21.3%
T3	7.6%	*14.8%	6.6%	6.4%	*13.0%	*12.8%	*9.8%	6.8%
T4	15.8%	16.4%	17.6%	*9.4%	*20.2%	*21.1%	*22.2%	*22.4%
T X	42.7%	*31.9%	*47.1%	46.2%	41.6%	*35.5%	*34.5%	43.2%
N negative	16.5%	14.8%	16.6%	*11.9%	*10.9%	15.9%	16.7%	*11.7%
N positive	30.2%	31.2%	*25.6%	30.1%	*26.3%	27.7%	32.1%	30.5%
N X	53.4%	54.0%	*57.8%	*58.0%	*62.8%	*56.5%	51.1%	*57.8%
M negative	22.5%	19.9%	21.6%	*15.0%	*15.9%	*11.7%	*17.9%	*16.7%
M positive	29.8%	*25.0%	*24.1%	*25.1%	*22.8%	29.6%	27.9%	29.0%
M X	47.7%	*55.0%	*54.3%	*59.9%	*61.2%	*58.8%	*54.2%	*54.3%
grade 1	2.1%	2.9%	*4.1%	1.8%	1.6%	*3.8%	2.6%	1.2%
grade 2	12.3%	*9.0%	*8.8%	9.9%	13.4%	13.1%	13.5%	*8.4%
grade 3+	29.8%	26.4%	*21.4%	*24.0%	*24.7%	*22.2%	*23.7%	29.2%
grade X	55.8%	*61.7%	*65.7%	*64.3%	*60.3%	*60.9%	*60.2%	*61.2%
MV yes	81.0%	*76.3%	*60.3%	*72.2%	*68.3%	*76.6%	*67.9%	*68.3%
MV no	17.7%	*22.7%	*36.8%	*27.1%	*31.5%	*22.7%	*30.5%	*28.9%
MV X	1.2%	1.0%	*2.9%	0.8%	*0.3%	0.7%	1.6%	*2.8%
symptomatic	90.9%	93.2%	92.5%	*93.1%	*94.6%	*95.4%	*93.5%	90.2%
incidental	4.1%	3.7%	3.1%	3.6%	3.7%	3.3%	*2.6%	4.3%
screen detected	0.4%	0.0%	0.1%	0.1%	0.1%	0.4%	0.1%	0.1%
presentation X	4.6%	3.1%	4.3%	3.1%	*1.6%	*0.8%	3.8%	5.4%
non-smoker	6.8%	8.5%	*10.1%	6.5%	*8.9%	*16.3%	*9.5%	*8.7%
ex-smoker	25.8%	23.2%	*21.9%	26.2%	22.6%	*19.4%	24.3%	*21.8%
smoker	52.8%	*57.8%	*56.6%	52.8%	*62.5%	53.4%	55.5%	*59.8%
smoking status X	14.7%	*10.6%	*11.4%	14.5%	*6.0%	*10.8%	*10.7%	*9.7%
ever married	82.8%	*75.0%	*76.6%	*76.1%	*74.2%	*79.7%	*77.7%	*74.8%
never married	13.6%	*22.0%	*18.9%	*20.4%	*23.8%	*17.8%	*18.8%	*22.5%
marital status X	3.6%	3.1%	4.6%	3.4%	*2.0%	2.5%	3.5%	2.6%

*Significant difference in proportion of cases, compared with Eastern region (χ^2 test, 1 df, P<0.05)

5. 3 Relative survival: descriptive analysis

Five-year relative survival estimates for national population, by period of diagnosis, age, sex, cell-type and other patient or tumour characteristics, are shown in *Table 5.3.1*. Survival curves, to five years after diagnosis, are plotted for the same variables in *Figure 5.3.1*. Five-year estimates by treatment status are shown in *Table 5.3.2*; and one-year, three-year and five-year estimates, nationally and regionally by diagnosis period, in *Table 5.3.3*.

Results and comparisons presented in this section are not adjusted for potential confounding variables, thus are potentially open to misinterpretation if taken at face value. More formal (multivariate) comparisons are made in *section 5.4*.

5.3.1 General summary

For lung cancer cases diagnosed in Ireland during 1994-2001 as a whole, relative survival to five years after diagnosis was estimated as 8.6% (95% CI 8.0-9.2%) (*Table 5.3.1*). Equivalent figures for males were 7.9% (7.1-8.5%), for females 10.0% (8.9-11.0%). Relative survival to one year averaged 23.7% (22.9-24.5%), and to three years 10.5% (9.8-11.0%) (*Table 5.3.3*).

5.3.2 Variation by patient and tumour characteristics

relative survival (to five years) was highest for age-groups under 45 years or, for other specific variables, cases that were of non-small-cell carcinoma morphologies; early stage; T category 1; node-negative; non-metastatic; grade 1 or 2; microscopically verified; incidentally detected; or in non-smokers or patients who were ever married (*Table 5.3.1* & *Figure 5.3.1*). Survival was lowest in the oldest age-group (75+), and, for other variables, cases that were of small-cell or non-specific morphologies; stage IV; T categories 3-4 or unknown; node-positive or nodal status unknown; metastatic; grade 3+ or unknown; lacking microscopic verification (or with MV status unknown); cases presenting symptomatically; or in smokers, or patients with unknown smoking or marital status. Note however that patients in a given univariate category may differ in other characteristics also - see section *5.4.1* for multivariate comparisons.

5.3.3 Variation by treatment status

Patients who received any tumour-directed treatment, or surgery, within six months of diagnosis had substantially higher five-year survival than patients who did not receive these treatments: averaging 12% v 4.5% for treatment v no treatment, and 35% v 4.2% for surgery v no surgery for 1994-2001 as a whole (*Table 5.3.2*). In contrast, survival was lower overall in patients who had radiotherapy or had chemotherapy compared with those did not. However, since patients given or not given particular treatments are likely to have differed, on average, in disease stage, cell-type or other characteristics, these figures do not provide any measure of treatment effectiveness.

5.3.4 National and regional trends

National estimates of five-year survival showed some indication of an improvement, though not statistically significant, from 8.2% (95% CI 7.4-9.0%) for cases diagnosed during 1994-97 to 9.0% (8.1-9.9%) for 1998-2001 (*Table 5.3.1*). Similar apparent improvements were evident for most regions of residence, but again were not clear-cut in terms of statistical significance (*Table 5.3.3*). See sections *5.4.2-3* for more formal comparisons, adjusted for age or other factors.

5.3.5 Regional variation

Five-year relative survival estimates during 1994-2001 ranged from 7.3% (95% CI 5.9-8.9%) for patients from the Southern region to 9.9% (7.5-12.5%) for the North-Eastern region (*Table 5.3.3*). However, confidence intervals overlapped markedly between regions, and regional rankings varied between diagnosis periods. See also *section 5.4.4*.

Table 5.3.1 National five-year relative survival for lung cancer patients, by patient and tumour characteristics, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population.

	1994-2001		1994-1997		1998-2001	
	5-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	8.6%	(8.0%-9.2%)	8.2%	(7.4%-9.0%)	9.0%	(8.1%-9.9%)
age 15-44	28.6%	(22.9%-34.5%)	29.1%	(20.6%-38.0%)	28.2%	(20.6%-36.2%)
age 45-54	11.7%	(9.6%-14.0%)	10.5%	(7.7%-13.6%)	13.3%	(10.2%-16.6%)
age 55-64	10.1%	(8.8%-11.5%)	8.4%	(6.8%-10.2%)	12.1%	(10.0%-14.4%)
age 65-74	8.7%	(7.7%-9.6%)	9.0%	(7.7%-10.3%)	8.0%	(6.6%-9.5%)
age 75+	5.6%	(4.6%-6.7%)	5.3%	(4.0%-6.8%)	6.1%	(4.6%-7.7%)
male	7.9%	(7.1%-8.5%)	7.5%	(6.6%-8.5%)	8.2%	(7.1%-9.3%)
female	10.0%	(8.9%-11.0%)	9.6%	(8.2%-11.0%)	10.4%	(8.9%-12.0%)
non-small-cell	11.0%	(10.1%-11.8%)	10.3%	(9.1%-11.4%)	11.9%	(10.5%-13.2%)
small-cell	5.0%	(3.8%-6.2%)	5.6%	(4.0%-7.5%)	4.1%	(2.7%-5.9%)
other/NOS	5.1%	(4.1%-6.1%)	4.9%	(3.7%-6.3%)	5.3%	(3.9%-6.8%)
stage I	35.9%	(30.9%-40.8%)	35.8%	(29.3%-42.4%)	35.2%	(27.3%-43.3%)
stage II	17.6%	(11.9%-24.1%)	14.9%	(8.3%-23.3%)	21.7%	(12.8%-32.1%)
stage III	8.1%	(6.1%-10.5%)	8.4%	(5.3%-12.3%)	7.7%	(4.9%-11.1%)
stage IV	2.4%	(1.8%-3.1%)	2.6%	(1.7%-3.6%)	2.3%	(1.6%-3.3%)
stage X[a]	9.4%	(8.6%-10.2%)	8.3%	(7.3%-9.3%)	*10.7%	(9.4%-12.1%)
T1	25.1%	(21.9%-28.3%)	23.1%	(18.9%-27.5%)	26.7%	(21.9%-31.8%)
T2	13.7%	(12.2%-15.2%)	12.8%	(10.9%-14.8%)	14.8%	(12.6%-17.1%)
T3	6.3%	(4.7%-8.1%)	7.2%	(4.9%-9.9%)	5.2%	(3.2%-7.8%)
T4	3.8%	(2.9%-4.8%)	4.0%	(2.6%-5.6%)	3.5%	(2.3%-5.0%)
T X	5.0%	(4.2%-5.7%)	4.7%	(3.8%-5.7%)	5.3%	(4.1%-6.6%)
N negative	26.2%	(23.8%-28.5%)	25.2%	(22.0%-28.5%)	26.7%	(23.0%-30.3%)
N positive	6.5%	(5.5%-7.4%)	6.4%	(5.1%-7.8%)	6.6%	(5.2%-8.0%)
N X	4.9%	(4.2%-5.5%)	4.8%	(4.0%-5.7%)	5.0%	(4.1%-6.0%)
M negative	16.5%	(14.7%-18.3%)	18.3%	(15.6%-21.0%)	14.8%	(12.4%-17.4%)
M positive[b]	2.5%	(1.9%-3.1%)	2.6%	(1.8%-3.6%)	2.3%	(1.6%-3.3%)
M X	9.1%	(8.2%-9.9%)	7.7%	(6.6%-8.7%)	*10.9%	(9.4%-12.3%)
grade 1	18.4%	(13.2%-24.3%)	10.9%	(6.22%-17.0%)	*30.0%	(20.1%-40.7%)
grade 2	17.3%	(15.0%-19.7%)	16.5%	(13.7%-19.5%)	17.9%	(14.2%-21.9%)
grade 3+	9.2%	(8.1%-10.4%)	8.6%	(7.1%-10.1%)	9.7%	(7.8%-11.7%)
grade X	6.2%	(5.5%-6.9%)	6.0%	(5.0%-6.9%)	6.6%	(5.6%-7.6%)
MV yes	9.8%	(9.1%-10.5%)	9.4%	(8.4%-10.3%)	10.2%	(9.0%-11.3%)
MV no	5.3%	(4.2%-6.3%)	4.9%	(3.6%-6.4%)	5.6%	(4.2%-7.3%)
MV X	3.1%	(0.9%-7.6%)	1.7%	(0.1%-7.9%)	4.9%	(1.2%-12.4%)
symptomatic	8.1%	(7.5%-8.7%)	8.0%	(7.2%-8.8%)	8.2%	(7.3%-9.1%)
incidental	20.0%	(15.6%-24.8%)	18.5%	(12.4%-25.7%)	21.3%	(15.1%-28.2%)
screen detected	-		-		-	
presentation X	9.0%	(6.0%-12.7%)	6.5%	(3.1%-11.5%)	12.9%	(8.7%-18.0%)
non-smoker	12.6%	(10.3%-15.0%)	14.2%	(10.9%-17.8%)	10.6%	(7.3%-14.5%)
ex-smoker	9.7%	(8.4%-11.0%)	9.0%	(7.3%-10.8%)	10.5%	(8.6%-12.5%)
smoker	7.8%	(7.1%-8.6%)	7.3%	(6.3%-8.2%)	8.5%	(7.3%-9.7%)
smoking X	7.2%	(5.7%-8.9%)	7.2%	(5.2%-9.5%)	6.9%	(4.7%-9.6%)
ever married	9.1%	(8.4%-9.7%)	8.6%	(7.7%-9.5%)	9.5%	(8.4%-10.5%)
never married	7.3%	(6.0%-8.7%)	7.1%	(5.4%-8.9%)	7.7%	(5.7%-9.9%)
marital status X	4.6%	(2.5%-7.6%)	5.1%	(2.3%-9.3%)	3.5%	(0.9%-8.8%)

[a]Unknown values shown as "X" for stage, T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status. [b]Minor discrepancies between stage IV and M positive cases are because some M positive cases were of morphologies for which TNM staging is not strictly applicable for this site. *Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

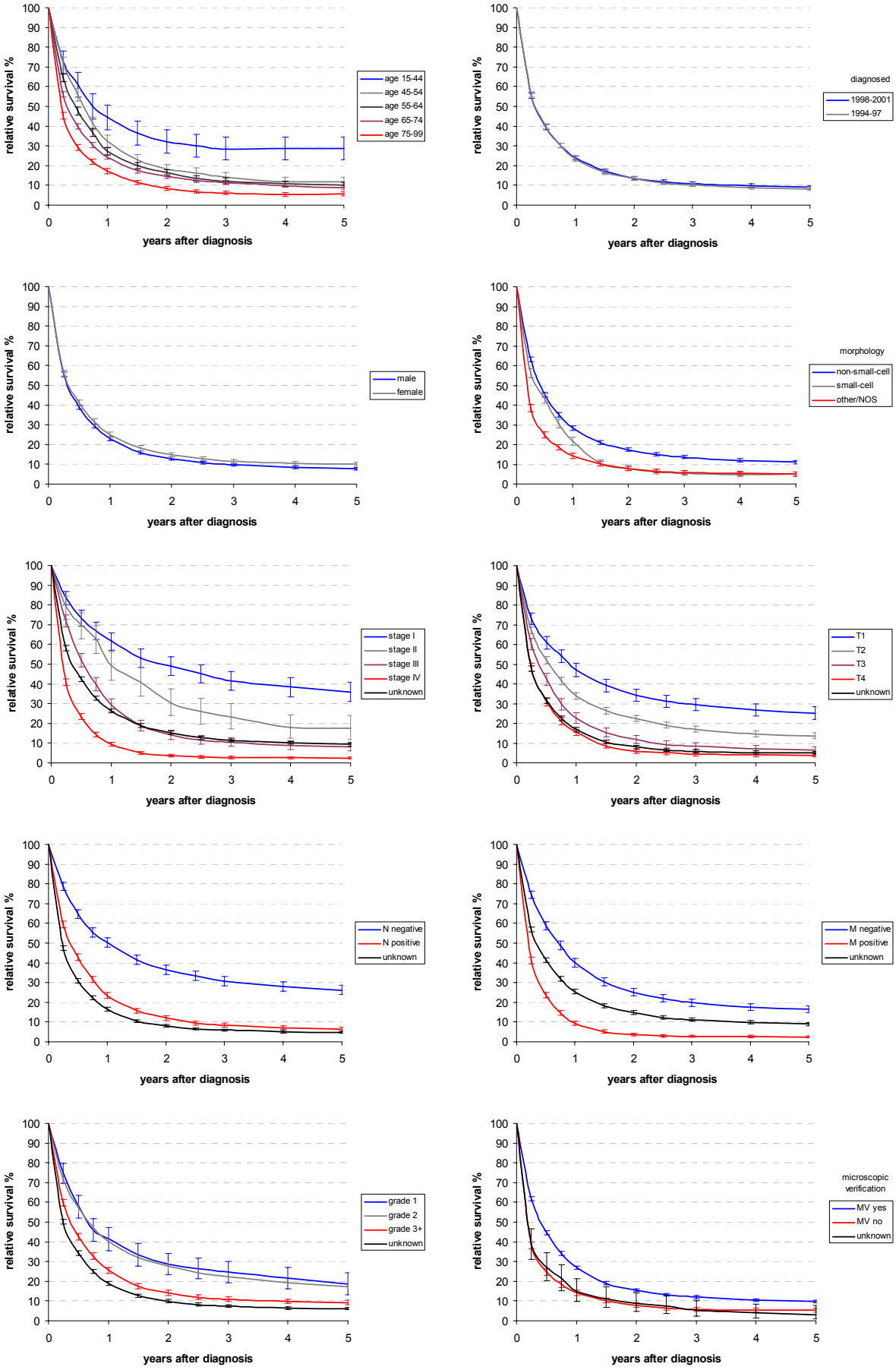
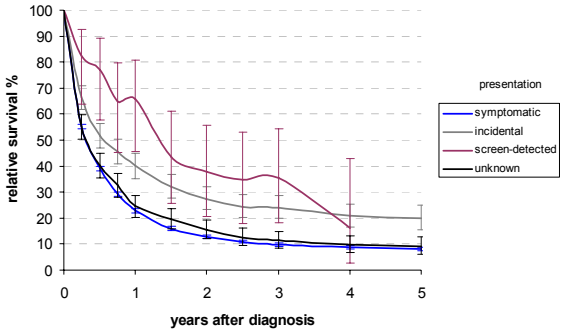
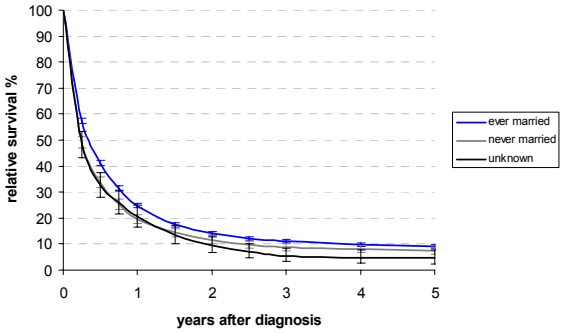


Figure 5.3.1 Relative survival up to five years after diagnosis for lung cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown.





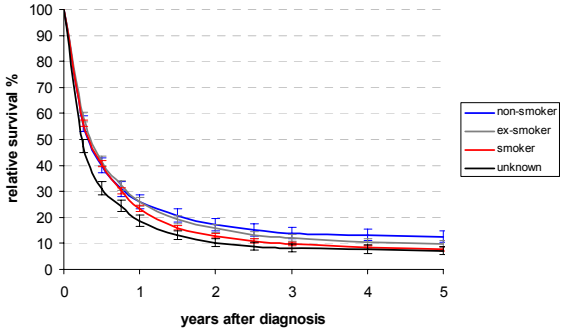


Figure 5.3.1 (continued)

Table 5.3.2 National five-year relative survival for lung cancer patients, by treatment status (within six months of diagnosis) and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population. Patients treated and not treated are likely to differ markedly in disease stage, age, cell-type or other characteristics, thus *differences in survival between treated and untreated patients below should not be interpreted as reflecting the effect of treatment.*

	1994-2001		1994-1997		1998-2001	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	8.6%	(8.0%-9.2%)	8.2%	(7.4%-9.0%)	9.0%	(8.1%-9.9%)
treatment	12.3%	(11.3%-13.2%)	12.0%	(10.7%-13.3%)	12.5%	(11.1%-13.9%)
no treatment	4.5%	(3.6%-5.2%)	4.2%	(3.3%-5.1%)	4.9%	(3.8%-6.0%)
surgery	34.7%	(32.0%-37.3%)	30.2%	(26.9%-33.5%)	*40.0%	(35.4%-44.4%)
no surgery	4.2%	(3.7%-4.6%)	4.0%	(3.4%-4.6%)	4.3%	(3.6%-5.0%)
radiotherapy	4.8%	(4.0%-5.6%)	4.6%	(3.5%-5.7%)	5.2%	(4.1%-6.4%)
no radiotherapy	10.4%	(9.6%-11.2%)	9.8%	(8.8%-10.8%)	11.0%	(9.7%-12.2%)
chemotherapy	5.0%	(3.9%-6.2%)	5.1%	(3.6%-6.8%)	4.8%	(3.3%-6.6%)
no chemotherapy	9.3%	(8.6%-10.0%)	8.8%	(7.9%-9.7%)	9.9%	(8.8%-10.9%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs.

Table 5.3.3 One-year, three-year and five-year relative survival for lung cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population (from the same region for regional estimates).

Region	1994-2001		1994-1997		1998-2001	
	1-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	23.7%	(22.9%-24.5%)	23.4%	(22.3%-24.5%)	24.0%	(22.8%-25.1%)
E	24.7%	(23.4%-26.0%)	24.4%	(22.6%-26.1%)	25.1%	(23.3%-26.9%)
M	24.8%	(21.2%-28.4%)	24.7%	(19.5%-30.1%)	24.8%	(20.0%-29.8%)
MW	24.0%	(21.1%-26.9%)	21.8%	(17.8%-26.1%)	25.8%	(21.8%-29.8%)
NE	21.8%	(19.1%-24.6%)	23.6%	(19.4%-27.8%)	20.3%	(16.8%-24.0%)
NW	23.8%	(20.7%-27.0%)	26.3%	(21.7%-31.0%)	21.5%	(17.4%-25.8%)
S	22.6%	(20.5%-24.6%)	21.2%	(18.4%-24.1%)	23.9%	(21.0%-26.8%)
SE	22.1%	(19.7%-24.6%)	21.3%	(18.0%-24.8%)	23.0%	(19.5%-26.4%)
W	23.7%	(21.0%-26.4%)	23.7%	(19.8%-27.6%)	23.7%	(20.0%-27.5%)
	1994-2001		1994-1997		1998-2001	
	3-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	10.5%	(9.8%-11.0%)	10.1%	(9.2%-10.9%)	10.8%	(9.9%-11.6%)
E	10.9%	(9.9%-11.8%)	10.3%	(9.0%-11.6%)	11.5%	(10.1%-12.9%)
M	10.8%	(8.2%-13.7%)	10.7%	(7.1%-15.1%)	11.0%	(7.6%-15.0%)
MW	10.4%	(8.3%-12.6%)	9.8%	(7.0%-13.2%)	11.0%	(8.1%-14.2%)
NE	10.2%	(8.2%-12.3%)	10.5%	(7.6%-13.9%)	9.8%	(7.2%-12.8%)
NW	11.8%	(9.4%-14.4%)	13.1%	(9.6%-17.0%)	10.5%	(7.4%-14.2%)
S	9.4%	(7.9%-10.9%)	8.4%	(6.5%-10.5%)	10.4%	(8.3%-12.7%)
SE	10.5%	(8.6%-12.4%)	10.7%	(8.2%-13.5%)	10.1%	(7.7%-12.9%)
W	9.5%	(7.6%-11.6%)	8.7%	(6.2%-11.6%)	10.5%	(7.7%-13.5%)
	1994-2001		1994-1997		1998-2001	
	5-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	8.6%	(8.0%-9.2%)	8.2%	(7.4%-9.0%)	9.0%	(8.1%-9.9%)
E	9.0%	(8.0%-9.9%)	8.3%	(7.1%-9.5%)	9.6%	(8.1%-11.2%)
M	9.4%	(6.9%-12.4%)	8.9%	(5.5%-13.2%)	10.1%	(6.6%-14.4%)
MW	8.2%	(6.2%-10.5%)	7.8%	(5.1%-11.1%)	8.5%	(5.6%-12.2%)
NE	9.0%	(6.9%-11.2%)	8.6%	(5.8%-11.9%)	9.6%	(6.8%-12.8%)
NW	9.9%	(7.5%-12.5%)	11.3%	(7.9%-15.3%)	7.9%	(4.7%-11.9%)
S	7.3%	(5.9%-8.9%)	6.5%	(4.7%-8.5%)	8.7%	(6.4%-11.2%)
SE	8.7%	(6.9%-10.6%)	9.3%	(6.8%-12.1%)	7.8%	(5.4%-10.7%)
W	8.1%	(6.2%-10.2%)	7.4%	(5.0%-10.3%)	8.8%	(6.0%-12.1%)

5.4 Relative survival: modelling

5.4.1 Variation by patient and tumour characteristics

For assessment of regional variation in relative survival during 1994-2001, a full relative survival model was run, potentially incorporating and adjusting for available patient and tumour characteristics. These included year of follow-up (years 1 to 5 after diagnosis), age-group, stage-related variables (T, N and M categories), grade, interaction between those variables and year of follow-up, and additional patient and tumour variables without interaction terms (sex, cell-type, microscopic verification status, method of presentation, marital status, smoking status, year of diagnosis). Excluding region and year (covered later), and variables that did not contribute significantly to model-fit, statistically significant excess hazard ratios (EHRs) were recorded as follows:

- During year 1 of follow-up (for variables assessed using an interaction term for follow-up year):
  - Higher EHR (lower relative survival) for age-groups 45-54 years (1.316 [95% CI 1.088-1.592]), 55-64 (1.604 [1.340-1.919]), 65-74 (1.944 [1.629-2.319]) and 75+ (2.392 [2.002-2.859]), compared with age-group 15-44 years.
  - Higher EHR for T categories 2 (1.321 [1.193-1.464]), 3 (1.651 [1.471-1.853]), 4 (1.946 [1.753-2.161], and unknown or non-applicable (1.709 [1.547-1.887]), compared with T category 1.
  - Higher EHR for N positive (1.689 [1.558-1.832]) and N unknown cases (1.886 [1.739-2.045]), compared with N negative cases.
  - Higher EHR for M positive (2.219 [2.071-2.378]) and M unknown cases (1.239 [1.159-1.324], compared with M negative cases.
  - Higher EHR for grade 3+ (1.227 [1.064-1.416] and grade unknown cases (1.207 [1.047-1.391]), compared with grade 1.
- For age, stage-related and grade variables, EHRs varied significantly during subsequent follow-up and cannot readily be summarized beyond year 1.
- Overall (for variables assessed without an interaction term for follow-up year):
  - Lower EHR (higher relative survival) for female patients (0.914 [0.877-0.954]), compared with males.
  - Higher EHR (lower relative survival) for cases of 'other or unspecified' morphology (1.391 [1.316-1.470]), compared with non-small-cell carcinoma.
  - Lower EHR for cases that presented incidentally (0.706 [0.630-0.792]), were screen detected (0.330 [0.203-0.536]) or whose method of presentation was unknown (0.831 [0.742-0.930]), compared with cases presenting symptomatically.
  - Higher EHR for current smokers (1.148 [1.067-1.235]) and patients of unknown smoking status (1.140 [1.041-1.249]), compared with non-smokers (never-smokers).
  - Higher EHR for patients who were never married (1.198 [1.137-1.262]), compared with those who were ever married.
- Microscopic verification status did not significantly improve model fit, after adjustment for other variables, and was excluded from the full model.

These findings are broadly consistent with the variations already noted for unadjusted relative survival (*Table 5.3.1*), for the overall period 1994-2001. A number of further differences were evident from the unadjusted estimates, including significantly low survival for small-cell carcinomas, cases lacking microscopic verification or of unknown MV status, and patients of unknown marital status. However, these differences were either not significant, or the variables did not significantly contribute to model-fit, after adjustment for available patient and tumour characteristics.

5.4.2 National and age-specific trends

There was no significant change, overall, in relative survival for lung cancer between diagnosis periods 1994-97 and 1998-2001, having adjusted for age, sex and cell-type (*Table 5.4.1*). In specific age-groups, a significant improvement was only seen for age-group 55-64, equivalent to a 10% reduction in excess risk of death.

5.4.3 Regional trends

Patients resident in the North-Eastern region showed a significant reduction in relative survival between 1994-97 and 1998-2001, equivalent to a 17% increase in excess risk of death (*Table 5.4.1*). Other regions showed no significant changes.

Table 5.4.1 Changes in relative survival between diagnosis-years 1994-97 and 1998-2001, stratified by age and region of residence, for patients diagnosed with lung cancer during 1994-2001. Excess hazard ratios in bold = significant difference from baseline (1994-1997) (EHR <1 = reduction in excess hazard thus improvement in relative survival, EHR >1 = increase in excess hazard thus reduction in relative survival). Only the basic model is shown for individual regions as regional sample sizes are generally too small too allow complex modelling.

	1998-2001 v 1994-97	
	[a]EHR (95% CI)	P
basic model: age-specific, sex-, celltype-adjusted		
age 15-44	1.053 (0.766-1.449)	0.747
age 45-54	0.918 (0.797-1.057)	0.236
age 55-64	**0.899** (0.823-0.983)	0.020
age 65-74	1.010 (0.949-1.076)	0.736
age 75+	1.056 (0.986-1.131)	0.115
basic model: sex-, age-, celltype-adjusted[b]		
total	0.996 (0.958-1.036)	0.878
E	0.982 (0.922-1.044)	0.568
M	1.017 (0.853-1.214)	0.845
MW	0.937 (0.812-1.081)	0.377
NE	**1.172** (1.014-1.353)	0.031
NW	1.091 (0.930-1.280)	0.281
S	0.964 (0.869-1.069)	0.490
SE	1.043 (0.921-1.181)	0.501
W	0.954 (0.832-1.094)	0.505
fuller model: sex-, age-, celltype-, stage-adjusted[b]		
total	0.991 (0.953-1.031)	0.678
final multivariate model[b]		
total	0.999 (0.960-1.040)	0.988

[a] EHR = excess hazard ratio (or "relative excess risk"]
[b]See *Table 5.4.*2 but region and diagnosis year excluded here.

5.4.4 Regional variation

Moderate regional variation in relative survival (as assessed by modelling of excess hazard ratios) was evident. For the period 1994-2001 as a whole, patients resident in the Mid-Western and North-Western regions had a significantly lower (by 8-10%) excess risk of death - i.e. higher relative survival - compared with patients from the Eastern region, based on comparisons adjusted for age, sex and cell-type (*Figure 5.4.1*, *Table 5.4.2*). This was significant only for North-Western region in 1994-97 and Mid-Western region in 1998-2001. After further adjustment, for stage-related variables, two further regions had significantly reduced excess risk of death – the Western region overall and in 1994-97, and the North-Eastern region in 1994-97. However, the North-Eastern and South-Eastern regions had significantly higher excess risk (lower survival) than the Eastern region during the most recent period, 1998-2001, after adjustment for stage.

In the fully adjusted model, taking account of a wider range of patient and tumour characteristics, three regions had a significantly low excess risk of death (compared with the Eastern region) during 1994-2001: Mid-Western (13% lower than the Eastern), North-Western (15% lower) and Western (14% lower) (*Figure 5.4.1*, *Table 5.4.2*). Again, regional variation was higher than in the basic model, and not fully consistent between the two diagnosis periods. However, three regions (Mid-Western, North-Western and Western) showed a significantly low excess risk in both 1994-97 and 1998-2001. Only one region (South-Eastern in 1998-2001) showed a significantly high excess risk of death based on the fully adjusted model (12% higher than for the Eastern region in 1998-2001).

In interpreting these analyses, the low average survival of lung cancer patients should be borne in mind. Statistically significant differences in survival may involve only small absolute gains or losses in survival. In addition to this, the modifying effects of stage-related and other variables on regional comparisons are difficult to interpret, given the particularly high proportions of lung cancer cases lacking specific data for many variables (see *Table 5.2.3*). This may be accentuated by the low survival figures involved and the tendency for survival to be particularly poor in patients lacking specific diagnostic or staging information (*section 5.4.1*).

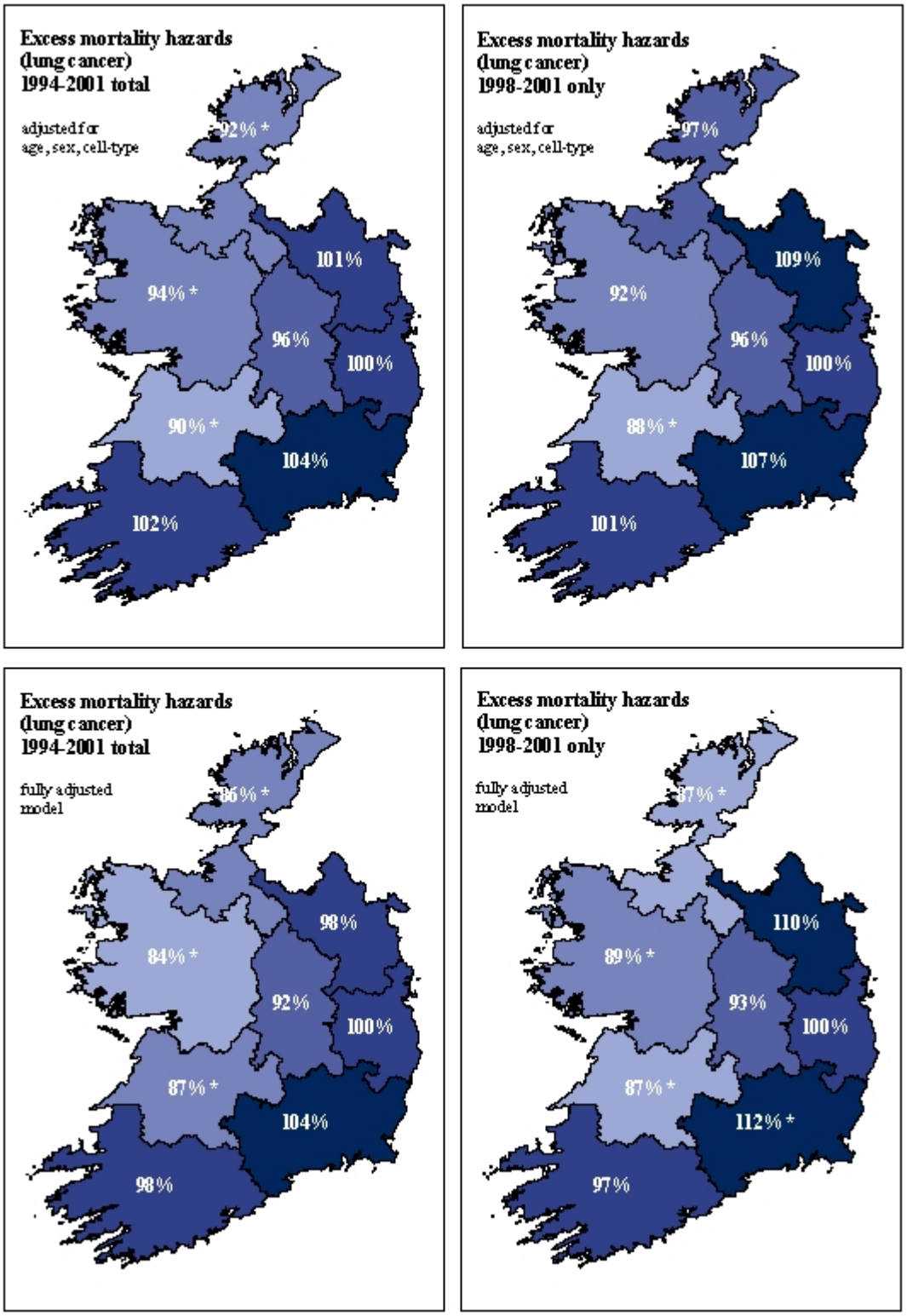


Figure 5.4.1 Regional variation in excess mortality hazards (based on relative survival) for lung cancer, expressed in comparison with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic model adjusted for age, sex & cell-type (top), fully-adjusted model (bottom). See *Table 5.4.2* for further details. * = significantly high or low excess risk (P<0.05).

Table 5.4.2 Variation in relative survival, by region of residence, for patients diagnosed with lung cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (EHR <1 = lower excess hazard thus higher relative survival than in Eastern region, EHR >1 = higher excess hazard thus lower relative survival).

	1994-2001		1994-1997		1998-2001	
	[a]EHR (95% CI)	P	EHR (95% CI)	P	EHR (95% CI)	P
basic model: sex-, age-, celltype-adjusted[b,c,d]						
E	1.000		1.000		1.000	
M	0.957 (0.872-1.050)	0.361	0.945 (0.824-1.083)	0.419	0.964 (0.849-1.095)	0.578
MW	**0.896** (0.828-0.970)	0.007	0.915 (0.816-1.027)	0.134	**0.876** (0.786-0.977)	0.017
NE	1.008 (0.933-1.088)	0.837	0.925 (0.827-1.035)	0.179	1.087 (0.978-1.208)	0.121
NW	**0.915** (0.841-0.995)	0.039	**0.867** (0.768-0.978)	0.021	0.971 (0.863-1.093)	0.634
S	1.017 (0.958-1.080)	0.562	1.021 (0.938-1.111)	0.627	1.007 (0.925-1.096)	0.866
SE	1.038 (0.969-1.112)	0.279	1.009 (0.915-1.112)	0.855	1.067 (0.968-1.177)	0.186
W	0.939 (0.871-1.011)	0.100	0.961 (0.864-1.068)	0.463	0.915 (0.824-1.017)	0.103
fuller model: sex-, age-, cell-, stage-adjusted[b,c,d,e]						
E	1.000		1.000		1.000	
M	0.954 (0.868-1.047)	0.324	0.905 (0.789-1.039)	0.158	0.982 (0.864-1.116)	0.788
MW	**0.891** (0.824-0.965)	0.005	**0.880** (0.784-0.988)	0.030	**0.893** (0.800-0.996)	0.043
NE	1.001 (0.926-1.081)	0.975	**0.870** (0.777-0.975)	0.017	**1.142** (1.027-1.271)	0.014
NW	**0.869** (0.798-0.946)	0.001	**0.837** (0.741-0.945)	0.004	0.896 (0.796-1.009)	0.072
S	0.983 (0.925-1.044)	0.582	0.963 (0.883-1.050)	0.395	0.991 (0.909-1.080)	0.843
SE	1.049 (0.979-1.124)	0.173	0.980 (0.888-1.081)	0.690	**1.131** (1.026-1.247)	0.013
W	**0.859** (0.797-0.926)	0.000	**0.808** (0.726-0.899)	0.000	0.909 (0.818-1.011)	0.079
final multivariate model[b,f]						
E	1.000		1.000		1.000	
M	0.924 (0.841-1.015)	0.103	0.903 (0.786-1.037)	0.150	0.931 (0.818-1.059)	0.279
MW	**0.871** (0.804-0.943)	0.001	**0.856** (0.762-0.961)	0.009	**0.868** (0.777-0.969)	0.012
NE	0.976 (0.903-1.055)	0.547	**0.857** (0.764-0.960)	0.008	1.104 (0.991-1.229)	0.071
NW	**0.855** (0.785-0.931)	0.000	**0.835** (0.739-0.944)	0.004	**0.872** (0.773-0.983)	0.026
S	0.978 (0.919-1.039)	0.478	0.969 (0.888-1.058)	0.486	0.973 (0.892-1.061)	0.538
SE	1.035 (0.966-1.109)	0.324	0.968 (0.877-1.069)	0.530	**1.119** (1.014-1.235)	0.024
W	**0.839** (0.779-0.905)	0.000	**0.785** (0.705-0.875)	0.000	**0.894** (0.804-0.994)	0.040

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]Models included interaction terms between follow-up interval (years 1-5) and age (plus stage-related variables in fuller and final models), equivalent to stratification by these variables, to allow for non-proportional hazards across follow-up time.
[c]Age-categories: EUROCARE age-groups 15-44, 45-54, 55-64, 65-74, 75+.
[d]Cell-type: non-small-cell (NSCLC), small-cell (SCLC) or other/unspecified lung cancer.
[e]Stage-related variables: T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[f]Final (full) multivariate model, also including: grade 1, 2, 3+ or unknown; method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever married, never married, unknown). [Microscopic verification status and individual year of observation did not significantly improve model-fit and were excluded.]

5.5 Treatment: Descriptive analysis

5.5.1 General comment

Analyses here are confined to *treatments administered within six months after diagnosis*. Variations in treatment between patient groups may, to some extent, reflect variations in the timing of treatment, but for this cancer the majority of first-line treatments should be included.

5.5.2 General summary of treatment

Of the total 11,683 lung cancer cases included in analyses for the period 1994-2001, 53% had some form of definitive or tumour-directed treatment within six months of diagnosis, 32% had radiotherapy, 15% had chemotherapy and 14% had surgery (*Table 5.5.1*). Equivalent figures for the most recent period, 1998-2001, were 5929 cases, of which 54% were treated, 34% had radiotherapy, 16% had chemotherapy and 13% had surgery (*Table 5.5.1*, *Figure 5.5.2*). A further breakdown by age is shown in *Table 5.5.1* and *Figure 5.5.1*.

The most frequent treatments or combinations were radiotherapy only (24% of cases 1994-2001), surgery only (12%), and chemotherapy only (8.9%). For the most recent period (1998-2001), equivalent figures were 25%, 10% and 9%, representing a significant increase in the use of radiotherapy and a significant decrease in surgery compared with 1994-97 (*Table 5.5.1*). Only chemotherapy plus radiotherapy (5.6% 1994-2001) and surgery plus radiotherapy (2.0%) made up more than 1% of treatments, and use of the former combination increased significantly between the periods 1994-97 and 1998-2001.

Equivalent figures by lung cancer cell-type are shown in *Table 5.5.2*. The main treatments for non-small-cell lung cancer (NSCLC) were radiotherapy (40% of 1994-2001 cases), surgery (23%) and to a lesser extent chemotherapy (11.5%); use of radiotherapy and chemotherapy fell significantly, but surgery increased, between 1994-97 and 1998-2001. Most NSCLC cases received a single treatment modality. For small-cell lung cancers (SCLC), chemotherapy was the main treatment (56% of 1994-2001 cases), radiotherapy to a lesser extent (27%); radiotherapy use increased significantly but chemotherapy use fell significantly between 1994-97 and 1998-2001. A substantial proportion of SCLC cases received multimodal treatment, in particular chemotherapy plus radiotherapy (17%).

Table 5.5.1 Summary of main treatment modalities and combinations (within six months of diagnosis) for lung cancer patients, by age and diagnosis period, 1994-2001. Only treatments or combinations making up at least 1% of cases in any period are listed.

	1994-2001						1994-97	1998-2001	
	age 15-44	44-54	55-64	65-74	75+	total	subtotal	subtotal	
total cases	234	898	2235	4494	3802	11 663	5734	5929	
any treatment	82.5%	76.3%	71.2%	56.5%	30.5%	52.9%	51.5%	54.2%	*
no treatment	17.5%	23.7%	28.8%	43.5%	69.5%	47.1%	48.5%	45.8%	*
any radiotherapy	43.6%	42.0%	41.2%	32.5%	22.3%	31.8%	29.4%	34.0%	*
any chemotherapy[a]	34.2%	32.6%	24.6%	15.4%	4.6%	15.3%	14.3%	16.3%	*
any surgery[b]	32.1%	22.4%	20.4%	16.6%	5.2%	14.4%	15.8%	13.0%	*
radiotherapy only	18.8%	22.8%	27.4%	24.8%	20.4%	23.6%	22.1%	25.0%	*
surgery only	23.5%	16.1%	15.7%	13.8%	4.7%	11.6%	12.8%	10.4%	*
chemotherapy only	14.1%	16.4%	13.4%	9.7%	3.2%	8.9%	8.7%	9.0%	
chemo + radio	17.5%	14.1%	9.6%	5.0%	1.3%	5.6%	4.8%	6.4%	*
surgery + radio	6.0%	4.0%	3.2%	2.2%	0.4%	2.0%	2.2%	1.8%	
others	2.6%	2.8%	1.9%	1.1%	0.6%	1.2%	1.0%	1.5%	*

[a]Chemotherapy and related treatments (excluding hormonal therapy). [b]Surgery and related treatments.
*Significant difference between diagnosis periods in percentage having this treatment (χ^2 tests), unadjusted for age or other variables.

Table 5.5.2 Summary of main treatment modalities and combinations (within six months of diagnosis) for lung cancer patients, by cell-type and diagnosis period, 1994-2001.

	NSCLC[a]			SCLC[b]			other[c]		
	94-01	**94-97**	**98-01**	**94-01**	**94-97**	**98-01**	**94-01**	**94-97**	**98-01**
total cases	6953	3456	3497	1623	799	824	3087	1479	1608
any treatment	64.9%	62.6%	*67.2%	67.3%	71.0%	*63.7%	18.2%	15.2%	*21.0%
no treatment	35.1%	37.4%	*32.8%	32.7%	29.0%	*36.3%	81.8%	84.8%	*79.0%
any radiotherapy	39.7%	37.6%	*41.8%	27.3%	23.8%	*30.7%	16.2%	13.4%	*18.8%
any chemotherapy[a]	11.5%	8.7%	*14.2%	55.7%	61.6%	*50.0%	2.8%	2.0%	*3.5%
any surgery[b]	23.1%	25.0%	*21.3%	3.0%	4.0%	2.1%	0.6%	0.7%	0.5%
radiotherapy only	30.8%	29.7%	*31.9%	9.7%	7.1%	*12.1%	14.6%	12.4%	*16.7%
surgery only	18.9%	20.6%	*17.2%	1.5%	1.8%	1.3%	0.4%	0.6%	0.2%
chemotherapy only	5.5%	3.8%	*7.1%	37.5%	43.9%	*31.2%	1.5%	1.1%	1.9%
chemo + radio	4.9%	3.9%	*5.9%	16.9%	15.6%	18.1%	1.3%	0.9%	1.6%
surgery + radio	3.3%	3.6%	3.0%	0.2%	0.3%	0.1%	0.1%	0.1%	0.2%
others	1.6%	1.0%	*2.1%	1.5%	2.3%	0.8%	0.4%	0.1%	0.6%

[a]Non-small-cell lung cancer. [b]Small-cell lung cancer. [c]Other morphologies (non-carcinomas and non-specific cancer).
*Significant difference between diagnosis periods in percentage having this treatment (χ^2 tests), unadjusted for age or other variables.

5.5.3 Region of surgical treatment v. region of residence

Only a minority of lung cancer patients receive surgical treatment, thus information on region of surgical treatment is of limited value compared with other major cancers. From the information available, however, it is clear the majority of patients, from six of the eight regions, had their main surgical treatment in the Eastern region (*Table 5.5.3*). This included all surgical patients from the Eastern regions and over 85% of those from the Midland, North-Eastern and North-Western regions, whether based on 1998-2001 or 1994-2001 data. Only in the Southern and Western regions did most patients have their surgical treatments locally (97% and 55% of 1994-2001 cases, respectively), although in the more recent period (1998-2001) 58% of Western patients had surgery in the Eastern region.

Table 5.5.3 Breakdown of lung cancer surgery, 1994-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases. Only surgical procedures within 6 months of diagnosis are included.

		Region of residence																	
Region where		**1994-2001 total**									**1998-2001 subtotal**								
treated		**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**	**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Eastern	%	**100.0**	**97.6**	**53.2**	**96.8**	**87.7**	2.6	**75.3**	44.6	**77.8**	**100.0**	**100.0**	**54.3**	**95.6**	**92.3**	4.2	**76.5**	**58.1**	**80.2**
Midland	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mid-Western	%	0.0	0.0	12.8	0.0	0.0	0.0	0.0	0.0	0.7	0.0	0.0	6.5	0.0	0.0	0.0	0.0	0.0	0.4
North-Eastern	%	0.0	0.0	0.0	3.2	0.0	0.0	0.0	0.0	0.2	0.0	0.0	0.0	4.4	0.0	0.0	0.0	0.0	0.4
North-Western	%	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Southern	%	0.0	0.0	25.5	0.0	0.0	**97.4**	20.1	0.0	16.9	0.0	0.0	30.4	0.0	0.0	**95.8**	19.1	0.0	15.4
South-Eastern	%	0.0	0.0	0.0	0.0	0.0	0.0	4.5	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	4.4	0.0	0.4
Western	%	0.0	2.4	8.5	0.0	12.3	0.0	0.0	**55.4**	3.9	0.0	0.0	8.7	0.0	7.7	0.0	0.0	41.9	3.3

5.5.4 Hospital caseloads (surgical cases)

Lung cancer cases were surgically treated (within six months of diagnosis) in a total of 29 hospitals in the Republic of Ireland during 1994-2001 (*Table 5.5.4*). In contrast to other major cancers (breast, colorectal and lung), there were indications that the number of hospitals where lung cancer patients had surgical treatment increased, and average surgical caseloads by hospital fell, during the period 1994-

2001. However, only a small proportion of lung cancer patients had surgical treatment, thus surgical caseload estimates may be less meaningful than for breast or colorectal cancer, for example.

About half (2-8 annually) of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each, accounting for between 44% and 11% of annual totals. About two-thirds (5-12) of the hospitals treated fewer than 20 surgical cases each in a given year (19% to 40% of annual totals), and almost all (8-12) treated fewer than 50 surgical cases (56% to 100% of annual totals).

Apparent declines in average surgical caseloads per hospital were supported by significant increases in the proportion of surgical cases treated in hospitals averaging fewer than 20, or fewer than 50, surgical cases annually.

5.5.5 Consultant caseloads (surgical cases)

A total of 99 individual consultants were coded as responsible for surgical managements of lung cancers diagnosed during 1994-2001. Of these, there were more during 1998-2001 (68) than 1994-97 (51), with between 20 and 34 consultants involved in any given year, though the overall trend was not clear-cut (*Table 5.5.5*).

Most surgical consultants in any given year treated fewer than 10 surgical cases each, accounting for 10%-21% of annual totals. Almost all treated fewer than 20 surgical cases each in a given year (10%-65% of annual totals), and in most years no consultant was responsible for more than 50 surgical cases. However, as noted under hospital caseloads, most lung cancer patients did not have surgical treatment.

There was some evidence that average surgical caseloads, by consultant, decreased over time. Reflecting this, significant increases during 1994-2001 were seen in the proportions of surgical patients treated by 'low volume' consultants, treating fewer than 10 or, especially, fewer than 20 surgical cases annually (*Table 5.5.5*). These trends may in part reflect decreases in the proportions of lung cancer patients having surgery (*section 5.6.2*), along with only a small annual increase (none for males) in total case-numbers annually (*section 5.1.1*).

Table 5.5.4 Summary of surgical caseloads by year of diagnosis and hospital, based on lung cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* hospital where surgical treatment received, excluding unidentified hospitals and those outside the Republic of Ireland

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01
hospitals (1+ case)	14	12	14	9	15	11	12	15		19	24
case average	19	20	16	22	14	19	15	14		12	8
<10 cases/year[a]	7	6	6	2	8	5	6	8		12	17
% of cases	*10.1*	*9.4*	*4.3*	*5.1*	*8.1*	*11.2*	*8.7*	*7.4*		*8.0*	*7.1*
<20 cases/year	9	8	9	5	12	7	8	11		14	19
% of cases	*20.1*	*22.6*	*19.1*	*30.1*	*39.2*	*25.2*	*26.8*	*28.9*	**	*18.5*	*19.3*
<50 cases/year	12	11	13	8	14	10	12	14		18	23
% of cases	*55.6*	*64.7*	*74.3*	*66.8*	*66.0*	*70.6*	*100*	*72.1*	***	*70.7*	*71.2*
50+ cases/year	2	1	1	1	1	1	0	1		1	1
% of cases	*44.4*	*35.3*	*25.7*	*33.2*	*34.0*	*29.4*	*0.0*	*27.9*		*29.3*	*28.8*

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated in hospitals of a given caseload.

Table 5.5.5 Summary of surgical caseloads by year of diagnosis and surgical consultant, based on lung cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* surgical consultant involved, excluding unknown consultants and those based outside the Republic of Ireland

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
consultants (1+ case)	29	20	20	23	26	22	27	34		51	68	
case average	9	12	12	9	8	10	7	6		5	3	
<10 cases/year[a]	22	14	14	17	20	14	19	26		45	60	
% of cases	*12.5*	*9.8*	*14.3*	*16.6*	*19.4*	*16.9*	*13.0*	*20.9*	**	*14.6*	*20.7*	***
<20 cases/year	24	14	15	17	23	19	25	31		45	64	
% of cases	*23.2*	*9.8*	*21.7*	*16.6*	*43.6*	*54.0*	*65.2*	*56.8*	***	*14.6*	*48.4*	***
<50 cases/year	27	20	20	23	25	22	27	34		51	68	
% of cases	*61.2*	*100*	*100*	*100*	*73.5*	*100*	*100*	*100*		*100*	*100*	
50+ cases/year	2	0	0	0	1	0	0	0		0	0	
% of cases	*38.8*	*0.0*	*0.0*	*0.0*	*26.5*	*0.0*	*0.0*	*0.0*		*0.0*	*0.0*	

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated by surgical consultants of a given caseload.

5.5.6 Variation by patient and tumour characteristics

More detailed comparisons are made under the section covering logistic regression analysis (*section 5.6.1*). Basic tabulations of treatment for each category of patient or tumour are shown in *Table 5.5.6*. Detailed comments are not provided here, but note that cases in older patients or of unknown cell-type tended to be less likely to receive a given treatment. It should also be noted that these tabulations are based on unadjusted data – i.e. patients or tumours compared under a given variable may also differ in other characteristics, some of which may be more important determinants of treatment.

See also *Table 5.5.1* and *Figure 5.5.1* for further summaries of treatments in relation to age.

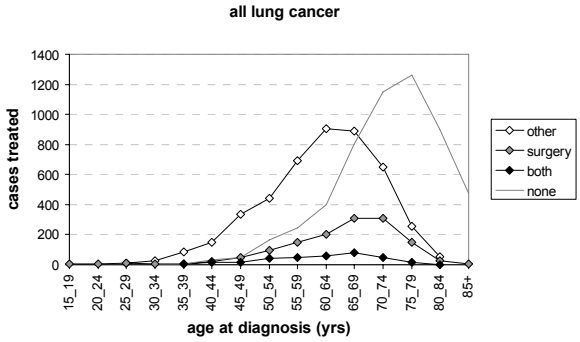


Figure 5.5.1 Age-profiles for tumour-directed treatments within six months of diagnosis for lung cancer cases diagnosed 1994-2001: numbers of cases having surgery (only), other treatments (radiotherapy, chemotherapy or hormone therapy but not surgery), both surgery and other treatments, or no treatment.

5.5.7 National trends

See *section 5.5.2*.

5.5.8 Regional variation

Regional variations in treatment, unadjusted for patients or tumour characteristics, are summarized for the period 1998-2001 in *Figure 5.5.2* (all lung cancer) and *Figure 5.5.3* (for major cell-types). For lung cancer as a whole, approximately two-fold variation between patients from different regions was apparent for surgery (range 8-16% of regional cases), radiotherapy (range 20-37%) and chemotherapy (range 10-22%) (*Figure 5.5.2*). There was apparently little in common between patterns for different modalities, except that use of all three modalities was high among patients from the Eastern region. Overall treatment varied somewhat less (range 43-62%), but was highest for the Eastern region. Regional variations in treatments for non-small-cell and small-cell lung cancers (*Figure 5.5.3*) were of broadly similar magnitude to those for lung cancer as a whole. However, overall treatment for both cell-types, surgery for NSCLC and chemotherapy for SCLC appeared to vary less between regions than for lung cancer as a whole. This suggests that some

regional variation may reflect regional differences in the specificity of diagnoses or in treatment of non-specific cancer types. Broadly similar patterns, or extent of regional variation, were also seen during 1994-97 (not presented). More rigorous comparisons of treatments between regions, taking account of age and where possible other patient and tumour characteristics, are presented under *section 5.6* for both 1994-97 and 1998-2001.

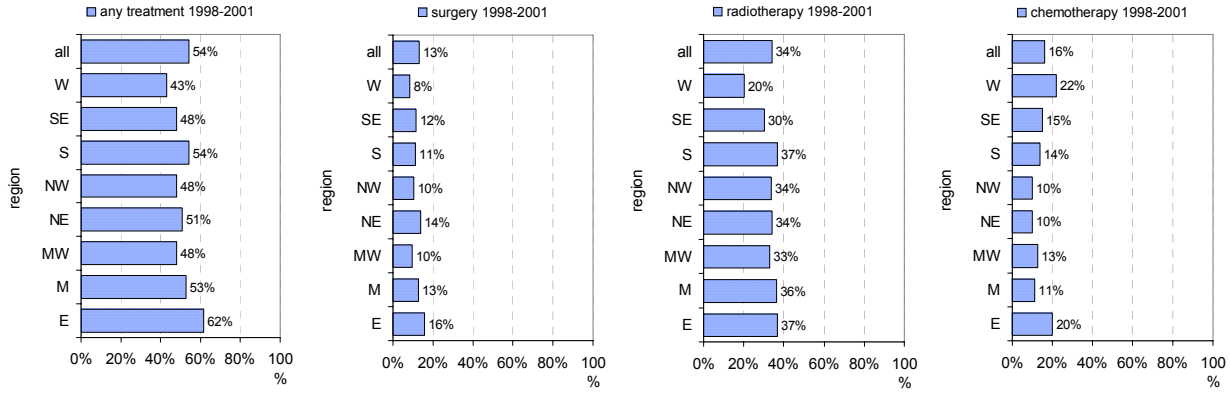


Figure 5.5.2 Percentage of lung cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence, 1998-2001.

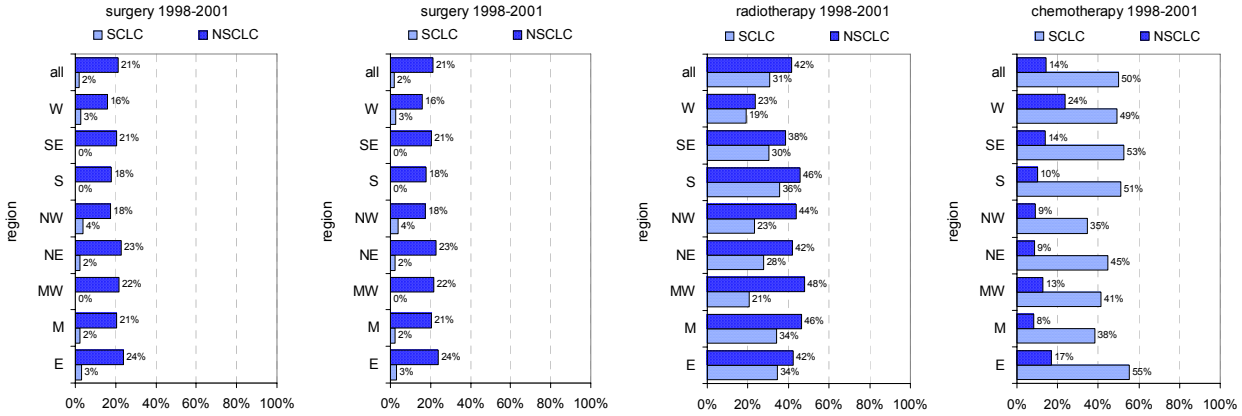


Figure 5.5.3 Percentage of lung cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence and cell-type, 1998-2001.

Table 5.5.6 Summary of treatment of lung cancer cases, 1998-2001, by patient and tumour characteristics: unadjusted percentages receiving treatment within six months of diagnosis. See *Table 5.2.2* for sample sizes.

	Overall treatment	Surgery	Radiotherapy	Chemotherapy
total cases	54.2%	13.0%	34.0%	16.3%
age 15-44[a]	84.6%	33.1%	45.4%	33.8%
age 45-54	78.2%	20.4%	44.5%	34.9%
age 55-64	71.7%	19.8%	42.9%	25.7%
age 65-74	58.0%	14.1%	35.1%	16.9%
age 75+	32.5%	4.8%	24.6%	4.9%
male	55.6%	13.2%	35.3%	16.2%
female	51.8%	12.6%	31.9%	16.5%
non-small-cell	67.2%	21.3%	41.8%	14.2%
small-cell	63.7%	2.1%	30.7%	50.0%
other/NOS	21.0%	0.5%	18.8%	3.5%
stage I	71.4%	46.6%	23.1%	8.4%
stage II	68.5%	52.8%	25.8%	12.4%
stage III	66.5%	9.9%	46.7%	29.1%
stage IV	52.0%	3.6%	37.4%	20.6%
stage X[a]	51.7%	15.3%	30.9%	12.3%
T1	63.7%	34.4%	24.6%	12.2%
T2	62.7%	29.1%	30.3%	14.2%
T3	61.2%	13.3%	43.9%	15.8%
T4	56.9%	4.4%	39.4%	23.3%
T X	43.2%	2.3%	33.0%	14.7%
N negative	71.2%	41.3%	27.1%	11.5%
N positive	62.2%	14.4%	39.3%	22.8%
N X	43.7%	3.2%	32.7%	13.6%
M negative	65.5%	19.6%	38.7%	22.1%
M positive	52.0%	3.7%	37.4%	20.8%
M X	50.8%	16.2%	29.8%	10.9%
grade 1	67.4%	41.7%	22.0%	6.8%
grade 2	77.3%	39.3%	38.2%	10.2%
grade 3+	68.9%	21.7%	38.9%	23.3%
grade X	44.5%	4.4%	31.9%	15.0%
MV yes	66.3%	17.5%	39.5%	21.0%
MV no	20.3%	0.3%	18.6%	3.1%
MV X	21.3%	0.0%	17.3%	4.0%
symptomatic	54.5%	12.2%	35.0%	16.6%
incidental	55.4%	27.9%	24.4%	10.1%
screen detected	36.8%	36.8%	10.5%	0.0%
presentation X	47.2%	13.0%	24.4%	16.7%
non-smoker	48.6%	11.2%	28.4%	15.9%
ex-smoker	58.2%	16.0%	35.1%	15.4%
smoker	56.4%	13.1%	36.1%	17.8%
smoking status X	40.8%	7.7%	27.1%	12.1%
ever married	56.9%	14.1%	35.3%	17.6%
never married	44.9%	9.3%	29.1%	12.0%
marital status X	35.4%	5.1%	27.4%	7.4%

[a]See *Table 5.5.1* for a further breakdown by age, for the overall period 1994-2001.

5.6 Treatment: logistic regression analysis

5.6.1 Variation by patient and tumour characteristics

Preliminary multivariate logistic regression models were used to assess variation in treatments in relation to patient and tumour characteristics other than region of residence and year of diagnosis (before examining those). Comparisons here are with baseline groups for relevant variables – diagnosis age 15-44, male, non-small-cell morphology, T category 1 (smallest size/local extension), N negative (no nodal involvement), M negative (no distant metastasis), tumour grade 1, microscopically verified (MV), symptomatic method of presentation, non-smoker and ever married – having adjusted for all variables shown in the relevant table (*Tables 5.6.1-4*). The main comparisons are based on data for 1994-2001 as a whole (or 1996-2001 for chemotherapy and hormonal therapy). However, attention is drawn to any significant differences in patterns between the diagnosis periods 1994-97 and 1998-2001.

Overall treatment

For 1994-2001 as a whole, treatment was significantly less likely, compared with baseline groups, for patients aged 55 or above; tumours of unspecified or non-carcinoma morphology; T category 4 or unknown; N category positive or unknown; M category positive or unknown; grade unknown; cases lacking microscopic verification; and for patients who were never married or whose marital status was unknown (*Table 5.6.1*). Treatment was significantly more likely for small-cell (compared with non-small-cell) carcinomas; tumours of grade 2; and ex-smokers. Patterns were very similar for the diagnosis periods 1994-97 and 1998-2001, and relative risk values showed no significant changes.

Surgery

Surgical treatment was significantly less likely for age-groups 45 or over; small-cell (compared with non-small-cell) carcinomas; and cases that were T category 2, 3, 4 or unknown; N category positive or unknown; metastatic; grade unknown; lacking microscopic verification; and for smokers and patients who were never married (*Table 5.6.2*). Surgical treatment was more likely for cases of unknown metastatic status or whose method of presentation was incidental, screen-detected or unknown. Patterns were broadly similar between diagnosis periods, and relative risk values differed significantly only for T categories 3 and 4 and M category unknown. However, the magnitude of variation relative to baseline groups appeared to be greater in the more recent period, 1998-2001.

Radiotherapy

Radiotherapy use was significantly lower for patients aged 65 or more; for small-cell and unspecified or non-carcinoma morphologies; M category unknown; cases whose method of presentation was incidental, screen-detected or unknown; and patients who were never married (*Table 5.6.3*). Radiotherapy use was higher for cases that were T category 3-4 or unknown; N category positive or unknown; grade 3+ or unknown; and for smokers and ex-smokers. These patterns were broadly similar for 1994-97 and 1998-2001, but the magnitude of variation in radiotherapy use by T category and grade appeared to be higher in the more recent period. Relative risks differed significantly between periods for T category unknown, and grade 2 and unknown.

Chemotherapy

Chemotherapy was significantly less likely for age-groups 55 or over; M category positive or unknown; and patients who were never married or of unknown marital status (*Table 5.6.4*). Chemotherapy was more likely for small-cell (compare with non-small-cell) carcinomas; T categories 2-4 and unknown; N category positive or unknown; and grade 3+ or unknown. Patterns were broadly similar between diagnosis periods, but relative risk values differed significantly for T categories 2-4 (less marked variation during 1998-2001) and M category unknown.

Table 5.6.1 Risk ratios for overall treatment of lung cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
age 15-44	1.000		1.000		1.000	
age 45-54	0.907 (0.809-0.987)	0.021	0.911 (0.754-1.033)	0.176	**0.907** (0.809-0.987)	0.021
age 55-64	**0.858** (0.759-0.943)	0.000	0.896 (0.747-1.016)	0.098	**0.858** (0.759-0.943)	0.000
age 65-74	**0.705** (0.597-0.808)	0.000	**0.719** (0.556-0.870)	0.000	**0.705** (0.597-0.808)	0.000
age 75+	**0.467** (0.367-0.576)	0.000	**0.473** (0.329-0.636)	0.000	**0.467** (0.367-0.576)	0.000
male	1.000		1.000		1.000	
female	0.970 (0.928-1.012)	0.167	0.983 (0.919-1.047)	0.609	0.970 (0.928-1.012)	0.167
NSCLC	1.000		1.000		1.000	
SCLC	**1.108** (1.068-1.146)	0.000	**1.217** (1.160-1.268)	0.000	**1.108** (1.068-1.146)	0.000
other/NOS	**0.639** (0.499-0.789)	0.000	**0.595** (0.411-0.804)	0.000	**0.639** (0.499-0.789)	0.000
T1	1.000		1.000		1.000	
T2	0.990 (0.924-1.052)	0.768	1.001 (0.908-1.087)	0.967	0.990 (0.924-1.052)	0.768
T3	1.014 (0.937-1.085)	0.710	1.047 (0.940-1.143)	0.369	1.014 (0.937-1.085)	0.710
T4	**0.927** (0.856-0.995)	0.038	0.907 (0.801-1.006)	0.069	**0.927** (0.856-0.995)	0.038
T X	**0.805** (0.737-0.873)	0.000	**0.782** (0.685-0.879)	0.000	**0.805** (0.737-0.873)	0.000
N negative	1.000		1.000		1.000	
N positive	**0.912** (0.866-0.956)	0.000	**0.912** (0.846-0.974)	0.005	**0.912** (0.866-0.956)	0.000
N X	**0.786** (0.736-0.834)	0.000	**0.775** (0.704-0.844)	0.000	**0.786** (0.736-0.834)	0.000
M negative	1.000		1.000		1.000	
M positive	**0.849** (0.800-0.897)	0.000	**0.836** (0.765-0.904)	0.000	**0.849** (0.800-0.897)	0.000
M X	**0.922** (0.879-0.964)	0.000	**0.922** (0.861-0.978)	0.006	**0.922** (0.879-0.964)	0.000
grade 1	1.000		1.000		1.000	
grade 2	**1.167** (1.076-1.245)	0.001	**1.176** (1.040-1.290)	0.013	**1.167** (1.076-1.245)	0.001
grade 3+	1.049 (0.952-1.137)	0.310	1.052 (0.910-1.179)	0.455	1.049 (0.952-1.137)	0.310
grade X	0.969 (0.867-1.064)	0.537	0.944 (0.795-1.083)	0.447	0.969 (0.867-1.064)	0.537
MV yes[c]	1.000		1.000		1.000	
MV no	**0.755** (0.603-0.908)	0.001	**0.774** (0.562-0.987)	0.037	**0.755** (0.603-0.908)	0.001
MV X	0.962 (0.741-1.154)	0.723	1.021 (0.700-1.275)	0.887	0.962 (0.741-1.154)	0.723
symptomatic	1.000		1.000		1.000	
incidental	0.951 (0.843-1.058)	0.373	0.846 (0.677-1.023)	0.090	0.951 (0.843-1.058)	0.373
screen detected	0.777 (0.432-1.173)	0.276	0.873 (0.353-1.449)	0.692	0.777 (0.432-1.173)	0.276
presentation X	1.017 (0.899-1.132)	0.772	0.883 (0.693-1.080)	0.247	1.017 (0.899-1.132)	0.772
non-smoker	1.000		1.000		1.000	
ex-smoker	**1.136** (1.048-1.222)	0.002	**1.152** (1.019-1.282)	0.025	**1.136** (1.048-1.222)	0.002
smoker	1.002 (0.921-1.083)	0.961	0.989 (0.869-1.111)	0.866	1.002 (0.921-1.083)	0.961
smoking status X	0.983 (0.881-1.085)	0.745	1.098 (0.942-1.253)	0.218	0.983 (0.881-1.085)	0.745
ever married	1.000		1.000		1.000	
never married	**0.751** (0.702-0.801)	0.000	**0.774** (0.701-0.849)	0.000	**0.751** (0.702-0.801)	0.000
marital status X	**0.789** (0.673-0.908)	0.001	**0.746** (0.586-0.918)	0.004	**0.789** (0.673-0.908)	0.001

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
There were no significant differences in RR between diagnosis periods.

Table 5.6.2 Risk ratios for surgical treatment of lung cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	**0.462** (0.310-0.670)	0.000	**0.556** (0.315-0.924)	0.022		**0.437** (0.249-0.730)	0.001
age 55-64	**0.426** (0.293-0.608)	0.000	**0.533** (0.312-0.866)	0.009		**0.377** (0.221-0.619)	0.000
age 65-74	**0.338** (0.232-0.485)	0.000	**0.475** (0.278-0.773)	0.002		**0.260** (0.151-0.435)	0.000
age 75+	**0.131** (0.085-0.199)	0.000	**0.201** (0.109-0.360)	0.000		**0.095** (0.052-0.172)	0.000
male	1.000		1.000			1.000	
female	1.063 (0.933-1.208)	0.349	1.100 (0.920-1.307)	0.288		1.036 (0.851-1.253)	0.720
NSCLC	1.000		1.000			1.000	
SCLC	**0.218** (0.161-0.295)	0.000	**0.247** (0.167-0.362)	0.000		**0.174** (0.104-0.289)	0.000
other/NOS	1.096 (0.601-1.801)	0.748	1.095 (0.530-1.926)	0.788		1.003 (0.302-2.433)	0.995
T1	1.000		1.000			1.000	
T2	**0.846** (0.727-0.976)	0.021	0.958 (0.787-1.143)	0.653		**0.721** (0.565-0.903)	0.004
T3	**0.522** (0.420-0.642)	0.000	**0.751** (0.576-0.953)	0.017	*	**0.308** (0.212-0.439)	0.000
T4	**0.223** (0.173-0.286)	0.000	**0.325** (0.231-0.449)	0.000	*	**0.149** (0.101-0.218)	0.000
T X	**0.151** (0.116-0.196)	0.000	**0.173** (0.120-0.246)	0.000		**0.123** (0.083-0.182)	0.000
N negative	1.000		1.000			1.000	
N positive	**0.498** (0.436-0.565)	0.000	**0.540** (0.452-0.637)	0.000		**0.460** (0.374-0.559)	0.000
N X	**0.186** (0.154-0.225)	0.000	**0.179** (0.138-0.231)	0.000		**0.203** (0.151-0.269)	0.000
M negative	1.000		1.000			1.000	
M positive	**0.345** (0.277-0.426)	0.000	**0.317** (0.233-0.426)	0.000		**0.389** (0.284-0.527)	0.000
M X	**1.331** (1.193-1.475)	0.000	1.111 (0.962-1.267)	0.146	*	**1.648** (1.386-1.933)	0.000
grade 1	1.000		1.000			1.000	
grade 2	**1.301** (1.060-1.549)	0.013	**1.518** (1.140-1.912)	0.006		1.131 (0.822-1.449)	0.419
grade 3+	0.957 (0.754-1.183)	0.702	1.111 (0.797-1.475)	0.513		0.833 (0.576-1.133)	0.267
grade X	**0.409** (0.301-0.548)	0.000	**0.509** (0.332-0.755)	0.000		**0.350** (0.220-0.539)	0.000
MV yes	1.000		1.000			1.000	
MV no	**0.026** (0.008-0.079)	0.000	**0.019** (0.003-0.099)	0.000		**0.035** (0.006-0.186)	0.000
MV X	-		-			-	
symptomatic	1.000		1.000			1.000	
incidental	**1.761** (1.364-2.229)	0.000	**1.542** (1.026-2.211)	0.037		**2.009** (1.422-2.740)	0.000
screen detected	**3.624** (1.639-5.591)	0.004	3.248 (0.845-5.590)	0.078		**4.241** (1.385-6.973)	0.016
presentation X	**1.630** (1.121-2.282)	0.011	1.380 (0.697-2.446)	0.339		**1.969** (1.244-2.939)	0.005
non-smoker	1.000		1.000			1.000	
ex-smoker	0.917 (0.718-1.160)	0.479	0.788 (0.562-1.084)	0.148		1.135 (0.785-1.611)	0.492
smoker	**0.797** (0.632-0.998)	0.049	**0.665** (0.484-0.901)	0.008		1.044 (0.734-1.462)	0.805
smoking status X	0.982 (0.718-1.321)	0.908	1.084 (0.712-1.587)	0.694		0.932 (0.575-1.470)	0.769
ever married	1.000		1.000			1.000	
never married	**0.663** (0.553-0.792)	0.000	**0.784** (0.618-0.987)	0.038		**0.553** (0.415-0.733)	0.000
marital status X	0.965 (0.606-1.483)	0.877	1.183 (0.657-1.972)	0.559		0.778 (0.349-1.608)	0.517

[a,b]See *Table 5.6.1*.
*Significant difference in RR between diagnosis periods.

Table 5.6.3 Risk ratios for radiotherapy of lung cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.928 (0.768-1.098)	0.407	0.910 (0.670-1.177)	0.500		0.927 (0.718-1.149)	0.516
age 55-64	0.924 (0.773-1.083)	0.346	0.935 (0.706-1.187)	0.609		0.909 (0.714-1.117)	0.387
age 65-74	**0.765** (0.631-0.912)	0.002	**0.743** (0.547-0.973)	0.030		**0.774** (0.598-0.970)	0.024
age 75+	**0.596** (0.480-0.729)	0.000	**0.550** (0.390-0.753)	0.000		**0.620** (0.465-0.801)	0.000
male	1.000		1.000			1.000	
female	0.946 (0.890-1.004)	0.069	0.931 (0.846-1.020)	0.128		0.950 (0.876-1.027)	0.205
NSCLC	1.000		1.000			1.000	
SCLC	**0.594** (0.538-0.653)	0.000	**0.545** (0.469-0.630)	0.000		**0.635** (0.558-0.718)	0.000
other/NOS	**0.505** (0.355-0.698)	0.000	**0.451** (0.270-0.718)	0.000		**0.608** (0.372-0.927)	0.018
T1	1.000		1.000			1.000	
T2	1.100 (0.969-1.241)	0.137	1.002 (0.832-1.193)	0.974		**1.195** (1.001-1.411)	0.049
T3	**1.541** (1.361-1.728)	0.000	**1.350** (1.116-1.601)	0.003		**1.712** (1.443-1.991)	0.000
T4	**1.380** (1.224-1.544)	0.000	**1.209** (1.003-1.434)	0.046		**1.508** (1.281-1.750)	0.000
T X	**1.275** (1.133-1.427)	0.000	1.103 (0.923-1.302)	0.270	*	**1.464** (1.245-1.699)	0.000
N negative	1.000		1.000			1.000	
N positive	**1.489** (1.366-1.616)	0.000	**1.521** (1.330-1.722)	0.000		**1.435** (1.278-1.598)	0.000
N X	**1.413** (1.289-1.541)	0.000	**1.495** (1.302-1.698)	0.000		**1.353** (1.194-1.521)	0.000
M negative	1.000		1.000			1.000	
M positive	0.957 (0.881-1.037)	0.295	1.054 (0.924-1.191)	0.421		**0.898** (0.805-0.996)	0.042
M X	**0.790** (0.727-0.857)	0.000	**0.858** (0.754-0.970)	0.014		**0.771** (0.689-0.857)	0.000
grade 1	1.000		1.000			1.000	
grade 2	1.216 (0.995-1.458)	0.055	1.031 (0.791-1.301)	0.812	*	**1.543** (1.116-2.037)	0.010
grade 3+	**1.289** (1.070-1.526)	0.008	1.127 (0.885-1.392)	0.317		**1.583** (1.163-2.062)	0.004
grade X	**1.368** (1.144-1.608)	0.001	1.113 (0.872-1.378)	0.373	*	**1.755** (1.313-2.241)	0.000
MV yes	1.000		1.000			1.000	
MV no	0.859 (0.629-1.129)	0.295	0.872 (0.550-1.278)	0.514		0.771 (0.480-1.140)	0.212
MV X	1.008 (0.655-1.418)	0.967	1.084 (0.571-1.716)	0.779		0.882 (0.461-1.424)	0.657
symptomatic	1.000		1.000			1.000	
incidental	**0.760** (0.633-0.903)	0.001	**0.753** (0.555-0.997)	0.048		**0.763** (0.606-0.944)	0.012
screen detected	**0.200** (0.049-0.708)	0.009	-			0.326 (0.078-1.056)	0.064
presentation X	**0.810** (0.667-0.973)	0.023	0.769 (0.547-1.048)	0.100		0.804 (0.631-1.003)	0.054
non-smoker	1.000		1.000			1.000	
ex-smoker	**1.194** (1.065-1.330)	0.003	**1.209** (1.017-1.418)	0.032		**1.179** (1.009-1.362)	0.038
smoker	**1.120** (1.004-1.242)	0.041	1.058 (0.895-1.239)	0.495		**1.176** (1.017-1.346)	0.029
smoking status X	1.068 (0.927-1.221)	0.352	1.163 (0.943-1.409)	0.151		1.003 (0.824-1.202)	0.973
ever married	1.000		1.000			1.000	
never married	**0.804** (0.740-0.872)	0.000	**0.809** (0.714-0.913)	0.000		**0.800** (0.714-0.892)	0.000
marital status X	0.837 (0.687-1.005)	0.058	**0.731** (0.536-0.971)	0.030		0.926 (0.713-1.168)	0.538

[a,b]See *Table 5.6.1*.
[c]The MV variable was dropped from the logistic model for NSCL and SCLC, as cases were all microscopically verified.
*Significant difference in RR between diagnosis periods.

Table 5.6.4 Risk ratios for chemotherapy of lung cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-97			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-44	1.000		1.000			1.000	
age 45-54	0.897 (0.691-1.132)	0.378	0.912 (0.595-1.302)	0.641		0.884 (0.627-1.193)	0.445
age 55-64	**0.671** (0.512-0.861)	0.001	**0.676** (0.435-0.997)	0.048		**0.655** (0.459-0.904)	0.009
age 65-74	**0.420** (0.313-0.554)	0.000	**0.388** (0.240-0.607)	0.000		**0.434** (0.297-0.618)	0.000
age 75+	**0.140** (0.098-0.197)	0.000	**0.137** (0.078-0.238)	0.000		**0.140** (0.089-0.218)	0.000
male	1.000		1.000			1.000	
female	1.008 (0.904-1.122)	0.876	1.055 (0.886-1.249)	0.541		0.947 (0.820-1.089)	0.451
NSCLC	1.000		1.000			1.000	
SCLC	**5.015** (4.712-5.312)	0.000	**7.441** (6.848-7.999)	0.000		**3.602** (3.268-3.935)	0.000
other/NOS	0.893 (0.513-1.503)	0.681	0.756 (0.305-1.768)	0.532		1.066 (0.522-2.003)	0.853
T1	1.000		1.000			1.000	
T2	**1.376** (1.079-1.739)	0.010	**1.897** (1.249-2.809)	0.003	*	1.140 (0.841-1.523)	0.392
T3	**1.657** (1.268-2.137)	0.000	**2.504** (1.609-3.751)	0.000	*	1.288 (0.910-1.785)	0.150
T4	**2.214** (1.768-2.736)	0.000	**3.103** (2.089-4.431)	0.000	*	**1.781** (1.347-2.308)	0.000
T X	**1.564** (1.234-1.962)	0.000	**2.206** (1.471-3.214)	0.000		1.300 (0.965-1.723)	0.083
N negative	1.000		1.000			1.000	
N positive	**1.878** (1.588-2.207)	0.000	**2.050** (1.550-2.668)	0.000		**1.726** (1.394-2.115)	0.000
N X	**1.307** (1.082-1.571)	0.006	1.263 (0.924-1.707)	0.141		**1.278** (1.003-1.611)	0.047
M negative	1.000		1.000			1.000	
M positive	**0.723** (0.623-0.837)	0.000	**0.756** (0.582-0.972)	0.029		**0.702** (0.585-0.838)	0.000
M X	**0.658** (0.569-0.757)	0.000	0.909 (0.721-1.137)	0.411	*	**0.518** (0.428-0.625)	0.000
grade 1	1.000		1.000			1.000	
grade 2	1.382 (0.803-2.326)	0.239	1.426 (0.601-3.235)	0.415		1.231 (0.606-2.392)	0.558
grade 3+	**2.336** (1.422-3.714)	0.001	**2.494** (1.119-5.204)	0.026		**2.084** (1.096-3.717)	0.026
grade X	**2.258** (1.373-3.600)	0.002	**2.410** (1.076-5.062)	0.033		**1.937** (1.016-3.480)	0.045
MV yes	1.000		1.000			1.000	
MV no	**0.385** (0.209-0.686)	0.001	0.434 (0.163-1.065)	0.070		**0.319** (0.142-0.685)	0.003
MV X	0.769 (0.301-1.704)	0.550	1.234 (0.324-3.135)	0.735		0.523 (0.135-1.628)	0.296
symptomatic	1.000		1.000			1.000	
incidental	0.757 (0.541-1.044)	0.091	0.632 (0.346-1.114)	0.116		0.789 (0.523-1.161)	0.237
screen detected	0.633 (0.141-2.225)	0.517	1.980 (0.354-5.142)	0.397		-	
presentation X	1.294 (0.965-1.701)	0.083	0.871 (0.473-1.525)	0.645		**1.453** (1.045-1.958)	0.027
non-smoker	1.000		1.000			1.000	
ex-smoker	1.039 (0.841-1.274)	0.716	1.182 (0.831-1.653)	0.346		0.919 (0.701-1.188)	0.527
smoker	0.861 (0.706-1.046)	0.134	1.032 (0.742-1.417)	0.844		**0.754** (0.584-0.965)	0.025
smoking status X	0.812 (0.622-1.050)	0.115	0.865 (0.553-1.326)	0.514		0.769 (0.550-1.059)	0.110
ever married	1.000		1.000			1.000	
never married	**0.574** (0.488-0.673)	0.000	**0.528** (0.407-0.681)	0.000		**0.611** (0.496-0.750)	0.000
marital status X	**0.510** (0.326-0.783)	0.002	0.598 (0.311-1.101)	0.102		**0.457** (0.243-0.831)	0.009

[a,b]See *Table 5.6.1*.
[c]The MV variable was dropped from the logistic model for NSCL and SCLC, as cases were all microscopically verified.
*Significant difference in RR between diagnosis periods.

5.6.2 National and regional trends

Overall treatment

Nationally, treatment increased significantly between 1996 and 2001, by *c*.2.5% annually in relative terms, based on analyses adjusted for age, sex and cell-type (*Table 5.6.5*). Patients from the Eastern region also showed a significant increase, by *c*.2.2% annually. Further adjustment for stage reduced the magnitude of the national trend slightly. However, there were clear differences in trends between non-small-cell and small-cell lung cancers, with significant increases in treatment seen for NSCLC only (nationally and in three regions).

Table 5.6.5 Average annual changes in the proportion of lung cancer patients having any tumour-directed treatment (within six months of diagnosis), overall, by region of residence and by cell-type, 1996-2001.

	1996-2001 annual All lung cancers [a]RR (95% CI)	P	1996-2001 annual NSCLC RR (95% CI)	P		1996-2001 annual SCLC RR (95% CI)	P
age-, sex-, celltype-adjusted[b]							
total	**1.025** (1.011-1.039)	0.000	**1.029** (1.015-1.042)	0.000	*	0.977 (0.952-1.001)	0.067
E	**1.022** (1.002-1.041)	0.028	**1.029** (1.010-1.048)	0.003	*	0.972 (0.939-1.003)	0.085
M	1.060 (0.988-1.132)	0.101	1.043 (0.975-1.108)	0.208		1.004 (0.834-1.164)	0.958
MW	1.062 (0.998-1.127)	0.055	**1.092** (1.023-1.159)	0.008		1.136 (0.912-1.390)	0.247
NE	1.042 (0.992-1.092)	0.097	1.035 (0.988-1.080)	0.134		0.956 (0.870-1.032)	0.275
NW	0.991 (0.930-1.052)	0.773	0.986 (0.923-1.049)	0.673		0.923 (0.827-1.008)	0.078
S	1.018 (0.982-1.055)	0.314	1.030 (0.995-1.063)	0.088		0.978 (0.916-1.033)	0.461
SE	1.047 (0.988-1.107)	0.113	1.027 (0.979-1.074)	0.262		0.991 (0.889-1.090)	0.874
W	1.006 (0.951-1.063)	0.809	1.010 (0.954-1.066)	0.716		1.000 (0.856-1.143)	0.997
age, sex, celltype-, stage-adjusted[b,c]							
total	**1.017** (1.002-1.031)	0.023	**1.025** (1.011-1.039)	0.000	*	**0.973** (0.948-0.998)	0.041

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Morphology: non-small-cell (NSCLC), small-cell (SCLC) or other/unspecified lung cancer (for overall category).
[c]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
*Significant difference in RR between NSCLC and SCLC morphologies, thus "all cancer" trends may not, strictly, be meaningful.

Surgery

The use of surgery fell significantly, by *c*.3.4% annually (*c*.5.0% after stage-adjustment) between 1996 and 2001 (*Table 5.6.6*). Regional trends were not statistically significant. The trends largely involved surgery of non-small-cell lung cancers, (significant decline after stage-adjustment).

Table 5.6.6 Average annual changes in the proportion of lung cancer patients having surgical treatment (within six months of diagnosis), overall, by region of residence and by cell-type, 1996-2001.

	1996-2001 annual All lung cancers RR (95% CI)	P	1996-2001 annual NSCLC RR (95% CI)	P
age-, sex-, celltype-adjusted				
total	**0.966** (0.935-0.998)	0.039	0.975 (0.946-1.004)	0.101
E	0.982 (0.938-1.027)	0.442	0.993 (0.951-1.036)	0.769
M	0.961 (0.830-1.108)	0.591	0.951 (0.830-1.084)	0.464
MW	0.960 (0.831-1.106)	0.583	0.994 (0.867-1.135)	0.936
NE	0.908 (0.813-1.012)	0.085	0.930 (0.845-1.019)	0.122
NW	1.028 (0.880-1.197)	0.721	0.991 (0.857-1.139)	0.907
S	0.952 (0.870-1.041)	0.290	0.958 (0.882-1.038)	0.303
SE	0.937 (0.828-1.058)	0.299	0.961 (0.859-1.070)	0.476
W	0.962 (0.835-1.105)	0.589	0.971 (0.847-1.111)	0.681
age-, sex-, celltype-, stage-adjusted				
total	**0.950** (0.912-0.989)	0.013	**0.962** (0.926-0.999)	0.048

Radiotherapy

Radiotherapy use increased significantly at national scale, by *c*.2.2% annually between 1996 and 2001, although the basic trend was not significant after further adjustment for stage (*Table 5.6.7*).

Significant increases were also seen among patients from the Mid-Western and North-Eastern regions, both overall (by 8.7-13% annually) and for non-small-cell morphologies.

Table 5.6.7 Average annual changes in the proportion of lung cancer patients having radiotherapy (within six months of diagnosis), overall, by region of residence and by cell-type, 1996-2001. Note that some trends differ significantly between morphological subgroups, thus may not strictly be meaningful except as an overall summary of trends.

	1996-2001 annual All lung cancers RR (95% CI)	P	1996-2001 annual NSCLC RR (95% CI)	P		1996-2001 annual SCLC RR (95% CI)	P
age-, sex-, celltype-adjusted							
total	**1.022** (1.003-1.042)	0.023	1.011 (0.990-1.032)	0.280		1.048 (0.991-1.107)	0.094
E	0.993 (0.965-1.021)	0.655	0.984 (0.954-1.014)	0.314		1.045 (0.966-1.129)	0.264
M	1.083 (0.991-1.181)	0.077	1.039 (0.950-1.129)	0.390		1.400 (0.894-2.193)	0.141
MW	**1.087** (1.006-1.172)	0.034	**1.109** (1.012-1.210)	0.026		1.390 (0.944-1.986)	0.093
NE	**1.130** (1.047-1.217)	0.002	**1.101** (1.016-1.190)	0.019		1.149 (0.897-1.445)	0.263
NW	1.006 (0.929-1.086)	0.876	0.962 (0.880-1.047)	0.385		1.053 (0.810-1.339)	0.686
S	1.019 (0.970-1.069)	0.439	1.021 (0.969-1.074)	0.420		1.069 (0.932-1.217)	0.329
SE	1.033 (0.964-1.104)	0.345	1.043 (0.968-1.120)	0.257	*	0.835 (0.687-1.000)	0.050
W	1.020 (0.941-1.102)	0.620	0.978 (0.894-1.067)	0.633	*	1.412 (0.990-1.962)	0.056
age-, sex-, celltype-, stage-adjusted							
total	1.016 (0.997-1.036)	0.095	1.008 (0.987-1.030)	0.413		1.048 (0.989-1.108)	0.106

*Significant difference in RR between NSCLC and SCLC morphologies.

Chemotherapy

Significant overall increases in chemotherapy use were seen nationally (by *c*.6.4% annually or *c*.4.6% after stage-adjustment) and among patients from the Eastern region (by *c*.14% annually) (*Table 5.6.8*). However, these trends largely reflected increased use of chemotherapy for non-small-cell cancers (significant nationally and for three regions). In contrast, chemotherapy use declined for small-cell cancers (by *c*.5% annually at national scale).

Table 5.6.8 Average annual changes in the proportion of lung cancer patients having chemotherapy (within six months of diagnosis), overall, by region of residence and by cell-type, 1996-2001.

	1996-2001 annual All lung cancers [a]RR (95% CI)	P	1996-2001 annual NSCLC RR (95% CI)	P		1996-2001 annual SCLC RR (95% CI)	P
age-, sex-, celltype-adjusted[b]							
total	**1.064** (1.029-1.100)	0.000	**1.162** (1.111-1.215)	0.000	*	**0.951** (0.924-0.978)	0.000
E	**1.139** (1.084-1.196)	0.000	**1.264** (1.181-1.351)	0.000	*	0.966 (0.928-1.003)	0.080
M	0.978 (0.803-1.186)	0.823	1.131 (0.860-1.479)	0.373		0.821 (0.641-1.006)	0.059
MW	1.048 (0.912-1.201)	0.501	1.037 (0.869-1.231)	0.680		1.043 (0.793-1.357)	0.755
NE	1.064 (0.929-1.215)	0.363	**1.320** (1.062-1.633)	0.012	*	0.931 (0.837-1.019)	0.132
NW	0.915 (0.766-1.089)	0.322	1.042 (0.789-1.375)	0.768		**0.868** (0.764-0.962)	0.005
S	1.057 (0.955-1.169)	0.278	**1.278** (1.102-1.481)	0.001	*	0.950 (0.889-1.006)	0.083
SE	1.040 (0.927-1.166)	0.494	1.061 (0.917-1.223)	0.423		0.971 (0.872-1.068)	0.571
W	0.958 (0.876-1.045)	0.338	0.979 (0.883-1.081)	0.690		0.951 (0.812-1.091)	0.496
age-, sex-, celltype-, stage-adjusted[b,c]							
total	**1.046** (1.010-1.082)	0.010	**1.143** (1.091-1.197)	0.000	*	**0.945** (0.917-0.973)	0.000

*Significant difference in RR between NSCLC and SCLC morphologies.

5.6.3 Regional variation

Regional variations in treatment use (relative risks compared with the Eastern region) are summarized in *Figures 5.6.1-3* for the overall period 1994-2001 and for the most recent diagnosis period, 1998-2001. Results of basic models adjusted for age, sex and cell-type and of fully adjusted models are presented for overall treatment, surgical treatment, radiotherapy and chemotherapy. More detailed summaries, overall, by cell-type and for periods 1994-97 and 1998-2001, are presented in *Table 5.6.9-12*.

Overall treatment

During 1994-2001 as a whole, patients from six regions (Midland, Mid-Western, North-Eastern, North-Western, South-Eastern and Western) were significantly less likely to be treated than those from the Eastern region, after adjustment for age, sex and tumour morphology (*Table 5.6.9a*). The same pattern was seen for 1994-97, and a similar pattern for 1998-2001 (additionally including lower use of treatment in the Southern region). Relative risk estimates (RRs) differed significantly between diagnosis periods for Southern region only.

Regional patterns changed only slightly after further adjustment for stage-related variables, and in some instances appeared to be accentuated. (This especially applied to 1998-2001, when adjusted treatment use was significantly low among patients from all regions other than the Eastern region.) Fuller adjustment for patient and tumour variables had little further effect, or slightly moderated, the pattern of variation.

Regional patterns for non-small-cell (*Table 5.6.9b*) and small-cell lung cancers (*Table 5.6.9c*), essentially mirrored those for lung cancer as a whole (i.e. generally lower use of treatment outside the Eastern region), albeit with less statistically significant variation especially for SCLC.

Table 5.6.9a Risk ratios for overall treatment of lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-, celltype-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.878** (0.798-0.958)	0.003	**0.850** (0.728-0.972)	0.016		**0.891** (0.785-0.995)	0.041
MW	**0.837** (0.767-0.908)	0.000	**0.768** (0.664-0.874)	0.000		**0.887** (0.793-0.978)	0.015
NE	**0.861** (0.793-0.928)	0.000	**0.824** (0.723-0.926)	0.001		**0.872** (0.781-0.961)	0.005
NW	**0.854** (0.780-0.928)	0.000	**0.887** (0.778-0.995)	0.041		**0.821** (0.720-0.921)	0.000
S	0.959 (0.906-1.010)	0.119	1.013 (0.936-1.088)	0.729	*	**0.903** (0.831-0.974)	0.007
SE	**0.805** (0.744-0.866)	0.000	**0.785** (0.697-0.875)	0.000		**0.819** (0.735-0.902)	0.000
W	**0.773** (0.708-0.839)	0.000	**0.795** (0.699-0.892)	0.000		**0.752** (0.664-0.842)	0.000
fuller model: sex-, age-, cell-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**0.844** (0.761-0.926)	0.000	**0.846** (0.719-0.973)	0.018		**0.845** (0.736-0.953)	0.005
MW	**0.829** (0.757-0.901)	0.000	**0.776** (0.668-0.887)	0.000		**0.868** (0.773-0.962)	0.006
NE	**0.867** (0.798-0.937)	0.000	**0.872** (0.766-0.977)	0.017		**0.855** (0.761-0.947)	0.002
NW	**0.852** (0.775-0.928)	0.000	0.890 (0.776-1.004)	0.059		**0.818** (0.714-0.921)	0.000
S	0.951 (0.896-1.004)	0.075	1.007 (0.926-1.086)	0.855	*	**0.897** (0.822-0.970)	0.005
SE	**0.765** (0.703-0.827)	0.000	**0.732** (0.642-0.826)	0.000		**0.788** (0.703-0.873)	0.000
W	**0.777** (0.710-0.844)	0.000	**0.855** (0.754-0.955)	0.005		**0.722** (0.634-0.813)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.867** (0.783-0.950)	0.002	0.882 (0.752-1.011)	0.074		**0.869** (0.759-0.977)	0.018
MW	**0.835** (0.762-0.908)	0.000	**0.785** (0.675-0.898)	0.000		**0.877** (0.781-0.972)	0.011
NE	**0.882** (0.811-0.952)	0.001	**0.886** (0.778-0.993)	0.038		**0.885** (0.790-0.978)	0.016
NW	**0.856** (0.778-0.934)	0.000	0.915 (0.798-1.030)	0.152		**0.808** (0.703-0.914)	0.000
S	0.965 (0.910-1.020)	0.219	1.033 (0.950-1.112)	0.429	*	**0.904** (0.828-0.979)	0.012
SE	**0.762** (0.699-0.826)	0.000	**0.739** (0.647-0.834)	0.000		**0.781** (0.695-0.868)	0.000
W	**0.788** (0.720-0.857)	0.000	**0.871** (0.769-0.973)	0.013	*	**0.732** (0.641-0.824)	0.000

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Age-group 15-44, 45-54, 55-64, 65-74, or 75+; cell-type (non-small-cell, small-cell, other/unknown).
[c]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[d]Age-group; sex; cell-type; T, N and M categories; grade; microscopic verification status; smoking status; marital status; individual year of diagnosis. [Method of presentation did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

Table 5.6.9b Risk ratios for overall treatment of non-small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.918 (0.837-0.995)	0.037	0.886 (0.761-1.004)	0.061		0.935 (0.827-1.032)	0.202
MW	**0.881** (0.803-0.955)	0.001	**0.795** (0.679-0.908)	0.000	*	0.957 (0.853-1.049)	0.384
NE	**0.877** (0.807-0.944)	0.000	**0.849** (0.738-0.956)	0.005		**0.882** (0.791-0.966)	0.005
NW	**0.862** (0.783-0.937)	0.000	**0.877** (0.761-0.987)	0.028		**0.846** (0.737-0.948)	0.002
S	0.968 (0.917-1.017)	0.212	0.997 (0.919-1.069)	0.947		0.936 (0.865-1.001)	0.055
SE	**0.884** (0.819-0.946)	0.000	**0.896** (0.799-0.989)	0.028		**0.868** (0.781-0.950)	0.001
W	**0.764** (0.694-0.833)	0.000	**0.813** (0.712-0.912)	0.000		**0.713** (0.616-0.809)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.912** (0.825-0.993)	0.034	0.909 (0.775-1.034)	0.164		0.932 (0.818-1.033)	0.203
MW	**0.896** (0.813-0.974)	0.009	**0.817** (0.691-0.940)	0.003		0.966 (0.858-1.061)	0.516
NE	**0.882** (0.807-0.953)	0.001	0.915 (0.796-1.027)	0.142		**0.871** (0.774-0.962)	0.005
NW	**0.854** (0.769-0.935)	0.000	0.894 (0.768-1.012)	0.081		**0.824** (0.707-0.934)	0.001
S	0.972 (0.916-1.024)	0.306	1.017 (0.933-1.094)	0.674		0.937 (0.862-1.006)	0.077
SE	**0.847** (0.778-0.914)	0.000	**0.856** (0.751-0.958)	0.005		**0.840** (0.747-0.927)	0.000
W	**0.781** (0.707-0.855)	0.000	**0.895** (0.787-0.998)	0.046	*	**0.687** (0.586-0.789)	0.000

[a,b] See *Table 5.6.9a*.
[d] Age-group; sex; T, N and M categories; grade; smoking status; marital status; individual year of diagnosis. [Method of presentation did not significantly improve model-fit for lung cancers as a whole and was excluded from the final model; microscopic verification was excluded for SCLC and NSCLC as all had MV.]
*Significant difference in RR between diagnosis periods.

Table 5.6.9c Risk ratios for overall treatment of small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P	1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]						
E	1.000		1.000		1.000	
M	0.893 (0.720-1.043)	0.179	0.841 (0.578-1.058)	0.175	0.947 (0.710-1.142)	0.633
MW	**0.678** (0.523-0.835)	0.000	**0.661** (0.437-0.888)	0.002	**0.700** (0.489-0.916)	0.005
NE	0.902 (0.757-1.029)	0.142	0.907 (0.727-1.055)	0.245	0.867 (0.624-1.082)	0.248
NW	0.874 (0.716-1.014)	0.082	0.990 (0.778-1.143)	0.920	**0.758** (0.533-0.977)	0.029
S	1.047 (0.951-1.128)	0.317	1.101 (0.984-1.186)	0.085	0.975 (0.817-1.111)	0.746
SE	**0.804** (0.672-0.929)	0.001	**0.735** (0.557-0.904)	0.001	0.878 (0.680-1.055)	0.190
W	0.897 (0.751-1.026)	0.126	0.900 (0.678-1.077)	0.307	0.905 (0.703-1.082)	0.318
final multivariate model[d]						
E	1.000		1.000		1.000	
M	0.877 (0.690-1.039)	0.150	0.818 (0.540-1.050)	0.142	0.946 (0.689-1.155)	0.655
MW	**0.631** (0.471-0.798)	0.000	**0.627** (0.392-0.873)	0.002	**0.631** (0.416-0.865)	0.001
NE	0.879 (0.725-1.017)	0.091	0.911 (0.721-1.065)	0.293	0.838 (0.572-1.077)	0.203
NW	0.851 (0.684-1.002)	0.055	0.991 (0.761-1.152)	0.933	**0.702** (0.472-0.937)	0.012
S	1.019 (0.909-1.112)	0.717	1.091 (0.957-1.186)	0.163	0.922 (0.739-1.082)	0.366
SE	**0.748** (0.607-0.885)	0.000	**0.695** (0.507-0.880)	0.001	**0.788** (0.575-0.991)	0.040
W	0.930 (0.779-1.060)	0.316	0.925 (0.694-1.102)	0.463	0.922 (0.705-1.107)	0.444

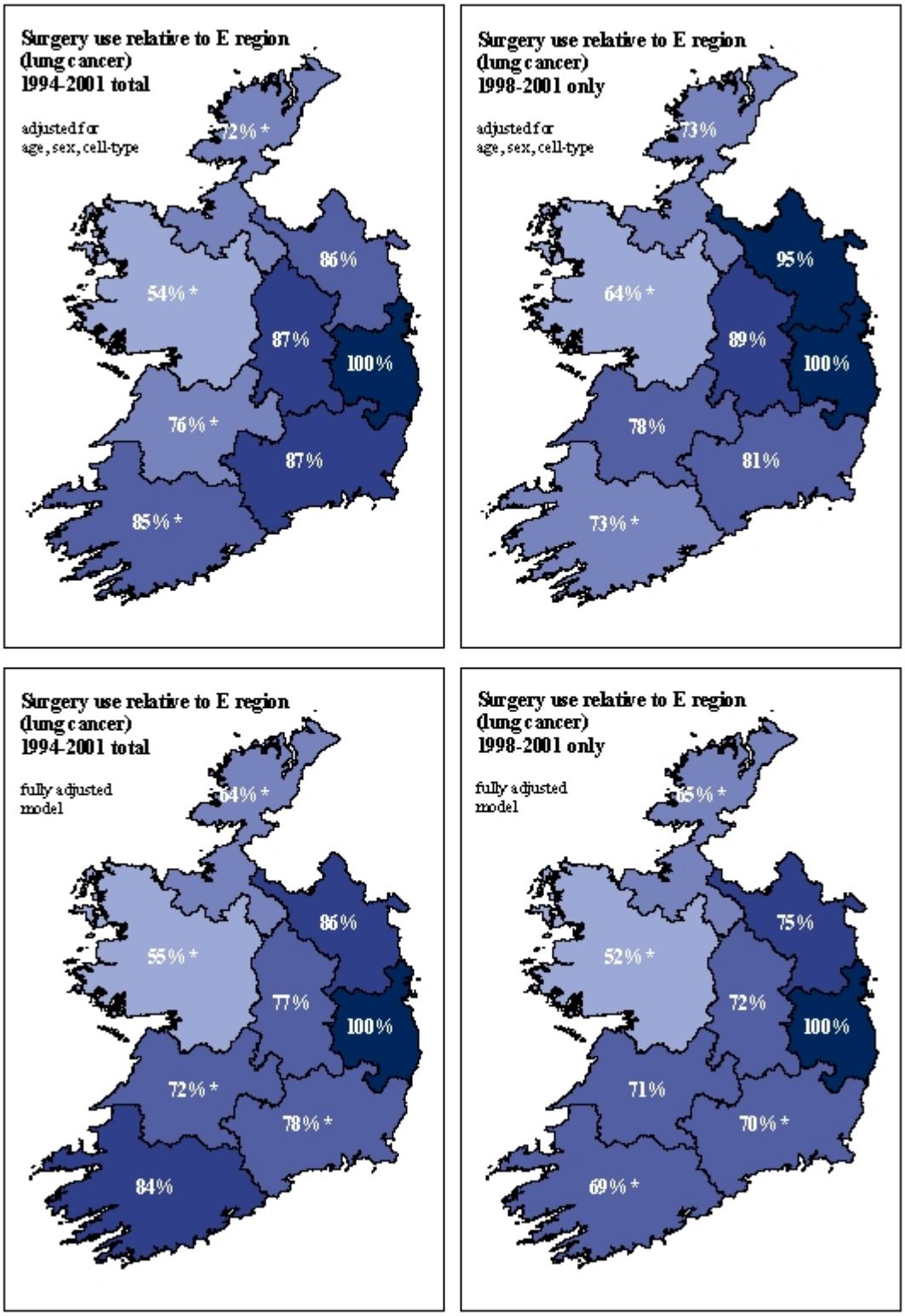


Figure 5.6.1 Regional variation in surgical treatment for lung cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic model adjusted for age, sex and cell-type (top), fully-adjusted model (bottom). See *Table 5.6.10* for further details. * = significantly high or low values (P<0.05).

Surgical treatment

Patients from four regions (Mid-Western, North-Western, Southern and Western) were significantly less likely to have surgical treatment than patients from the Eastern region during 1994-2001, after adjustment for age, sex and tumour cell-type (*Figure 5.6.1*, *Table 5.6.10a*). Use of surgical treatment was significantly low for three of these regions (Mid-Western, North-Western and Western) during 1994-97 and two of the regions (Southern and Western) during 1998-2001.

Regional patterns for 1994-2001 as a whole were accentuated somewhat (significantly low use of surgery in six regions) after further adjustment for stage. But a more complete model adjusting more patient and tumour characteristics indicated significantly low use of surgical treatment in four regions (Mid-Western, North-Western and Western in common with the basic model, and additionally the South-Eastern region). The full model indicated lower use of surgery in two regions (North-Western and Western) for 1994-97, and four (Southern and South-Eastern) for 1998-2001, compared with the Eastern region. However, there were no differences in relative risk estimates (RRs) between diagnosis periods for any of the regions or models examined.

These patterns were essentially the same for non-small-cell cancers (*Table 5.6.10b*) as for lung cancers as a whole. Samples sizes were too small to examine regional patterns in surgery for small-cell cancers.

Table 5.6.10a Risk ratios for surgical treatment of lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
basic model: sex-, age-, celltype-adjusted[b]						
E	1.000		1.000		1.000	
M	0.868 (0.694-1.077)	0.203	0.862 (0.630-1.159)	0.336	0.885 (0.639-1.205)	0.447
MW	**0.760** (0.613-0.935)	0.009	**0.743** (0.550-0.988)	0.041	0.784 (0.574-1.056)	0.112
NE	0.864 (0.716-1.037)	0.119	0.789 (0.597-1.029)	0.082	0.951 (0.733-1.218)	0.698
NW	**0.720** (0.573-0.899)	0.003	**0.710** (0.517-0.962)	0.027	0.731 (0.523-1.007)	0.056
S	**0.846** (0.733-0.974)	0.020	0.961 (0.796-1.150)	0.673	**0.728** (0.580-0.908)	0.005
SE	0.865 (0.729-1.021)	0.088	0.920 (0.732-1.145)	0.467	0.805 (0.620-1.035)	0.093
W	**0.544** (0.433-0.680)	0.000	**0.466** (0.336-0.640)	0.000	**0.643** (0.467-0.876)	0.005
fuller model: sex-, age-, cell-, stage-adjusted[b,c]						
E	1.000		1.000		1.000	
M	**0.716** (0.540-0.940)	0.016	0.788 (0.531-1.138)	0.211	0.708 (0.467-1.049)	0.087
MW	**0.701** (0.537-0.906)	0.006	0.717 (0.494-1.021)	0.066	0.708 (0.480-1.026)	0.069
NE	0.833 (0.660-1.041)	0.111	1.016 (0.724-1.390)	0.922	**0.713** (0.513-0.979)	0.036
NW	**0.681** (0.515-0.892)	0.005	**0.660** (0.443-0.962)	0.030	0.710 (0.473-1.044)	0.083
S	**0.793** (0.663-0.944)	0.009	0.906 (0.715-1.135)	0.399	**0.687** (0.519-0.901)	0.006
SE	**0.807** (0.655-0.988)	0.038	0.845 (0.638-1.103)	0.222	0.759 (0.550-1.033)	0.081
W	**0.570** (0.436-0.740)	0.000	**0.561** (0.382-0.810)	0.002	**0.611** (0.417-0.881)	0.008
final multivariate model[d]						
E	1.000		1.000		1.000	
M	0.774 (0.577-1.024)	0.074	0.887 (0.595-1.282)	0.537	0.721 (0.461-1.098)	0.131
MW	**0.715** (0.543-0.931)	0.012	0.729 (0.495-1.047)	0.089	0.713 (0.477-1.045)	0.084
NE	0.863 (0.676-1.090)	0.221	0.988 (0.691-1.374)	0.946	0.752 (0.532-1.047)	0.093
NW	**0.641** (0.477-0.851)	0.002	**0.631** (0.416-0.936)	0.021	**0.650** (0.424-0.978)	0.038
S	0.840 (0.699-1.005)	0.057	0.998 (0.783-1.254)	0.988	**0.690** (0.514-0.916)	0.010
SE	**0.778** (0.625-0.962)	0.020	0.826 (0.617-1.090)	0.182	**0.699** (0.496-0.972)	0.033
W	**0.549** (0.415-0.719)	0.000	**0.594** (0.403-0.860)	0.005	**0.516** (0.343-0.766)	0.001

[a,b,c]See *Table 5.6.9a*.

[d]Age-group; cell-type; T, N and M categories; grade; microscopic verification status; method of presentation; marital status. [Sex, smoking status and year of diagnosis did not significantly improve model-fit and were excluded from the final model.]

Table 5.6.10b Risk ratios for surgical treatment of non-small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997		1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
basic model: sex-, age-adjusted[b]						
E	1.000		1.000		1.000	
M	0.891 (0.722-1.085)	0.260	0.907 (0.679-1.182)	0.488	0.884 (0.648-1.178)	0.415
MW	**0.794** (0.648-0.964)	0.019	**0.745** (0.557-0.976)	0.032	0.852 (0.636-1.117)	0.255
NE	0.885 (0.741-1.046)	0.157	0.804 (0.615-1.030)	0.087	0.977 (0.768-1.223)	0.847
NW	**0.726** (0.582-0.897)	0.003	**0.748** (0.553-0.989)	0.042	**0.706** (0.506-0.965)	0.028
S	**0.848** (0.740-0.968)	0.014	0.935 (0.782-1.105)	0.442	**0.761** (0.613-0.934)	0.009
SE	0.877 (0.746-1.024)	0.099	0.896 (0.719-1.101)	0.307	0.859 (0.673-1.079)	0.198
W	**0.572** (0.458-0.707)	0.000	**0.495** (0.360-0.671)	0.000	**0.667** (0.489-0.894)	0.006
fuller model: sex-, age-, stage-adjusted[b,c]						
E	1.000		1.000		1.000	
M	**0.746** (0.566-0.966)	0.026	0.838 (0.575-1.176)	0.324	0.712 (0.471-1.041)	0.082
MW	**0.744** (0.572-0.952)	0.018	**0.700** (0.482-0.986)	0.041	0.805 (0.552-1.138)	0.231
NE	0.859 (0.686-1.061)	0.164	1.006 (0.722-1.350)	0.967	0.759 (0.551-1.024)	0.073
NW	**0.670** (0.507-0.871)	0.002	**0.695** (0.469-0.995)	0.047	**0.654** (0.433-0.959)	0.029
S	**0.804** (0.675-0.950)	0.010	0.880 (0.697-1.093)	0.257	**0.737** (0.561-0.954)	0.020
SE	0.829 (0.676-1.006)	0.058	0.813 (0.614-1.054)	0.122	0.841 (0.618-1.120)	0.246
W	**0.599** (0.459-0.771)	0.000	**0.588** (0.403-0.837)	0.002	**0.641** (0.438-0.915)	0.013
final multivariate model[d]						
E	1.000		1.000		1.000	
M	0.798 (0.601-1.039)	0.097	0.923 (0.632-1.290)	0.660	0.722 (0.464-1.082)	0.119
MW	**0.747** (0.571-0.963)	0.024	**0.702** (0.477-0.998)	0.049	0.807 (0.546-1.153)	0.251
NE	0.885 (0.700-1.103)	0.287	0.995 (0.703-1.351)	0.977	0.788 (0.563-1.075)	0.138
NW	**0.629** (0.469-0.831)	0.001	**0.665** (0.440-0.968)	0.033	**0.595** (0.383-0.896)	0.012
S	**0.837** (0.700-0.993)	0.042	0.955 (0.755-1.187)	0.695	**0.728** (0.547-0.953)	0.020
SE	**0.794** (0.641-0.974)	0.026	0.791 (0.591-1.036)	0.091	0.771 (0.553-1.050)	0.102
W	**0.572** (0.434-0.744)	0.000	**0.612** (0.418-0.872)	0.006	**0.546** (0.362-0.805)	0.002

[a,b,c]See *Table 5.6.9a*.
[d]Age-group; T, N and M categories; grade; method of presentation; marital status. [Sex, smoking status and year of diagnosis did not significantly improve model-fit and were excluded from the final model; microscopic verification was also excluded as all NSCLC cases had MV.]
There were no significant differences in RR between diagnosis periods.

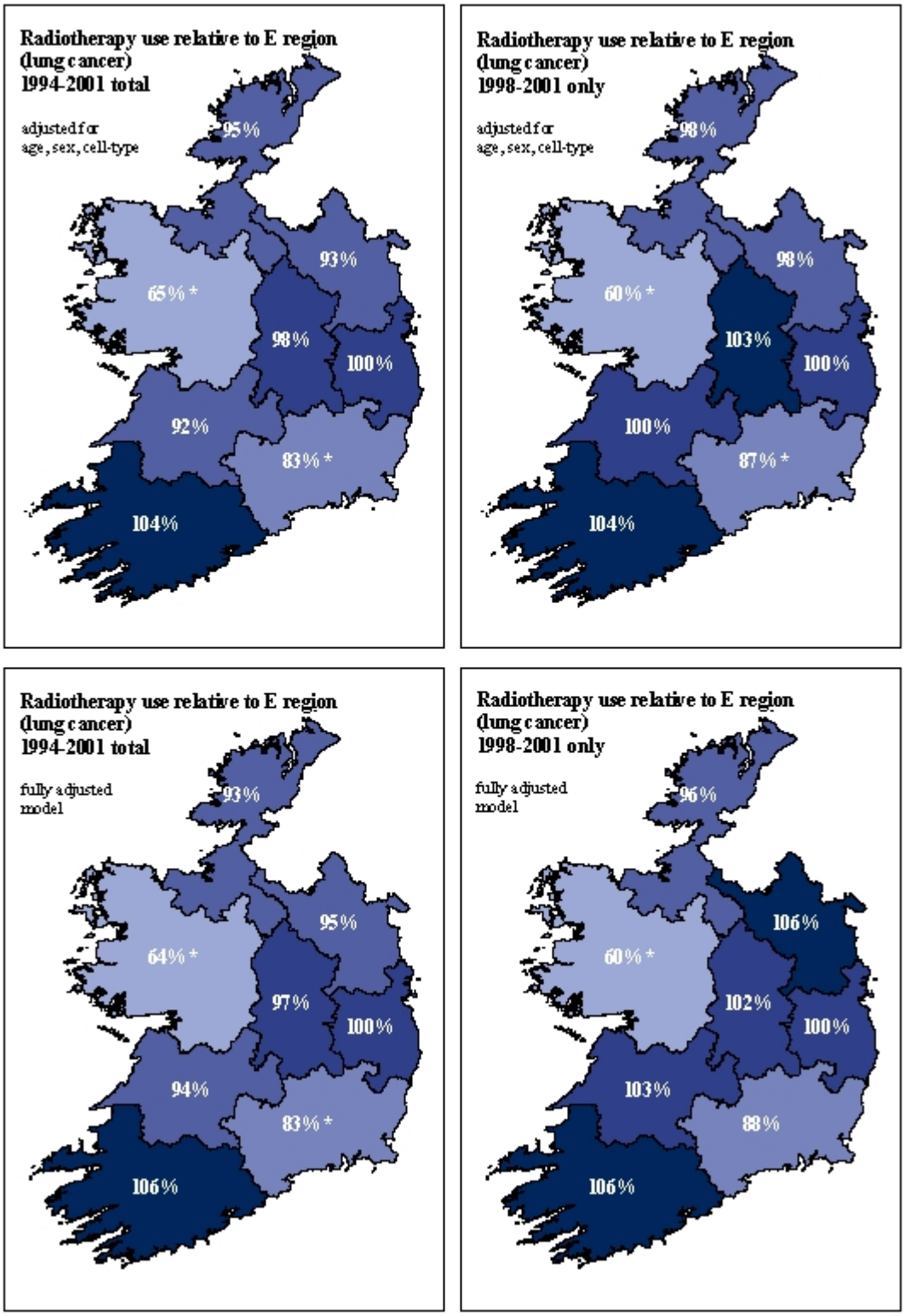


Figure 5.6.2 Regional variation in radiotherapy for lung cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic model adjusted for age, sex and cell-type (top), fully-adjusted model (bottom). See *Table 5.6.11* for further details. * = significantly high or low values (P<0.05).

Radiotherapy

Regional variation was less marked for radiotherapy use than for surgical treatment. For the overall period (1994-2001), patients from two regions (South-Eastern and Western) were significantly less likely to have radiotherapy than those from the Eastern region (*Figure 5.6.2*, *Table 5.6.11a*). This applied, in terms of general pattern and magnitude of regional variation, for the three models examined (from basic to fully adjusted). In the basic model, radiotherapy usage was low in patients from the same two regions for both the 1994-97 and 1998-2001 diagnosis periods, and also low for the Mid-Western region for 1994-97. In the final model, patients from the Mid-Western, South-Eastern and Western regions during 1994-97, but only the Western region during 1998-2001, had significantly low use of radiotherapy compared with the Eastern region. The only significant difference in relative risk values (RRs) between periods was for the Mid-Western region (in the stage-adjusted model).

The regional patterns for non-small-cell lung cancer were similar to those for lung cancers as a whole. The main exception was significantly higher radiotherapy use in NSCLC patients from the Mid-Western region compared with the Eastern region, for 1998-2001 (*Table 5.6.11b*). For small-cell lung cancer, radiotherapy usage was again significantly low among patients from the Western region (as for NSCLC and overall lung cancer); but, in contrast to NSCLC, was also significantly low for the Mid-Western region during 1998-2001 (*Table 5.6.11c*).

Table 5.6.11a Risk ratios for radiotherapy of lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-, celltype-adjusted[b]							
E	1.000		1.000			1.000	
M	0.975 (0.857-1.099)	0.690	0.883 (0.714-1.073)	0.220		1.030 (0.875-1.194)	0.712
MW	0.920 (0.821-1.026)	0.140	**0.798** (0.658-0.956)	0.014		1.001 (0.867-1.143)	0.986
NE	0.928 (0.831-1.030)	0.165	0.853 (0.713-1.008)	0.063		0.977 (0.849-1.113)	0.742
NW	0.949 (0.843-1.062)	0.373	0.907 (0.753-1.077)	0.275		0.981 (0.838-1.134)	0.808
S	1.036 (0.958-1.117)	0.363	1.031 (0.916-1.153)	0.598		1.035 (0.930-1.145)	0.509
SE	**0.832** (0.749-0.921)	0.000	**0.792** (0.673-0.924)	0.003		**0.867** (0.753-0.990)	0.035
W	**0.649** (0.568-0.737)	0.000	**0.699** (0.578-0.837)	0.000		**0.599** (0.495-0.717)	0.000
fuller model: sex-, age-, cell-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.970 (0.852-1.096)	0.643	0.886 (0.715-1.079)	0.239		1.012 (0.855-1.179)	0.883
MW	0.928 (0.827-1.036)	0.190	**0.800** (0.658-0.960)	0.016	*	1.014 (0.877-1.158)	0.843
NE	0.956 (0.857-1.061)	0.415	0.855 (0.713-1.013)	0.071		1.041 (0.906-1.183)	0.557
NW	0.930 (0.823-1.044)	0.226	0.902 (0.747-1.074)	0.257		0.949 (0.806-1.103)	0.512
S	1.038 (0.958-1.121)	0.349	1.026 (0.908-1.151)	0.669		1.040 (0.932-1.152)	0.468
SE	**0.827** (0.742-0.917)	0.000	**0.775** (0.656-0.908)	0.001		**0.874** (0.757-0.998)	0.048
W	**0.629** (0.549-0.717)	0.000	**0.674** (0.555-0.810)	0.000		**0.584** (0.481-0.702)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.969 (0.850-1.096)	0.632	0.903 (0.729-1.099)	0.324		1.021 (0.862-1.191)	0.795
MW	0.936 (0.833-1.044)	0.244	**0.814** (0.669-0.976)	0.026		1.026 (0.888-1.173)	0.712
NE	0.950 (0.850-1.055)	0.348	0.858 (0.715-1.017)	0.080		1.056 (0.918-1.201)	0.430
NW	0.934 (0.826-1.049)	0.261	0.924 (0.764-1.100)	0.386		0.955 (0.810-1.112)	0.572
S	1.055 (0.972-1.140)	0.191	1.047 (0.926-1.175)	0.451		1.063 (0.952-1.178)	0.268
SE	**0.834** (0.749-0.926)	0.001	**0.791** (0.669-0.926)	0.003		0.879 (0.761-1.005)	0.061
W	**0.636** (0.555-0.725)	0.000	**0.677** (0.556-0.815)	0.000		**0.599** (0.493-0.719)	0.000

[a,b,c]See *Table 5.6.9a*.
[d]Age-group; sex; cell-type; T, N and M categories; grade; method of presentation; smoking status; marital status; individual year of diagnosis. [Microscopic verification status did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

Table 5.6.11b Risk ratios for radiotherapy of non-small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	1.039 (0.909-1.173)	0.559	0.953 (0.766-1.154)	0.640		1.101 (0.925-1.280)	0.264
MW	0.959 (0.840-1.084)	0.520	**0.792** (0.633-0.970)	0.024	*	1.114 (0.946-1.284)	0.185
NE	0.983 (0.874-1.097)	0.777	0.947 (0.783-1.123)	0.550		0.994 (0.851-1.142)	0.937
NW	0.983 (0.861-1.110)	0.794	0.954 (0.781-1.141)	0.629		1.012 (0.844-1.188)	0.884
S	1.061 (0.976-1.148)	0.157	1.029 (0.905-1.158)	0.646		1.080 (0.964-1.198)	0.178
SE	**0.870** (0.773-0.972)	0.013	**0.827** (0.689-0.978)	0.026		0.904 (0.772-1.044)	0.180
W	**0.661** (0.567-0.764)	0.000	**0.773** (0.633-0.928)	0.005	*	**0.548** (0.430-0.687)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	1.058 (0.923-1.197)	0.400	0.996 (0.801-1.205)	0.972		1.121 (0.936-1.309)	0.201
MW	0.992 (0.867-1.122)	0.909	**0.793** (0.630-0.977)	0.029	*	**1.183** (1.006-1.360)	0.042
NE	0.999 (0.886-1.116)	0.993	0.929 (0.762-1.109)	0.434		1.077 (0.924-1.233)	0.324
NW	0.968 (0.842-1.099)	0.632	0.956 (0.776-1.150)	0.652		0.992 (0.818-1.175)	0.939
S	1.087 (0.997-1.179)	0.057	1.057 (0.926-1.193)	0.396		1.113 (0.989-1.238)	0.073
SE	**0.875** (0.774-0.980)	0.021	**0.824** (0.682-0.980)	0.028		0.923 (0.785-1.069)	0.297
W	**0.637** (0.544-0.741)	0.000	**0.723** (0.585-0.878)	0.001		**0.539** (0.420-0.681)	0.000

[a,b]See *Table 5.6.9a*.
[d]Age-group; sex; T, N and M categories; grade; method of presentation; smoking status; marital status; individual year of diagnosis. [Microscopic verification status was excluded from the final model for NSCLC and SCLC cases as all had MV.]
*Significant difference in RR between diagnosis periods.

Table 5.6.11c Risk ratios for radiotherapy of small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P	1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]						
E	1.000		1.000		1.000	
M	0.938 (0.621-1.337)	0.742	0.558 (0.225-1.224)	0.158	1.107 (0.701-1.581)	0.634
MW	0.683 (0.440-1.013)	0.059	0.851 (0.425-1.524)	0.618	**0.576** (0.320-0.960)	0.033
NE	0.737 (0.502-1.043)	0.088	0.742 (0.423-1.219)	0.254	0.778 (0.448-1.231)	0.312
NW	0.807 (0.539-1.155)	0.256	0.971 (0.535-1.598)	0.917	0.687 (0.387-1.118)	0.142
S	1.134 (0.909-1.384)	0.255	1.191 (0.845-1.606)	0.304	1.098 (0.814-1.414)	0.517
SE	0.981 (0.733-1.273)	0.896	1.151 (0.751-1.658)	0.498	0.839 (0.550-1.203)	0.366
W	**0.540** (0.342-0.822)	0.003	**0.433** (0.176-0.970)	0.041	**0.556** (0.321-0.902)	0.015
final multivariate model[d]						
E	1.000		1.000		1.000	
M	0.871 (0.564-1.271)	0.499	0.509 (0.199-1.156)	0.114	1.142 (0.710-1.640)	0.552
MW	**0.636** (0.403-0.960)	0.030	0.937 (0.464-1.666)	0.843	**0.559** (0.305-0.947)	0.029
NE	0.735 (0.495-1.049)	0.093	0.780 (0.439-1.290)	0.356	0.744 (0.416-1.205)	0.253
NW	0.761 (0.499-1.110)	0.166	0.940 (0.498-1.598)	0.838	0.683 (0.378-1.124)	0.145
S	1.081 (0.846-1.346)	0.517	1.099 (0.744-1.542)	0.619	1.067 (0.766-1.409)	0.682
SE	0.929 (0.684-1.223)	0.620	1.018 (0.637-1.525)	0.935	0.797 (0.509-1.168)	0.265
W	**0.522** (0.326-0.804)	0.002	0.470 (0.189-1.051)	0.068	**0.556** (0.318-0.911)	0.018

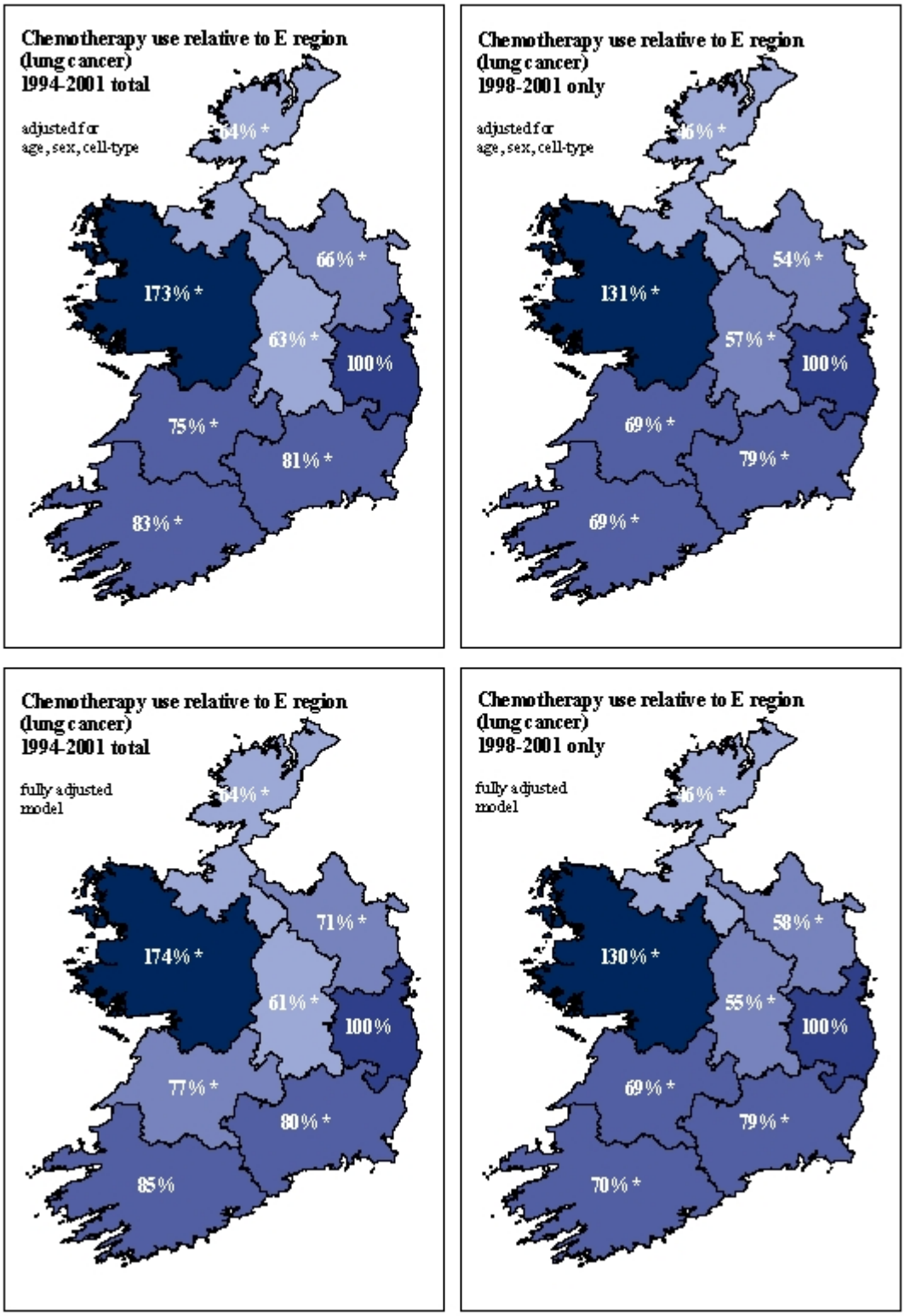


Figure 5.6.3 Regional variation in chemotherapy for lung cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic model adjusted for age, sex and cell-type (top), fully-adjusted model (bottom). See *Table 5.6.12* for further details. * = significantly high or low values (P<0.05).

Chemotherapy

Regional variation in chemotherapy use was very marked, although there were substantial differences between diagnosis periods 1994-97 and 1998-2001. For 1994-2001 as a whole, patients from six regions were significantly less likely to receive chemotherapy than those from the Eastern region, after adjustment for age, sex and cell-type (*Figure 5.6.3*, *Table 5.6.12a*). However, patients from the Western region were significantly more likely to have chemotherapy, and this also applied in for 1994-97 and 1998-2001 (although the relative risk value was significantly lower in the latter period). For other regions during 1994-97, radiotherapy usage did not differ significantly from the Eastern region. In contrast, six regions during 1998-2001 had significantly low radiotherapy usage compared with the Eastern region. For two of these regions, RR values were significantly lower in the latter period.

Further adjustment for stage-related or other variables had little effect on the pattern and magnitude of regional variations seen. Based on the fullest model (and 1994-2001 data), patients from five regions (Midland, Mid-Western, North-Eastern, North-Western and South-Eastern) were significantly less likely, and patients from the Western region significantly more likely, to receive radiotherapy than those from the Eastern region. As in the basic model, apart from the finding from the Western region, regional variation was largely confined to 1998-2001.

Findings for lung cancer as a whole were largely mirrored by those for non-small-cell cancers (*Table 5.6.12b*), while chemotherapy use for small-cell cancers was significantly low in several regions (*Table 5.6.12c*).

Table 5.6.12a Risk ratios for chemotherapy of lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: sex-, age-, celltype-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.626** (0.472-0.822)	0.001	0.718 (0.451-1.116)	0.145		**0.565** (0.394-0.796)	0.001
MW	**0.750** (0.598-0.934)	0.010	0.856 (0.588-1.221)	0.401		**0.686** (0.515-0.902)	0.006
NE	**0.664** (0.530-0.826)	0.000	0.794 (0.564-1.100)	0.170		**0.540** (0.395-0.730)	0.000
NW	**0.641** (0.497-0.820)	0.000	0.965 (0.662-1.375)	0.850	*	**0.464** (0.325-0.654)	0.000
S	**0.834** (0.713-0.971)	0.019	1.056 (0.832-1.326)	0.646	*	**0.688** (0.555-0.846)	0.000
SE	**0.808** (0.669-0.971)	0.023	0.825 (0.604-1.112)	0.213		**0.786** (0.618-0.989)	0.040
W	**1.725** (1.493-1.976)	0.000	**2.523** (2.066-3.013)	0.000	*	**1.310** (1.066-1.587)	0.011
fuller model: sex-, age-, cell-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**0.605** (0.452-0.800)	0.000	0.718 (0.451-1.116)	0.145		**0.541** (0.374-0.771)	0.000
MW	**0.751** (0.598-0.937)	0.011	0.856 (0.588-1.221)	0.401		**0.693** (0.519-0.915)	0.009
NE	**0.698** (0.556-0.870)	0.001	0.794 (0.564-1.100)	0.170		**0.576** (0.418-0.784)	0.000
NW	**0.616** (0.476-0.791)	0.000	0.965 (0.662-1.375)	0.850	*	**0.444** (0.309-0.629)	0.000
S	**0.836** (0.711-0.978)	0.025	1.056 (0.832-1.326)	0.646	*	**0.698** (0.561-0.863)	0.001
SE	**0.772** (0.635-0.932)	0.007	0.825 (0.604-1.112)	0.213		**0.774** (0.605-0.980)	0.033
W	**1.694** (1.462-1.946)	0.000	**2.523** (2.066-3.013)	0.000	*	**1.272** (1.030-1.548)	0.026
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.606** (0.451-0.805)	0.000	0.702 (0.431-1.113)	0.137		**0.550** (0.378-0.788)	0.001
MW	**0.767** (0.609-0.959)	0.020	0.938 (0.642-1.340)	0.735		**0.692** (0.516-0.916)	0.010
NE	**0.706** (0.561-0.882)	0.002	0.841 (0.593-1.173)	0.316		**0.582** (0.421-0.794)	0.000
NW	**0.640** (0.493-0.824)	0.000	1.008 (0.686-1.446)	0.963	*	**0.457** (0.317-0.650)	0.000
S	0.854 (0.725-1.001)	0.052	1.076 (0.836-1.367)	0.562	*	**0.695** (0.555-0.863)	0.001
SE	**0.800** (0.658-0.967)	0.021	0.774 (0.559-1.059)	0.112		**0.787** (0.614-0.998)	0.049
W	**1.743** (1.503-2.003)	0.000	**2.547** (2.070-3.061)	0.000	*	**1.303** (1.054-1.586)	0.015

[a,b,c]See *Table 5.6.9a*.
[d]Age-group; sex; cell-type; T, N and M categories; grade; microscopic verification status; smoking status; marital status; individual year of diagnosis. [Method of presentation did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

Table 5.6.12b Risk ratios for chemotherapy of non-small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.553** (0.363-0.830)	0.004	0.685 (0.334-1.364)	0.288		**0.474** (0.281-0.779)	0.003
MW	0.861 (0.639-1.147)	0.311	1.253 (0.790-1.946)	0.332	*	**0.667** (0.449-0.971)	0.034
NE	**0.549** (0.390-0.766)	0.000	0.596 (0.320-1.089)	0.094		**0.488** (0.323-0.726)	0.000
NW	**0.590** (0.405-0.851)	0.004	0.848 (0.458-1.530)	0.593		**0.468** (0.290-0.743)	0.001
S	**0.669** (0.529-0.843)	0.001	0.789 (0.529-1.165)	0.237		**0.598** (0.447-0.794)	0.000
SE	0.969 (0.761-1.225)	0.800	1.286 (0.866-1.878)	0.210		0.810 (0.595-1.086)	0.164
W	**2.140** (1.788-2.533)	0.000	**3.625** (2.784-4.607)	0.000	*	**1.460** (1.127-1.852)	0.005
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.548** (0.354-0.836)	0.005	0.780 (0.374-1.571)	0.496		**0.455** (0.264-0.766)	0.003
MW	0.878 (0.643-1.186)	0.403	1.488 (0.924-2.330)	0.100	*	**0.660** (0.436-0.978)	0.038
NE	**0.551** (0.387-0.778)	0.001	0.650 (0.344-1.202)	0.173		**0.511** (0.333-0.773)	0.001
NW	**0.556** (0.375-0.816)	0.002	0.872 (0.458-1.610)	0.670		**0.462** (0.280-0.745)	0.001
S	**0.657** (0.513-0.838)	0.001	0.777 (0.509-1.174)	0.235		**0.593** (0.435-0.799)	0.000
SE	0.972 (0.755-1.241)	0.828	1.270 (0.833-1.902)	0.262		0.826 (0.600-1.118)	0.222
W	**2.219** (1.838-2.646)	0.000	**3.864** (2.927-4.955)	0.000	*	**1.434** (1.092-1.842)	0.010

[a,b]See *Table 5.6.9a*.
[d]Age-group; sex; T, N and M categories; grade; microscopic verification status; smoking status; marital status; individual year of diagnosis. [Method of presentation did not significantly improve model-fit for either NSCLC and SCLC and was excluded from the final models for these cell-types; microscopic verification was also excluded as all NSCLC and SCLC cases had MV.]
*Significant difference in RR between diagnosis periods.

Table 5.6.12c Risk ratios for chemotherapy of small-cell lung cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
basic model: sex-, age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.778** (0.582-0.980)	0.031	0.827 (0.544-1.093)	0.223		0.760 (0.492-1.058)	0.116
MW	**0.624** (0.460-0.807)	0.000	**0.552** (0.333-0.815)	0.001		**0.700** (0.467-0.966)	0.028
NE	0.872 (0.704-1.037)	0.132	0.907 (0.703-1.092)	0.348		0.764 (0.501-1.054)	0.112
NW	**0.794** (0.615-0.977)	0.027	0.964 (0.716-1.172)	0.761		**0.621** (0.391-0.901)	0.009
S	1.038 (0.915-1.153)	0.529	1.084 (0.931-1.211)	0.264		0.969 (0.772-1.161)	0.765
SE	**0.808** (0.658-0.958)	0.012	**0.719** (0.529-0.915)	0.004		0.914 (0.683-1.145)	0.477
W	0.897 (0.727-1.062)	0.231	0.932 (0.683-1.147)	0.570		0.901 (0.662-1.141)	0.432
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.743** (0.535-0.961)	0.021	0.793 (0.503-1.075)	0.163		0.691 (0.413-1.019)	0.065
MW	**0.588** (0.422-0.779)	0.000	**0.513** (0.295-0.789)	0.001		**0.607** (0.381-0.886)	0.006
NE	0.835 (0.658-1.011)	0.067	0.898 (0.682-1.093)	0.329		0.715 (0.439-1.034)	0.081
NW	**0.778** (0.590-0.971)	0.024	0.970 (0.706-1.189)	0.815	*	**0.544** (0.326-0.826)	0.002
S	1.044 (0.908-1.168)	0.516	1.108 (0.940-1.242)	0.193		0.922 (0.704-1.138)	0.491
SE	**0.769** (0.613-0.929)	0.005	**0.719** (0.517-0.927)	0.007		0.822 (0.581-1.077)	0.175
W	0.952 (0.771-1.121)	0.594	0.951 (0.690-1.172)	0.699		0.925 (0.664-1.183)	0.582

*Significant difference in RR between diagnosis periods.

5.7 Discussion: lung cancer

The major findings here are:

- no significant changes in relative survival of patients between the periods 1994-97 and 1998-2001, except for an improvement for age-group 55-64 and a reduction in survival for patients from the North-Eastern region;
- significantly higher relative survival in patients from at least two regions (Mid-Western and North-Western) compared with the Eastern region, and (after fuller adjustment for patient and tumour characteristics) significantly lower survival in those from the South-Eastern region (1998-2001 only);
- significant increases in overall treatment, radiotherapy and chemotherapy use, but decreases in surgery use, nationally and in some regions, between 1996 and 2001;
- significant regional variation in treatments, mainly involving lower use of overall treatment, surgery, chemotherapy and to a lesser extent radiotherapy for patients from outside the Eastern region.

Survival trends

The lack of any notable or general improvement in relative survival for this cancer, within the period examined, is not unexpected. Lung cancer is, on average, far more fatal and less treatable than other cancers considered in this report. The scope for improvements in treatment and survival is also, currently, less, in the absence of effective approaches to population-based screening that might lead to substantially earlier detection.

Regional variation in survival

This was less marked than for the other cancers considered in this report (breast, colorectal and prostate cancers). Also, in contrast to those cancers, the variation seen largely involved higher relative survival for patients from a number of regions compared with the Eastern region. Reflecting the poor survival rates for this cancer, absolute differences between regions were small and the clinical significance of the variation seen is unclear.

Survival: international context

For males, the average five-year relative survival for Irish patients diagnosed with lung cancer during 1994-97 was lower than the European average for patients diagnosed during 1990-94 (EUROCARE-3 results summarized in *Table 5.7.1*). For female patients, Irish and average European survival figures were similar. More recent Europe-wide figures are not yet available. Note that figures tabulated here are age-standardized to the EUROCARE-3 patient population, thus the Irish figures differ slightly from those tabulated earlier in this chapter.

Table 5.7.1 Comparison of five-year relative survival for lung cancer patients, Ireland 1994-97 and 1998-2001, and Europe 1990-94, age-adjusted to the EUROCARE-3 standard patient population for this cancer.[a]

	Ireland 1994-97 5-yr survival (95% CI)		Ireland 1998-2001 survival (95% CI)		Europe 1990-94[b] survival (95% CI)		[range][c]
male	7.7%	(6.7%-8.7%)	8.4%	(7.3%-9.5%)	9.7%	(9.3%-10.0%)	[6.1%-13.4%]
female	9.8%	(8.4%-11.3%)	11.2%	(9.6%-12.9%)	9.6%	(9.0%-10.2%)	[5.9%-16.2%]

[a]Capocaccia *et al*. (2003) and unpublished. [b]EUROCARE-3: Sant *et al*. (2003), including cancer of the trachea (not included in Irish data).
[c]Range of national figures: highest Austria (male), Switzerland (female).

Treatment trends

Radiotherapy use, and overall treatment, increased nationally by the equivalent of between 2% and 3% annually in relative terms between 1996 and 2001, while chemotherapy use increased to a greater extent (by *c*.6% annually). Regional trends for these modalities were generally not clear-cut, but were consistent with either stable or increasing use of treatment. There was some evidence that trends differed between small-cell and non-small-cell lung cancers, particularly for chemotherapy (decrease in usage for SCLC compared with an increase for NSCLC). In contrast to radiotherapy and chemotherapy, the use of surgical treatment fell nationally, and also appeared to fall at regional scale. It is not clear to what extent this reflects (or is compensated for by) increases in use of the other modalities.

Regional variation in treatment

There was a general tendency for higher proportions of patients from the Eastern region to be treated than those from other regions, overall and based on specific modalities.

This tendency was strongest for chemotherapy, but for this modality regional variation was much more marked in the most recent diagnosis period, 1998-2001, with significantly lower use among patients from six of the eight regions (compared with none during 1994-97). Chemotherapy use was actually highest in the Western region, in both periods, but (relative to the Eastern region) was lower in the more recent period. The change in regional variation for chemotherapy use between diagnosis periods appears to reflect a more substantial annual increase in chemotherapy use among patients from the Eastern region compared with other regions.

Regional variation in surgical treatment was also substantial (significantly low use in up to four regions), but with less clear-cut differences between diagnosis periods. Radiotherapy usage varied least between regions, but was significantly low among patients from the South-Eastern and Western regions (especially the latter during 1998-2001).

In general, the extent of adjustment for patient and tumour characteristics (in addition to age, sex and cell-type included in the basic model) had little effect on the patterns or magnitude of regional variation in treatment. Likewise, these patterns were broadly reflected by analyses confined to the most common cell-type, non-small-cell lung cancer.

Treatment: international context

Comparisons are made here with first-course treatments reported for cancers in the USA as part of the National Cancer Data Base (http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm). Data have been extracted from the latter for cases other than stage 0, diagnosed during 1998-2001, to provide nearest-equivalent data on treatments of invasive lung cancers. Possible minor differences between the Irish and US data in the timing of treatment included, or the histological definitions used, should be borne in mind, but the data should be broadly comparable.

For both non-small-cell and small-cell lung cancer, Irish patients were significantly less likely to receive treatment, whether radiotherapy, chemotherapy or surgery, than in the USA (*Table 5.7.2*). A significantly smaller proportion of small-cell lung cancer cases had treatment, whether radiotherapy, chemotherapy or surgery, than in the USA (*Table 5.7.2*). Of specific single or multi-modal treatments, fewer Irish cases had chemotherapy plus radiotherapy, and more had radiotherapy only, for both SCLC and NSCLC. Irish NSCLC cases were less likely to have surgery only, chemotherapy only or surgery plus chemotherapy plus radiotherapy. High proportions of SCLC in both populations had chemotherapy only.

Standard treatment modalities for lung cancer

Evidence-based summaries of standard treatment options, by stage or other prognostic grouping, are available as part of the US National Cancer Institute's PDQ Cancer Information Summaries: (http://www.cancer.gov/cancertopics/pdq/cancerdatabase).

A brief summary is provided below, by broad modality (see also *Appendix 1*).

Small-cell lung cancer

Surgery: Curative intent [or survival-prolonging] in combination with adjuvant chemotherapy or chemotherapy plus radiotherapy for disease of limited stage.

Radiotherapy: Adjuvant for limited stage; adjuvant or palliative for extensive stage.

Chemotherapy: Curative (as single modality) or adjuvant for limited and extensive stage.

Non-small-cell lung cancer

Surgery: Curative (as single modality or in combination with adjuvant chemotherapy or radiotherapy) for stage I; curative (in combination with adjuvant radiotherapy and chemotherapy) for stages I-IIIA; curative (in combination) for stage IIIB.

Radiotherapy: Curative (as single modality) for stages I-II; curative or adjuvant for IIIA-IIIB; palliative for stage IV.

Chemotherapy: Adjuvant for stages I-IIIA; curative or adjuvant for stage IIIB; mainly palliative for stage IV.

Table 5.7.2 Comparison of main treatment modalities and combinations for patients with invasive lung cancer, Ireland and USA, in diagnosis period 1998-2001. US data were not specified in detail for some treatments, and may be based on slightly different definitions of lung cancer cell-type.

	non-small-cell lung cancer			small-cell lung cancer		
	Ireland 1998-2001		USA[a©] 1998-2001	Ireland 1998-2001		USA[a©] 1998-2001
any treatment	67.2%	***	80.9%	63.7%	***	81.6%
no treatment	32.8%	***	19.1%	36.3%	***	18.4%
any radiotherapy	41.8%	***	≥44.6%	30.7%	***	[c]≥45.4%
any chemotherapy	14.2%	***	≥32.5%	50.0%	***	≥69.9%
any surgery[b]	21.3%	***	32.5%	2.1%	**	≥4.4%
radiotherapy only	31.9%	***	18.6%	12.1%	***	6.1%
surgery only	17.2%	***	23.0%	1.3%	-	-
chemotherapy only	7.1%	***	9.9%	31.2%	ns	30.7%
chemo + radio	5.9%	***	19.2%	18.1%	***	39.2%
surgery + radio	3.0%	ns	3.4%	0.1%	-	-
surge + radio + chemo	0.3%	***	3.4%	0.2%	-	-
others	1.7%	-	3.3%	0.6%	-	5.5%

- = data not available or statistical comparison not possible.
[a]Source of US data: National Cancer Data Base of first-course treatments reported by hospitals approved by the American College of Surgeons Commission on Cancer; cases of stage 0 have been excluded but cases of unknown stage have been included and assumed to be invasive; see http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm.

[b]US surgical data are for surgery of primary site only.
(P<0.05), ** (P<0.01), *** (P<0.001): significant differences between Ireland and USA in proportion of patients treated (χ^2 tests, 1.d.f.).
[c]≥ indicates that overall use of these treatments among patients in the USA may be higher than shown, as figures less frequent single modalities or combinations of modalities are not quoted on the NCDB website.

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Chapter 6. PROSTATE CANCER

Summary

Trends in incidence, mortality and patient/tumour characteristics

Numbers of cases and age-standardized incidence rates showed very marked and significant upward trends, but no significant trends were evident in numbers of deaths or mortality rate.

Increases in the proportions of cases in younger men, and in overall recorded incidence, provided stronger evidence of trends towards earlier detection than did recorded changes in stage distribution or method of presentation of cases.

Survival

1994-2001 average

Relative survival to five years after diagnosis was estimated as 69.5% (95% CI 67.9-70.9%) nationally.

Survival trends

Five-year survival was 63.0% (95% CI 60.8-65.1%) for cases diagnosed during 1994-97 and 75.9% (73.7-77.9%) for 1998-2001 – a marked improvement in average recorded survival. Relative survival modelling confirmed significant improvements between diagnosis periods 1994-97 and 1998-2001. The improvement represented about a 40% reduction in the age-adjusted excess risk of death. Patients from seven of the eight regions showed also significant improvements in relative survival, equivalent to 30-51% reductions in the age-adjusted excess risk of death.

A substantial proportion of the improvements seen could involve lead-time bias, whereby earlier detection of cases extends recorded survival time, in addition to or even in the absence of any true survival benefit. Improvements in survival were seen in patients below age 75 but not in older patients. This age-discrepancy would be consistent with increasingly earlier diagnosis (e.g. through screening) among younger patients, in particular.

Regional variation in survival

Overall during 1994-2001, only one region (Southern) showed a significant excess mortality risk, compared with the Eastern region, after adjusting for patient and tumour characteristics. (Regional variation was much more marked in the basic, age-adjusted model.) However, regional disparities in survival were more obvious for the 1998-2001 diagnosis period. Then, patients from four regions had significantly higher excess risks: Mid-Western (54% higher than for Eastern region), North-Eastern (47% higher), Southern (35% higher) and Western region (39% higher). Possible changes in the coding or quality of explanatory variables may account for some of the apparent increase in 'unexplained' regional variation.

International comparison of survival

The five-year relative survival of Irish patients diagnosed during 1994-97 (63%) was similar to or slightly lower than the European average based on 1990-94 diagnoses.

Treatment

Proportions of patients treated: main modalities and combinations

77% of patients had some form of definitive or tumour-directed treatment within six months of diagnosis, 48% had surgical treatment, 37% had hormonal therapy and 8% had radiotherapy, overall for 1994-2001. Equivalent figures for 1998-2001 were 78% treated, 43% surgery, 41% hormonal therapy and 10% radiotherapy.

The most frequent treatments or combinations were surgery only (34% of cases 1994-2001), hormonal therapy only (22%), and surgery plus hormonal therapy (12%).

Region of treatment versus region of residence

For five of the eight regions, most patients resident in those regions had their main surgery in the same region (*Table 6.5.2*). The exceptions were the Midland, North-Eastern and South-Eastern regions, where, respectively, 60%, 78% and 48% of surgical cases were treated in the Eastern region, based on 1994-2001 diagnoses.

Hospital caseloads

Prostate cancer cases were surgically treated in a total of 47 hospitals in the Republic of Ireland during 1994-2001. There was no strong evidence of any trend in overall numbers of hospitals providing surgical treatment. Between one-third and half of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each; about two-thirds treated fewer than 20 surgical cases each in a given year and almost all treated fewer than 50 cases. There was a tendency for average hospital caseload to increase during the

period 1994-2001, with smaller proportions of surgical cases treated in 'low volume' hospitals.

Surgical consultant caseloads

At least 118 individual consultants were responsible for surgical managements of prostate cancers during 1994-2001, increasing from 75 in 1994-97 to 94 in 1998-2001. Half of the surgical consultants in any given year treated fewer than 10 surgical cases each; about three-quarters treated fewer than 20 cases in a year and almost all treated fewer than 50 cases. Average annual caseloads showed no obvious trend over time, but significant declines were seen in the proportions of surgical patients treated by 'low volume' consultants.

Treatment trends

National surgery usage fell significantly between 1996 and 2001, by about 9% annually in relative terms after adjustment for age and stage. Seven of the eight regions also showed significant age-adjusted reductions in surgery, by 4%-20% annually.

Use of radiotherapy increased significantly between 1996 and 2001, by about 16% annually (age- and stage-adjusted). Much of this increase appeared to be concentrated in three regions (North-Western, Southern and South-Eastern).

There was a small but significant increase in use of hormonal therapy between 1996 and 2001, by 3-4% per year at national scale. Significant increases were seen for patients from Midland and Southern regions, by 9%-20%, but a decrease for Western region.

Regional variation in treatment

During 1994-2001 as a whole, the use of surgery was significantly lower among patients in four regions (Midland, Southern and, most markedly, North-Western and Western), compared with the Eastern region, after adjustment for patient and tumour characteristics. But surgery use relative to the Eastern region differed significantly between periods for five regions. This involved a widening of regional variation in comparison with Eastern region in the more recent period.

Overall, there was significantly (and substantially) greater use of radiotherapy in patients from the Southern and Western regions, and lower use in patients from the North-Eastern region, compared with the Eastern region. But relative use of radiotherapy differed significantly between 1994-97 and 1998-2001 for three regions (North-Western, Southern and South-Eastern), in each instance reflecting an increase in radiotherapy use compared with the Eastern region.

Use of hormonal therapy was substantially lower for patients from the Eastern region, compared with all other regions, during 1994-2001. Hormonal use varied less in the more recent period, but variation was still substantial.

There were stronger indications for this cancer than for others considered in this report (breast, colorectal and lung cancers) that low usage of a given treatment modality in a region may have been balanced, to some extent, by higher use of another modality. For this cancer, treatment comparisons are also complicated by the lack of comprehensive data on the use of 'watchful waiting' as initial choice of therapy. If the use of watchful waiting has reflected regional or institutional factors, or varied over time within some or all regions, it is likely to have influenced the geographic and temporal patterns seen for other treatments.

International comparison of treatment

Irish patients were significantly less likely to receive treatment than in the USA. This largely involved significantly lower use of radiotherapy in Ireland. Overall use of surgery was similar in both populations.

6.1 Incidence and mortality statistics

On average, there were 1371 cases of and 519 deaths from invasive prostate cancer annually in Irish men during 1994-2001 (*Table 6.1.1*). Over this period, numbers of cases and age-standardized incidence rates showed very marked and significant upward trends, but no significant trends were evident in numbers of deaths or mortality rates.

Table 6.1.1 Incidence of and mortality from invasive prostate cancer, Republic of Ireland, 1994-2001.

	annual average numbers		age-standardized rate[a]	
1994-2001	**male**		**male**	
Incidence (cases)	1371		85.9	
Incidence trend (per year)[b]	+7.8%	***	+6.7%	***
Mortality (deaths)	519		32.7	
Mortality trend (per year)	+1.1%	ns	-0.2%	ns

[a]European age-standardized rate per 100,000 persons per year.
[b]Estimated annual percentage change (ns not significant, * P<0.05, **P<0.01, ***P<0.001).

6.2 Cases included for treatment and survival analyses; patient and tumour characteristics

Analyses cover invasive cancers of the prostate (ICD-10 code C61) diagnosed in 10,352 men aged 15-99 years during 1994-2001. Full details of exclusion/inclusion criteria are shown in *Table 6.2.1*.

Table 6.2.1 Summary of inclusions and exclusions for prostate cancer analyses.

Case definition	**total**
all registered tumours[a]	10,996
ages 15-99 only	10,994
excluding death-certificate-only & autopsy-only cases	10,656
invasive tumours only	10,634
first tumours[b]	**10,352**

[a] Including in situ carcinomas, and tumours of unspecified behaviour, but excluding lymphomas (classified separately within ICD-10).
[b] Or most serious tumour diagnosed same date.

A breakdown of basic patient and tumour characteristics is given in *Table 6.2.2*, including comparisons between diagnosis periods 1994-97 and 1998-2001. Note proportional changes in these variables do not always show the same trends as absolute numbers of cases (which have increased markedly overall). The variables and category-values shown are those considered, later in this chapter, for inclusion in statistical models aimed at describing and if possible explaining regional variation and time-trends in survival and treatment.

Statistically significant changes between 1994-97 and 1998-2001 in proportions of patients or tumours with particular characteristics involved:

- Increases in patients aged under 55 and 55-64, decreases in those 75-84 and 85+ at diagnosis.
- Decreases in stage I and stage IV cancers, increase in unknown stage.
- Decreases in tumours in T1 and T unknown categories, increases in T2 and T3.
- Decrease in node-positive cancers.
- Increases in cases without metastases and of unknown metastatic status, decrease in metastatic cases.
- Decreases in grade 1 and grade 3+ tumours, increase in grade 2.
- Increase in microscopically verified (MV) cases, decrease in non-MV cases.
- Decrease in symptomatic cases, increases in incidental and screen-detected cases and unknown method of presentation.
- Decrease in patients recorded as never married, increase in unknown marital status.
- Increase in patients with unknown smoking status.

At face value, increases in the proportions of cases in younger men, and in overall recorded incidence (*section 6.1*), provided stronger evidence of trends towards earlier detection than did other relevant variables. Expected changes over time in the stage distribution or method of presentation of cases are far from obvious, based on the data available. Notably, there were large increases for the T2 but not T1 category, and larger increases for cases whose method of presentation was unclear than for screen-detected or incidentally detected cases.

Variation in patient and tumour characteristics by region of residence is summarized in *Table 6.2.3*.

Table 6.2.2 Summary of patient and tumour characteristics for prostate cancer patients included in survival and treatment analyses, 1994-2001.

	diagnosed 1994-2001		diagnosed 1994-1997		diagnosed 1998-2001	
	number	% of cases	number	% of cases	number	% of cases
total	10352		4453		5899	
age 15-54	322	3.1%	104	2.3%	218	*3.7%
age 55-64	1696	16.4%	575	12.9%	1121	*19.0%
age 65-74	4082	39.4%	1715	38.5%	2367	40.1%
age 75-84	3473	33.5%	1686	37.9%	1787	*30.3%
age 85+[a]	779	7.5%	373	8.4%	406	*6.9%
stage I	102	1.0%	73	1.6%	29	*0.5%
stage II	377	3.6%	147	3.3%	230	3.9%
stage III	120	1.2%	51	1.1%	69	1.2%
stage IV	2099	20.3%	1090	24.5%	1009	*17.1%
stage X[b]	7654	73.9%	3092	69.4%	4562	*77.3%
T1	1466	14.2%	755	17.0%	711	*12.1%
T2	2643	25.5%	828	18.6%	1815	*30.8%
T3	766	7.4%	272	6.1%	494	*8.4%
T4	389	3.8%	181	4.1%	208	3.5%
T X	5088	49.1%	2417	54.3%	2671	*45.3%
N negative	1217	11.8%	511	11.5%	706	12.0%
N positive	173	1.7%	98	2.2%	75	*1.3%
N X	8962	86.6%	3844	86.3%	5118	86.8%
M negative	2780	26.9%	1133	25.4%	1647	*27.9%
M positive	1803	17.4%	941	21.1%	862	*14.6%
M X	5769	55.7%	2379	53.4%	3390	*57.5%
grade 1	1662	16.1%	932	20.9%	730	*12.4%
grade 2	3777	36.5%	1312	29.5%	2465	*41.8%
grade 3+	2387	23.1%	1093	24.5%	1294	*21.9%
grade X	2526	24.4%	1116	25.1%	1410	23.9%
MV[c] yes	9012	87.1%	3790	85.1%	5222	*88.5%
MV no	1254	12.1%	626	14.1%	628	*10.6%
MV X	86	0.8%	37	0.8%	49	0.8%
symptomatic	8347	80.6%	3932	88.3%	4415	*74.8%
incidental	776	7.5%	275	6.2%	501	*8.5%
screen detected	108	1.0%	25	0.6%	83	*1.4%
presentation X	1121	10.8%	221	5.0%	900	*15.3%
non-smoker	3584	34.6%	1618	36.3%	1966	*33.3%
ex-smoker	1781	17.2%	828	18.6%	953	*16.2%
smoker	2013	19.4%	1009	22.7%	1004	*17.0%
smoking X	2974	28.7%	998	22.4%	1976	*33.5%
ever married	8232	79.5%	3528	79.2%	4704	79.7%
never married	1652	16.0%	755	17.0%	897	*15.2%
marital status X	468	4.5%	170	3.8%	298	*5.1%

[a]Age-groups used for this cancer differ from those for other cancers in this report. [b]Unknown values shown as "X" for stage and other variables. [c]MV = microscopic verification (histology or cytology).

*Significant change in the proportion of cases in this category (χ^2 test, 1 df, $P<0.05$); but note that some further changes may be significant if cases in "unknown" categories are excluded.

Table 6.2.3 Summary of patient and tumour characteristics, by region of residence, for prostate cancer patients included in survival and treatment analyses, 1994-2001. Account is taken of the potential confounding affect of these variables in statistical models of regional variation in survival (*section 6.4.4*) and treatment (*section 6.6.3*).

	Eastern	Mid-Western	Midland	North-Eastern	North-Western	Southern	South-Eastern	Western
total cases	3103	645	805	833	794	1730	1275	1167
age 15-54	3.8%	*2.2%	2.7%	2.9%	2.5%	2.8%	3.4%	2.7%
age 55-64	20.0%	*14.0%	*15.7%	*14.2%	*11.7%	*16.2%	*15.6%	*14.3%
age 65-74	40.5%	37.8%	42.0%	43.2%	36.8%	38.0%	39.9%	*36.4%
age 75-84	28.2%	*37.8%	*33.7%	*33.1%	*39.0%	*36.1%	*32.7%	*39.1%
age 85+	7.4%	8.2%	6.0%	6.6%	*9.9%	6.9%	8.4%	7.5%
stage I	0.4%	0.8%	*1.5%	0.4%	*1.0%	*1.8%	*2.0%	0.5%
stage II	3.0%	3.3%	3.4%	3.6%	2.6%	*6.0%	*6.1%	*0.3%
stage III	1.3%	1.2%	0.6%	0.8%	1.5%	1.3%	1.3%	0.6%
stage IV	19.4%	*25.6%	18.0%	20.6%	20.2%	19.3%	20.1%	*22.7%
stage X	76.0%	*69.1%	76.5%	74.5%	74.7%	*71.5%	*70.5%	75.8%
T1	10.8%	*17.4%	*21.7%	8.5%	*5.3%	*21.7%	*15.9%	*13.2%
T2	20.9%	23.1%	*31.1%	*29.9%	*9.6%	*38.8%	*29.0%	19.5%
T3	9.6%	*6.4%	*3.1%	*12.2%	*5.5%	*6.4%	*7.1%	*4.5%
T4	4.2%	*6.0%	3.2%	4.4%	4.3%	*2.5%	3.5%	3.0%
T X	54.5%	*47.1%	*40.9%	*44.9%	*75.3%	*30.5%	*44.4%	*59.8%
N negative	11.2%	9.6%	9.1%	11.4%	*7.3%	*13.3%	*22.7%	*5.1%
N positive	1.6%	2.2%	2.2%	1.4%	2.5%	1.4%	1.4%	1.3%
N X	87.1%	88.2%	88.7%	87.2%	*90.2%	85.3%	*75.8%	*93.6%
M negative	30.6%	28.8%	*20.1%	*25.0%	28.1%	*25.7%	30.5%	*18.9%
M positive	16.5%	*21.7%	14.5%	17.4%	17.1%	17.5%	16.9%	*20.2%
M X	52.9%	49.5%	*65.3%	*57.6%	54.8%	*56.9%	52.6%	*60.9%
grade 1	13.6%	*19.7%	*22.2%	*18.8%	*8.6%	*16.9%	*18.8%	15.1%
grade 2	46.0%	*33.6%	*24.8%	*33.4%	*24.9%	*36.2%	*37.6%	*30.2%
grade 3+	24.1%	24.7%	*15.0%	22.8%	*17.4%	*26.8%	23.1%	23.3%
grade X	16.3%	*22.0%	*37.9%	*25.0%	*49.1%	*20.1%	*20.5%	*31.4%
MV yes	93.9%	*87.6%	*75.5%	*85.4%	*79.5%	*86.1%	*86.0%	*85.4%
MV no	4.9%	*11.8%	*22.6%	*13.8%	*20.4%	*13.7%	*12.9%	*14.1%
MV X	1.2%	0.6%	1.9%	0.8%	*0.1%	*0.2%	1.1%	0.5%
symptomatic	73.9%	*85.6%	*85.0%	*84.2%	*91.7%	*81.3%	*84.4%	*77.6%
incidental	8.0%	*4.7%	*4.5%	*5.3%	*3.7%	*16.2%	*5.0%	*3.9%
screen detected	1.2%	0.6%	0.5%	*0.1%	1.8%	1.3%	1.3%	0.7%
presentation X	16.9%	*9.1%	*10.1%	*10.4%	*2.9%	*1.2%	*9.3%	17.8%
non-smoker	28.5%	*33.8%	*38.5%	31.2%	27.8%	*47.7%	*36.6%	*34.1%
ex-smoker	18.7%	15.7%	16.0%	*22.2%	*23.7%	*9.7%	*15.2%	20.1%
smoker	16.1%	18.8%	*24.7%	*20.2%	*23.9%	*18.7%	*19.4%	*22.6%
smoking status X	36.6%	*31.8%	*20.7%	*26.4%	*24.6%	*23.9%	*28.8%	*23.1%
ever married	85.6%	*76.0%	*76.8%	*78.3%	*73.6%	*79.2%	*79.8%	*72.3%
never married	9.7%	*19.7%	*17.1%	*18.2%	*25.4%	*15.8%	*16.8%	*20.9%
marital status X	4.7%	4.3%	6.1%	3.5%	*1.0%	5.0%	3.5%	*6.8%

*Significant difference in proportion of cases, compared with Eastern region (χ^2 test, 1 df, $P<0.05$)

6.3 Relative survival: descriptive analysis

Five-year relative survival estimates for national population, by period of diagnosis, age and other patient or tumour characteristics, are shown in *Table 6.3.1*. Survival curves, to five years after diagnosis, are plotted for the same variables in *Figure 6.3.1*. Five-year survival estimates by treatment status are shown in *Table 6.3.2*; and one-year, three-year and five-year estimates, nationally and regionally by diagnosis period, in *Table 6.3.3*.

Results and comparisons presented in this section are not adjusted for potential confounding variables, thus are potentially open to misinterpretation if taken at face value. More formal (multivariate) comparisons are made in *section 6.4*.

6.3.1 General summary

For prostate cancers diagnosed in Irish men during 1994-2001 as a whole, relative survival to five years after diagnosis was estimated as 69.5% (95% CI 67.9-70.9%) (*Table 6.3.1*). Relative survival to one year averaged 89.1% (88.2-89.7%), and to three years 76.2% (75.0-77.3%) (*Table 6.3.3*).

6.3.2 Variation by patient and tumour characteristics

Relative survival (to five years) was highest for patients aged 55-64 years, or, for other specific variables, cases that were stages I-II or unknown stage; T categories 1-3; node-negative; non-metastatic; microscopically verified; or screen-detected or with method of presentation unknown; and patients who were non-smokers, ever married or of unknown smoking or marital status (*Table 6.3.1*, *Figure 6.3.1*). The very high relative survival (*c*.100%) for stage III cases may be an artifact, if fully-staged cases are a highly selected group for this cancer. Survival was lowest among women in the oldest age-groups (75+), and for cases that were grade 3+ or unknown; stage IV; T category 4; node-positive; metastatic; lacking microscopic verification; symptomatic; and among smokers or patients who were never married. Note however that patients in a given univariate category may differ with respect to other characteristics - see section *6.4.1* for multivariate comparisons.

6.3.3 Variation by treatment status

Patients who received any tumour-directed treatment, surgery or radiotherapy within six months of diagnosis had slightly or moderately higher five-year survival than patients who did not receive these treatments: averaging 70% v 67% for treatment v no treatment, 76% v 63% for surgery v no surgery, and 75% v 69% for radiotherapy v no radiotherapy for 1994-2001 as a whole (*Table 6.3.2*). This was reversed for patients having hormonal therapy, 56% v 77% for treated v not treated. These patterns were consistent between diagnosis periods for surgery and hormonal therapy, but not for radiotherapy or overall treatment. It should be noted that patients given or not given particular treatments may have differed greatly in disease stage or other characteristics. Thus these figures do not provide any useful measure of treatment effectiveness

6.3.4 National and regional trends

National estimates of five-year survival were 63.0% (95% CI 60.8-65.1%) for cases diagnosed during 1994-97 and 75.9% (73.7-77.9%) for 1998-2001 (*Table 6.3.1, Figure 6.3.1*) – a marked improvement in average recorded survival. Similar improvements in survival were apparent for all regions of residence (*Table 6.3.3*). See sections *6.4.2-3* for more formal comparisons, adjusted for age or other factors.

6.3.5 Regional variation

Five-year relative survival estimates during 1994-2001 ranged from 62.3% (95% CI 56.9-67.5%) for patients from the Mid-Western region to 77.4% (74.7-79.9%) for the Eastern region (*Table 6.3.3*). See *section 6.4.4* for more formal comparisons.

Table 6.3.1 National five-year relative survival for prostate cancer patients, by patient and tumour characteristics, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population.

	1994-2001		1994-1997		1998-2001	
	5-yr survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	69.5%	(67.9%-70.9%)	63.0%	(60.8%-65.1%)	*75.9%	(73.7%-77.9%)
age 15-54	73.1%	(66.4%-78.7%)	64.6%	(54.2%-73.4%)	80.6%	(72.0%-87.1%)
age 55-64	79.8%	(77.0%-82.3%)	70.5%	(66.0%-74.6%)	*86.9%	(83.3%-90.0%)
age 65-74	73.8%	(71.6%-75.8%)	64.8%	(61.7%-67.7%)	*82.7%	(79.7%-85.5%)
age 75-84	62.1%	(59.0%-65.1%)	61.0%	(56.9%-65.0%)	62.8%	(57.9%-67.6%)
age 85+[a]	55.2%	(46.1%-64.8%)	54.5%	(42.5%-67.7%)	55.9%	(42.3%-71.0%)
grade 1	90.7%	(87.2%-93.8%)	87.4%	(82.8%-91.6%)	*97.3%	(92.0%-101%)
grade 2	83.8%	(81.3%-86.1%)	75.1%	(71.3%-78.8%)	*90.1%	(86.8%-93.1%)
grade 3+	53.9%	(50.8%-57.0%)	48.6%	(44.5%-52.6%)	*59.8%	(55.1%-64.4%)
grade X	47.7%	(44.6%-50.7%)	41.6%	(37.5%-45.7%)	*53.3%	(48.7%-57.7%)
stage I	75.9%	(60.7%-89.3%)	70.9%	(54.1%-85.9%)	92.2%	(52.7%-117%)
stage II	90.0%	(83.4%-95.5%)	91.7%	(81.7%-99.6%)	89.8%	(80.6%-96.8%)
stage III	100.8%	(89.8%-107%)	97.4%	(79.9%-108%)	106.2%	(91.0%-110%)
stage IV	25.7%	(23.2%-28.2%)	23.9%	(20.8%-27.1%)	27.9%	(23.7%-32.1%)
stage X[b]	80.1%	(78.3%-81.8%)	74.7%	(72.1%-77.2%)	*85.6%	(83.1%-87.9%)
T1	82.8%	(79.0%-86.4%)	76.2%	(70.9%-81.1%)	*91.7%	(86.0%-96.7%)
T2	79.0%	(76.0%-81.7%)	72.6%	(67.8%-77.1%)	*82.2%	(78.2%-85.8%)
T3	78.7%	(73.6%-83.4%)	69.6%	(61.7%-77.0%)	*85.9%	(79.1%-91.7%)
T4	31.2%	(25.3%-37.5%)	28.0%	(20.4%-36.3%)	33.1%	(24.1%-42.8%)
T X	62.2%	(59.9%-64.3%)	57.3%	(54.4%-60.2%)	*68.9%	(65.5%-72.2%)
N negative	87.8%	(84.1%-91.1%)	82.9%	(77.2%-88.0%)	*93.3%	(88.4%-97.3%)
N positive	43.7%	(34.3%-53.0%)	43.7%	(32.4%-54.9%)	46.7%	(28.6%-64.2%)
N X	67.4%	(65.7%-69.0%)	60.8%	(58.4%-63.0%)	73.8%	(71.3%-76.1%)
M negative	86.5%	(83.7%-89.1%)	82.2%	(78.1%-85.9%)	*91.8%	(87.8%-95.3%)
M positive	21.5%	(19.0%-24.1%)	20.0%	(16.9%-23.3%)	23.1%	(18.9%-27.6%)
M X	76.4%	(74.3%-78.3%)	70.8%	(67.7%-73.7%)	*81.9%	(79.0%-84.6%)
MV yes	75.6%	(74.0%-77.2%)	69.2%	(66.8%-71.4%)	*82.1%	(79.8%-84.2%)
MV no	24.6%	(21.0%-28.4%)	24.6%	(20.0%-29.6%)	25.0%	(19.2%-31.4%)
MV X	43.8%	(28.1%-60.9%)	45.9%	(23.9%-70.9%)	36.7%	(16.3%-61.9%)
symptomatic	66.2%	(64.5%-67.8%)	61.3%	(59.0%-63.5%)	*71.9%	(69.4%-74.3%)
incidental	79.0%	(73.3%-84.3%)	66.8%	(58.1%-75.2%)	*88.9%	(81.1%-95.4%)
screen detected	93.8%	(75.7%-106%)	102.2%	(69.2%-124%)	92.3%	(71.3%-104%)
presentation X	87.7%	(83.1%-91.9%)	83.7%	(74.0%-92.6%)	88.3%	(82.5%-93.3%)
non-smoker	73.4%	(70.8%-75.9%)	67.1%	(63.6%-70.5%)	*80.0%	(76.2%-83.6%)
ex-smoker	62.0%	(58.3%-65.5%)	58.1%	(53.2%-62.9%)	65.3%	(59.6%-70.7%)
smoker	57.3%	(54.0%-60.6%)	53.7%	(49.3%-58.0%)	*63.4%	(58.2%-68.3%)
smoking X	77.9%	(75.0%-80.5%)	69.8%	(65.2%-74.1%)	*83.5%	(79.9%-86.9%)
ever married	71.7%	(70.0%-73.3%)	65.3%	(62.9%-67.6%)	*78.3%	(75.9%-80.6%)
never married	56.5%	(52.7%-60.2%)	51.3%	(46.3%-56.3%)	62.1%	(56.2%-67.8%)
marital status X	75.1%	(67.6%-82.0%)	67.3%	(55.8%-78.2%)	78.2%	(67.4%-87.7%)

[a]Age-groups used for this cancer differ from those for other cancers in this report.
[b]Unknown values shown as "X" for stage, T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

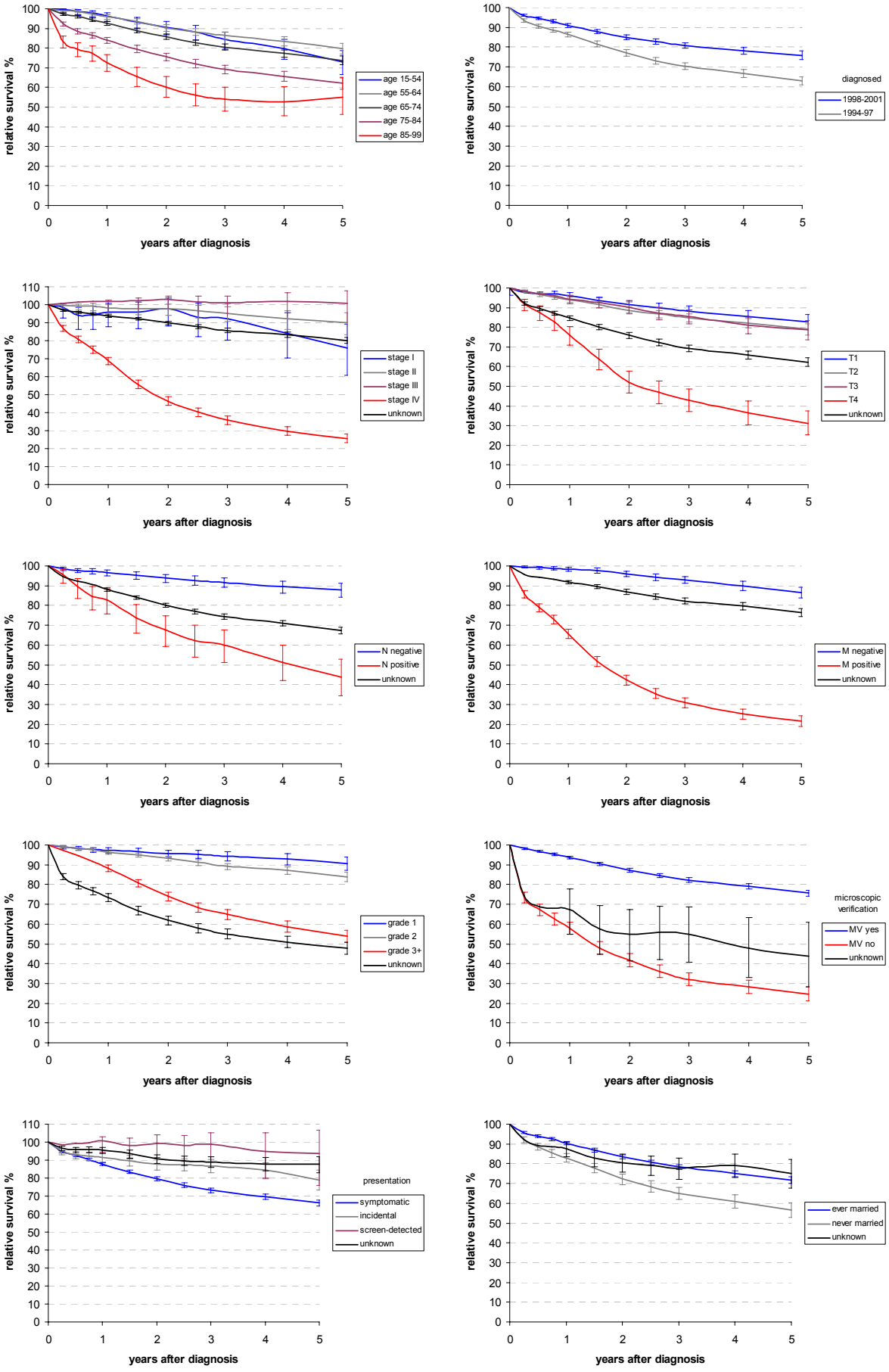

Figure 6.3.1 Relative survival up to five years after diagnosis for prostate cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown.

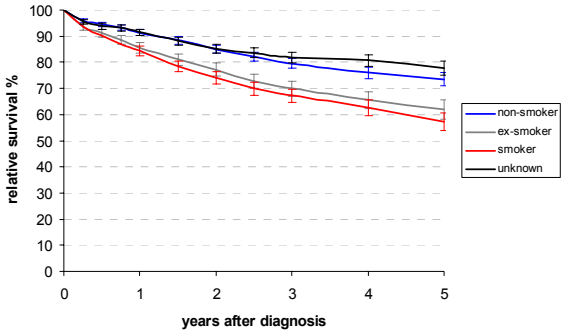

Figure 6.3.1 (continued)

Table 6.3.2 National five-year relative survival for prostate cancer patients, by treatment status (within six months of diagnosis) and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population. Patients treated and not treated are likely to differ markedly in disease stage, age or other characteristics, thus *differences in survival between treated and untreated patients below should not be interpreted as reflecting the effect of treatment*.

	1994-2001		1994-1997		1998-2001	
	survival	**(95% CI)**	**survival**	**(95% CI)**	**survival**	**(95% CI)**
total	69.5%	(67.9%-70.9%)	63.0%	(60.8%-65.1%)	*75.9%	(73.7%-77.9%)
treatment	70.1%	(68.3%-71.7%)	64.3%	(61.9%-66.7%)	*75.9%	(73.4%-78.2%)
no treatment	67.5%	(64.3%-70.6%)	59.0%	(54.6%-63.4%)	*76.1%	(71.4%-80.5%)
surgery	76.0%	(73.9%-78.1%)	71.4%	(68.5%-74.2%)	*82.2%	(79.0%-85.2%)
no surgery	63.4%	(61.2%-65.4%)	53.2%	(50.1%-56.2%)	*70.9%	(67.9%-73.8%)
radiotherapy	75.2%	(70.5%-79.5%)	52.9%	(45.1%-60.4%)	*87.1%	(81.8%-91.6%)
no radiotherapy	69.0%	(67.4%-70.6%)	63.6%	(61.3%-65.7%)	*74.8%	(72.4%-77.0%)
hormone therapy	56.5%	(53.9%-58.9%)	48.3%	(44.6%-51.9%)	*62.4%	(58.8%-65.9%)
no hormone	76.8%	(74.9%-78.5%)	69.8%	(67.2%-72.3%)	*85.0%	(82.3%-87.5%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs.

Table 6.3.3 One-year, three-year and five-year relative survival for prostate cancer patients, unadjusted for age, by region of residence and period of diagnosis, 1994-2001. Relative survival is the survival of cancer patients as a percentage of the expected survival of persons of the same age and sex in the general population (from the same region for regional estimates).

Region	1994-2001		1994-97		1998-2001	
	1-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	89.1%	(88.2%-89.7%)	86.5%	(85.1%-87.6%)	*91.0%	(90.0%-91.8%)
E	91.9%	(90.6%-93.1%)	89.6%	(87.3%-91.6%)	*93.7%	(92.0%-95.0%)
M	87.5%	(84.0%-90.4%)	82.7%	(76.6%-87.6%)	90.8%	(86.5%-94.2%)
MW	89.8%	(86.9%-92.2%)	88.0%	(83.5%-91.6%)	91.5%	(87.5%-94.5%)
NE	86.8%	(83.8%-89.4%)	84.2%	(79.2%-88.3%)	88.9%	(85.1%-92.0%)
NW	86.2%	(83.0%-88.9%)	81.3%	(75.6%-86.1%)	89.2%	(85.3%-92.4%)
S	87.0%	(84.9%-88.8%)	84.9%	(81.4%-87.9%)	88.5%	(85.8%-90.7%)
SE	89.0%	(86.7%-91.0%)	87.6%	(83.9%-90.8%)	90.1%	(87.1%-92.6%)
W	88.9%	(86.4%-91.0%)	85.3%	(81.3%-88.7%)	*91.9%	(88.8%-94.4%)
	1994-2001		1994-97		1998-2001	
	3-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	76.2%	(75.0%-77.3%)	70.3%	(68.5%-72.1%)	*80.8%	(79.3%-82.1%)
E	82.1%	(80.0%-83.9%)	76.5%	(73.2%-79.6%)	*86.2%	(83.7%-88.5%)
M	72.8%	(67.9%-77.4%)	63.9%	(56.1%-71.2%)	*79.3%	(73.0%-84.9%)
MW	73.2%	(69.0%-77.2%)	68.8%	(62.5%-74.6%)	77.5%	(71.6%-82.8%)
NE	75.3%	(71.2%-79.2%)	68.9%	(62.4%-74.9%)	*80.7%	(75.4%-85.4%)
NW	71.8%	(67.3%-75.9%)	65.8%	(58.5%-72.5%)	75.6%	(70.0%-80.7%)
S	74.7%	(71.8%-77.4%)	67.2%	(62.4%-71.6%)	*80.0%	(76.3%-83.4%)
SE	75.4%	(72.0%-78.5%)	70.7%	(65.5%-75.6%)	79.2%	(74.9%-83.1%)
W	72.6%	(68.9%-76.0%)	67.0%	(61.5%-72.2%)	*77.5%	(72.6%-81.9%)
	1994-2001		1994-97		1998-2001	
	5-yr survival	(95% CI)	survival	(95% CI)	survival	(95% CI)
total	69.5%	(67.9%-70.9%)	63.0%	(60.8%-65.1%)	*75.9%	(73.7%-77.9%)
E	77.4%	(74.7%-79.9%)	70.8%	(66.9%-74.6%)	*84.1%	(80.4%-87.5%)
M	63.5%	(57.1%-69.7%)	53.1%	(44.5%-61.7%)	*72.3%	(62.8%-81.2%)
MW	62.3%	(56.9%-67.5%)	56.9%	(49.9%-63.8%)	70.2%	(61.6%-78.2%)
NE	67.3%	(61.9%-72.5%)	61.0%	(53.6%-68.1%)	74.1%	(66.1%-81.4%)
NW	64.5%	(58.8%-70.0%)	58.2%	(50.1%-66.2%)	68.1%	(59.4%-76.3%)
S	67.8%	(63.9%-71.5%)	59.3%	(53.9%-64.6%)	*75.7%	(70.1%-80.8%)
SE	69.0%	(64.8%-73.1%)	65.2%	(59.1%-70.9%)	72.3%	(66.0%-78.2%)
W	66.4%	(61.8%-70.8%)	60.3%	(54.1%-66.4%)	*73.7%	(66.9%-80.0%)

*Significant changes (improvements) in survival between diagnosis periods, unadjusted for age, based on non-overlap of 95% CIs; some other changes may also be significant.

6.4 Relative survival: modelling

6.4.1 Variation by patient and tumour characteristics

For assessment of regional variation in relative survival during 1994-2001, a full relative survival model was run, potentially incorporating and adjusting for available patient and tumour characteristics. These included year of follow-up (years 1 to 5 after diagnosis), age-group, M category and grade, interaction between those variables and year of follow-up, and additional patient and tumour variables without interaction terms (T and N categories, microscopic verification status, method of presentation, marital status, smoking status, year of diagnosis). Excluding region and year (covered later), and variables that did not contribute significantly to model-fit, statistically significant excess hazard ratios (EHRs) were recorded as follows:

- During year 1 of follow-up (for variables assessed using an interaction term for follow-up year):
  - Higher EHR (lower relative survival) for age-groups, 65-74 (1.841 [95% CI 1.027-3.301]), 75-84 (2.931 [1.641-5.235]) and 85+ (3.704 [2.029-6.761]), compared with age-group 15-54 years.
  - Higher EHR for M positive (8.511 [5.5581-13.03]) and M unknown cases (2.897 [1.887-4.446], compared with M negative cases.
  - Higher EHR for grade 3+ (2.549 [1.688-3.849] and grade unknown cases (2.874 [1.898-4.354]), compared with grade 1.
- For age, M category and grade, EHRs varied significantly during subsequent follow-up and cannot readily be summarized beyond year 1.
- Overall (for variables assessed without an interaction term for follow-up year):
  - Higher EHR for T categories 4 (2.147 [95% CI 1.688-2.730]) and unknown or non-applicable (1.329 [1.095-1.613]), compared with T category 1.
  - Higher EHR for N positive (1.934 [1.374-2.722]) and N unknown cases (1.588 [1.239-2.035]), compared with N negative cases.
  - Higher HER for cases lacking microscopic verification (2.387 [2.013-2.831]) or of unknown MV status (3.099 [2.073-4.631]), compared with microscopically verified cases.
  - Lower EHR (higher relative survival) for cases that presented incidentally (0.785 [0.623-0.988]) or whose method of presentation was unknown (0.672 [0.529-0.852]), compared with cases presenting symptomatically.
  - Higher EHR for ex-smokers ([1.545 [1.352-1.765]) and current smokers (1.502 [1.326-1.702]), compared with non-smokers (never-smokers).
  - Higher EHR for patients who were never married (1.286 [1.149-1.440]), compared with those who were ever married.

These findings are in general consistent with the variations already noted for unadjusted relative survival (*Table 6.3.1*), for the overall period 1994-2001. However, unadjusted relative survival was significantly low cases that were grade 2 (compared with grad 1), and significantly high for screen-detected cases (compared with symptomatic cases), differences that were not significant after adjustment for other patient and tumour characteristics.

6.4.2 National and age-specific trends

Relative survival improved significantly (i.e. excess hazard ratios fell significantly) between diagnosis periods 1994-97 and 1998-2001. The improvement represented about a 40% reduction in the age-adjusted excess risk of death (*Table 6.4.1*). A similar reduction was seen after full adjustment for other patient and tumour characteristics, including grade and other stage-related variables. Less complete adjustment, for age and stage-related variables only, appeared to reduce the magnitude of the reduction.

However, improvement was largely confined to patients below 75 years of age, with a 48-59% reduction in excess risk for age-groups 15-54 to 65-74 and no significant reduction for older patients (unadjusted models, *Table 6.4.1*).

6.4.3 Regional trends

Patients from seven of the eight regions showed significant improvements in relative survival between 1994-97 and 1998-2001, equivalent to 30-51% reductions in the age-adjusted excess risk of death (*Table 6.4.1*).

6.6.4 Regional variation

For 1994-2001 as a whole, the age-adjusted excess risk of death was significantly higher (by 35-69%), thus relative survival was lower, in patients from all regions other than the Eastern region (*Table 6.4.2*). The pattern was similar for diagnosis periods 1994-97 and 1998-2001, with only the South-Eastern region (in 1994-97) not differing significantly from the Eastern region.

After adjustment for stage-related variables (including grade for this cancer), regional variations were reduced substantially, with only three regions having a significantly higher excess risk compared with the Eastern region for 1994-

2001. In fact, for patients diagnosed during 1994-97 only one region (Southern) showed a significant excess risk after stage-adjustment, whereas for patients diagnosed during 1998-2001 excess risks were seen for five regions.

Fuller adjustment, for age, stage-related and other variables further reduced the amount, and also the magnitude, of regional variation in relative excess risk. Only patients from the Southern region now showed an excess risk (25% higher than for the Eastern region) based on 1994-2001, or (23% higher) based on 1994-97 diagnoses. Patients from the Western region, diagnosed during 1994-97, in fact had a significantly (27%) lower excess risk compare with the Eastern region. But disparities were again more obvious for the 1998-2001 diagnosis period. In particular, patients from four regions had significantly higher excess risks: Mid-Western (54% higher than for the Eastern region), North-Eastern (47% higher), Southern (35% higher) and Western region (39% higher).

There was some evidence that regional variations in stage or other variables, or in the completeness of information on these variables, better 'explained' regional survival disparities for patients diagnosed during earlier years (1994-97).

Table 6.4.1 Changes in relative survival between diagnosis-years 1994-97 and 1998-2001, stratified by age and region of residence, for patients diagnosed with prostate cancer during 1994-2001. Excess hazard ratios in bold = significant difference from baseline (1994-1997). (EHR <1 = reduction in excess hazard thus improvement in relative survival, EHR >1 = increase in excess hazard thus reduction in relative survival). Only the basic model is shown for individual regions as regional sample sizes are generally too small too allow complex modelling.

	1998-2001 v 1994-97 [a]EHR (95% CI)	P
basic model: age-specific		
age 15-54	**0.517** (0.311-0.860)	0.011
age 55-64	**0.413** (0.311-0.548)	0.000
age 65-74	**0.456** (0.380-0.546)	0.000
age 75-84	0.863 (0.729-1.020)	0.086
age 85+	0.977 (0.708-1.347)	0.888
basic model: age- adjusted[b]		
total	**0.614** (0.552-0.683)	0.000
E	**0.575** (0.454-0.728)	0.000
M	**0.486** (0.335-0.706)	0.000
MW	**0.690** (0.493-0.964)	0.030
NE	**0.697** (0.492-0.987)	0.042
NW	**0.588** (0.411-0.842)	0.004
S	**0.639** (0.503-0.811)	0.000
SE	0.760 (0.566-1.019)	0.068
W	**0.604** (0.445-0.819)	0.001
fuller model: sex-, age-, stage-adjusted[b]		
total	**0.730** (0.664-0.804)	0.000
final multivariate model[b]		
total	**0.584** (0.475-0.718)	0.000

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]See *Table 6.4.2* but region and diagnosis year excluded here.

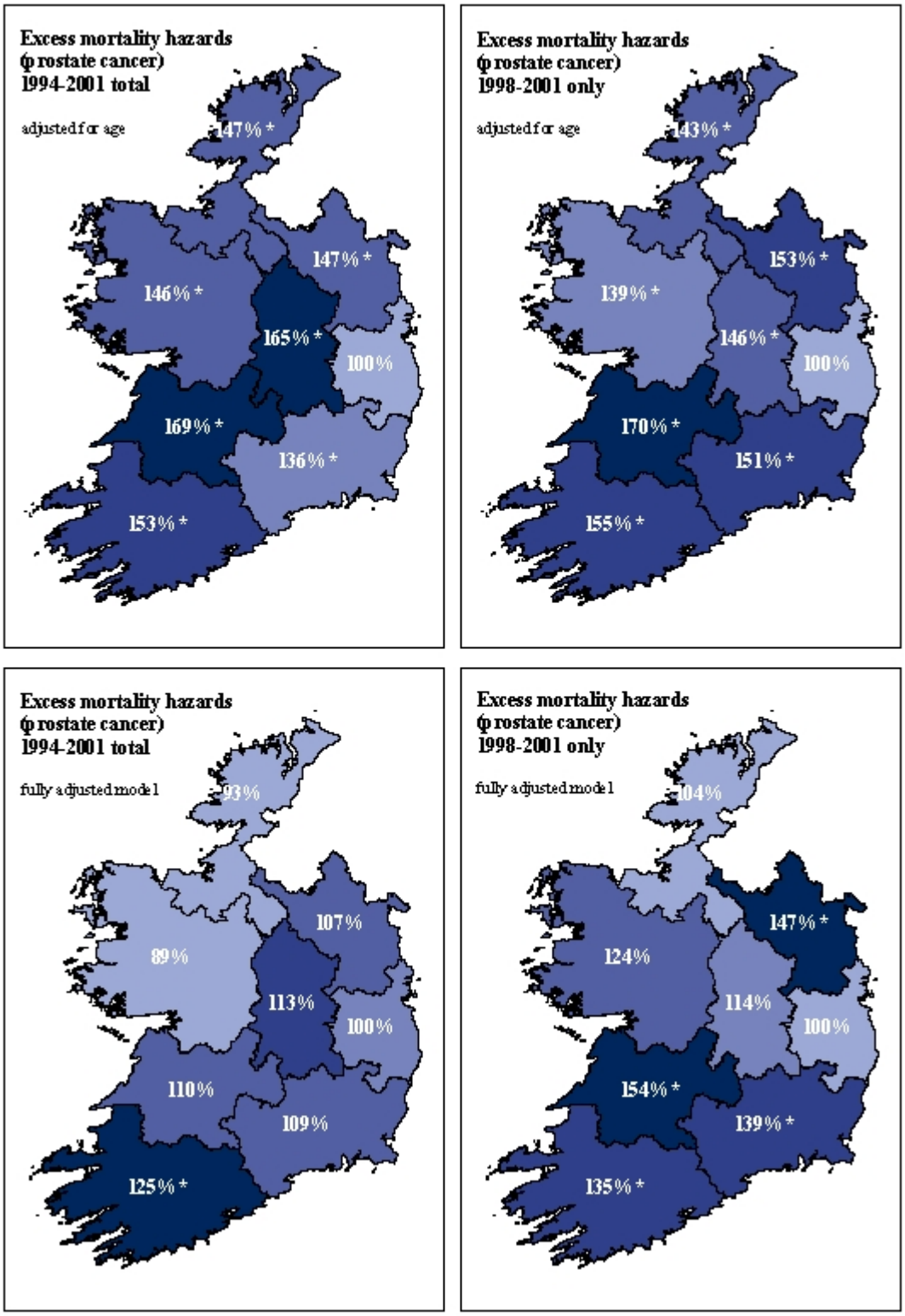

Figure 6.4.1 Regional variation in excess mortality hazards (based on relative survival) for prostate cancer, expressed in comparison with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom).
See *Table 6.4.2* for further details. * = significantly high or low excess risk (P<0.05).

Table 6.4.2 Variation in relative survival, by region of residence, for patients diagnosed with prostate cancer during 1994-2001. Analysis is based on survival up to five years from diagnosis. Excess hazard ratios in bold = significant difference from Eastern region (EHR <1 = lower excess hazard thus higher relative survival than in Eastern region, EHR >1 = higher excess hazard thus lower relative survival).

	1994-2001		1994-1997		1998-2001	
	[a]EHR (95% CI)	P	EHR (95% CI)	P	EHR (95% CI)	P
basic model: age-adjusted[b,c]						
E	1.000		1.000		1.000	
M	**1.646** (1.329-2.040)	0.000	**1.826** (1.391-2.396)	0.000	**1.463** (1.042-2.054)	0.028
MW	**1.690** (1.391-2.053)	0.000	**1.567** (1.227-2.000)	0.000	**1.700** (1.239-2.333)	0.001
NE	**1.470** (1.196-1.807)	0.000	**1.396** (1.068-1.825)	0.014	**1.530** (1.115-2.099)	0.008
NW	**1.470** (1.194-1.811)	0.000	**1.565** (1.189-2.060)	0.001	**1.434** (1.048-1.962)	0.024
S	**1.529** (1.301-1.798)	0.000	**1.540** (1.251-1.897)	0.000	**1.548** (1.207-1.987)	0.001
SE	**1.356** (1.130-1.627)	0.001	1.207 (0.946-1.539)	0.129	**1.512** (1.152-1.986)	0.003
W	**1.455** (1.211-1.749)	0.000	**1.452** (1.153-1.829)	0.002	**1.393** (1.037-1.871)	0.027
fuller model: age-, stage-adjusted[b,c,d]						
E	1.000		1.000		1.000	
M	1.221 (0.998-1.494)	0.051	1.198 (0.919-1.560)	0.180	1.212 (0.882-1.666)	0.234
MW	**1.421** (1.178-1.712)	0.000	1.150 (0.902-1.465)	0.258	**1.836** (1.373-2.454)	0.000
NE	**1.267** (1.051-1.528)	0.013	0.944 (0.734-1.216)	0.659	**1.708** (1.290-2.262)	0.000
NW	0.991 (0.816-1.204)	0.932	1.018 (0.787-1.318)	0.887	1.002 (0.749-1.341)	0.986
S	**1.380** (1.190-1.599)	0.000	**1.352** (1.108-1.650)	0.003	**1.489** (1.196-1.855)	0.000
SE	**1.286** (1.089-1.517)	0.003	1.032 (0.827-1.287)	0.777	**1.588** (1.234-2.044)	0.000
W	1.024 (0.866-1.210)	0.778	0.822 (0.659-1.025)	0.083	**1.301** (1.006-1.683)	0.044
final multivariate model[b,e]						
E	1.000		1.000		1.000	
M	1.128 (0.923-1.377)	0.236	1.098 (0.843-1.429)	0.486	1.139 (0.827-1.569)	0.423
MW	1.104 (0.913-1.335)	0.304	0.934 (0.728-1.198)	0.591	**1.544** (1.152-2.069)	0.004
NE	1.072 (0.889-1.292)	0.464	0.845 (0.655-1.090)	0.197	**1.472** (1.111-1.949)	0.007
NW	0.934 (0.772-1.129)	0.483	0.869 (0.670-1.126)	0.290	1.038 (0.777-1.386)	0.798
S	**1.248** (1.073-1.450)	0.004	**1.231** (1.003-1.511)	0.046	**1.350** (1.075-1.696)	0.010
SE	1.086 (0.919-1.284)	0.330	0.921 (0.738-1.151)	0.474	**1.387** (1.072-1.794)	0.013
W	0.894 (0.755-1.057)	0.191	**0.725** (0.580-0.908)	0.005	1.239 (0.958-1.604)	0.102

[a]EHR = excess hazard ratio (or "relative excess risk") estimated by a generalized linear model (GLM) with a Poisson error structure, fitted to exact survival times and collapsed observations.
[b]Models included interaction terms between follow-up interval (years 1-5) and age (plus M category and grade in fuller and final models), equivalent to stratification by these variables, to allow for non-proportional hazards across follow-up time.
[c]Age-categories (specific to for prostate cancer): EUROCARE age-groups 15-54, 55-64, 65-74, 75-84, 85+.
[d]Stage-related variables: T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown; and (for prostate cancer only) tumour grade 1, 2, 3+, unknown.
[e]Final (full) multivariate model, also including: microscopic verification (yes, no, or unknown); method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever, never, unknown); individual year of diagnosis.

6.5 Treatment: Descriptive analysis

6.5.1 General comment

Although analyses here are restricted to *treatments within six months of diagnosis*, for prostate cancer a substantial proportion of 'initial' treatment is given later than six months after diagnosis. However, it is not always straightforward to distinguish such 'late' treatment from treatment given to patients whose initial management was watchful waiting. In addition, data for earlier years are likely to be less complete for such later treatments. Treatments later than six months have therefore been excluded from analysis below, in line with other cancers considered in this report. A possible implication of this is that temporal or regional variation in proportions of patients treated (within six months) may, in part, reflect differences in the timing of treatment.

6.5.2 General summary of treatment

Of the total 10,352 prostate cancer cases included in analyses for the period 1994-2001, 77% had some form of definitive or tumour-directed treatment within six months of diagnosis, 48% had surgical treatment (excluding orchiectomy), 37% had hormonal therapy (including orchiectomy) and 8% had radiotherapy (*Table 6.5.1*). Equivalent figures for the most recent period, 1998-2001, were 5899 cases, of which 78% were treated (a small but significant increase compared with 1994-97), 43% had surgery (significant decrease), 41% had hormonal therapy (significant increase) and 10% had radiotherapy (significant increase) (*Table 6.5.1*, *Figure 6.5.2*). A further breakdown, by age, is shown in *Table 6.5.1* and *Figure 6.5.1*.

The most frequent treatments or combinations were surgery only (34% of cases 1994-2001), hormonal therapy only (22%), and surgery plus hormonal therapy (12%). For the most recent period (1998-2001), equivalent figures were 30%, 26% and 11%, representing a significant decrease in proportional use of surgery and a significant increase in hormonal therapy compared with 1994-97 (*Table 6.5.1*).

Table 6.5.1 Summary of main treatment modalities and combinations (within six months of diagnosis) for prostate cancer patients, 1994-2001. Only treatment combinations totalling at least 1% of cases in any period are listed.

	1994-2001						1994-97	1998-2001	
	age 15-54	55-64	65-74	75-84	85+	total	subtotal	subtotal	
total cases	322	1696	4082	3473	779	10 352	4453	5899	
any treatment	83.5%	83.1%	78.4%	73.7%	67.7%	76.9%	75.6%	77.9%	*
no treatment	16.5%	16.9%	21.6%	26.3%	32.3%	23.1%	24.4%	22.1%	*
any surgery[a]	59.6%	54.9%	48.1%	44.7%	36.3%	47.6%	53.5%	43.1%	*
any hormonal therapy	27.3%	29.1%	38.4%	40.6%	40.3%	37.4%	32.1%	41.4%	*
any radiotherapy	14.9%	16.3%	10.0%	2.3%	1.3%	7.9%	5.4%	9.9%	*
surgery only	47.2%	42.5%	33.3%	31.3%	26.6%	34.0%	39.5%	29.9%	*
hormone only	12.4%	14.9%	21.7%	26.3%	29.3%	22.4%	18.0%	25.7%	*
surgery + hormone	8.4%	8.8%	12.4%	12.7%	9.8%	11.6%	12.1%	11.2%	
radiotherapy only	6.5%	8.9%	4.8%	1.1%	0.4%	3.9%	2.3%	5.2%	*
hormone + radio	4.0%	3.2%	2.7%	0.5%	0.9%	2.0%	1.1%	2.6%	*
surgery + radio	1.9%	2.5%	1.8%	0.5%	0.0%	1.3%	1.4%	1.3%	
others	3.1%	2.4%	1.7%	1.4%	0.8%	1.7%	1.2%	2.1%	*

[a]Surgery and related treatments. *Significant difference between diagnosis periods in unadjusted percentage having this treatment (χ^2 tests).

6.5.3 Region of surgical treatment v. region of residence

For five of the eight regions, most patients resident in those regions had their main surgery in the same region (*Table 6.5.2*). The exceptions were the Midland, North-Eastern and South-Eastern regions, where, respectively, 60%, 78% and 48% of surgical cases were treated in the Eastern region, based on 1994-2001 diagnoses. The patterns were similar for the most recent four-year period, 1998-2001, with 63%, 76% and 49% of surgical cases for those regions being treated in the Eastern region. For South-Eastern region, however, almost as many surgical cases were treated locally (46% for 1994-2001 and 1998-2001).

Table 6.5.2 Breakdown of prostate cancer surgery, 1994-2001, by region of residence and region where main surgery was performed, expressed as percentages of surgically-treated cases. Only surgical procedures within 6 months of diagnosis are included.

		Region of residence																	
Region where		**1994-2001 total**									**1998-2001 subtotal**								
treated		**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**	**E**	**M**	**MW**	**NE**	**NW**	**S**	**SE**	**W**	**Total**
Eastern	%	**99.3**	**59.6**	12.1	**77.6**	33.3	3.4	**48.4**	21.6	**58.6**	**99.3**	**63.2**	17.0	**75.6**	40.4	3.1	**49.2**	30.5	**62.0**
Midland	%	0.3	35.3	0.3	0.0	0.0	0.0	0.0	0.0	2.4	0.4	32.2	0.7	0.0	0.0	0.0	0.0	0.0	2.4
Mid-Western	%	0.1	0.6	**66.6**	0.0	0.0	0.1	1.2	0.3	5.5	0.1	1.2	**55.1**	0.0	0.0	0.3	0.8	0.0	3.4
North-Eastern	%	0.2	0.0	0.0	21.3	0.0	0.0	0.0	0.0	2.1	0.2	0.0	0.0	23.3	0.0	0.0	0.0	0.0	2.5
North-Western	%	0.0	0.0	0.0	0.9	**63.0**	0.0	0.0	4.0	3.2	0.0	0.0	0.0	0.8	**53.9**	0.0	0.0	3.7	2.2
Southern	%	0.1	0.0	10.5	0.0	0.0	**96.5**	4.9	0.0	15.4	0.0	0.0	17.0	0.0	0.0	**96.6**	3.9	0.0	15.0
South-Eastern	%	0.1	0.9	4.6	0.2	0.0	0.0	45.6	0.0	6.7	0.0	1.2	5.4	0.4	0.0	0.0	46.1	0.0	6.9
Western	%	0.0	3.5	5.9	0.0	1.8	0.0	0.0	**74.1**	6.0	0.0	2.3	4.8	0.0	1.1	0.0	0.0	**65.8**	5.3
Northern Ireland	%	0.0	0.0	0.0	0.0	1.8	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0	4.5	0.0	0.0	0.0	0.2

6.5.4 Hospital caseloads (surgical cases)

Prostate cancer cases were surgically treated in a total of 47 hospitals in the Republic of Ireland during 1994-2001 (*Table 6.5.3*). There was no strong evidence of any trend in overall numbers of hospitals providing surgical treatment, although fewer hospitals were involved for cases diagnosed in 2000 (34) and 2001 (35) compared with earlier years.

Between one-third and half (12-24 annually) of the hospitals involved in surgery in any given year treated fewer than 10 surgical cases each, accounting for between 7% and 15% of annual case-totals. About two-thirds (23-30) of the hospitals treated fewer than 20 surgical cases each in a given year (26% to 42% of annual totals), and almost all (31-38) treated fewer than 50 cases (60% to 90% of annual totals).

There was a tendency for average hospital caseload to increase during the period 1994-2001, with smaller proportions of surgical cases treated in 'low volume' hospitals. However, trends in the proportion of patients treated in hospitals with different caseloads were somewhat variable, although the overall trend towards higher surgical caseloads was also evident from data grouped by four-year period.

6.5.5 Consultant caseloads (surgical cases)

At least 118 individual consultants were coded as responsible for surgical managements of prostate cancers during 1994-2001. There was some evidence that the numbers of consultant involved increased during 1994-2001; for example, 94 consultants were recorded during 1998-2001 compared with 75 during 1994-97 (*Table 6.5.4*).

In general, half of the surgical consultants in any given year treated fewer than 10 surgical cases each, accounting for 9%-22% of annual case-totals. About three-quarters of the consultants treated fewer than 20 surgical cases each in a given year (31%-53% of annual totals), and almost all treated fewer than 50 cases (71%-86% of annual totals).

Average annual caseloads showed no obvious trend over time, but significant declines were seen in the proportions of surgical patients treated by 'low volume' consultants (*Table 6.5.4*). For example, the proportion treated by consultants with annual caseloads of 20 or fewer surgical cases fell from 45% of surgical patients during 1994-2001 to 36% during 1994-2001. Note, however, that trends could be exaggerated somewhat if recording of multiple surgical treatments has been more complete in recent years.

Table 6.5.3 Summary of surgical caseloads by year of diagnosis and hospital, based on prostate cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* hospital where surgical treatment received, excluding unidentified hospitals and those outside the Republic of Ireland.

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
hospitals (1+ case)	39	37	41	39	40	36	34	35		45	43	
case average	13	16	17	17	17	17	19	21		14	16	
<10 cases/year[a]	17	24	21	20	20	16	14	12		26	24	
% of cases	*12.2*	*15.3*	*9.2*	*10.3*	*10.2*	*8.1*	*6.8*	*7.4*	***	*13.5*	*11.6*	*
<20 cases/year	28	30	29	25	28	24	23	24		35	30	
% of cases	*42.5*	*29.5*	*26.9*	*23.2*	*25.8*	*26.5*	*27.8*	*30.8*	**	*33.8*	*25.0*	***
<50 cases/year	36	36	38	36	37	33	31	31		42	40	
% of cases	*90.3*	*63.7*	*67.1*	*69.0*	*68.3*	*65.4*	*65.3*	*60.3*	***	*69.6*	*66.8*	*
50+ cases/year	3	1	3	3	3	3	3	4		3	3	
% of cases	*9.7*	*36.3*	*32.9*	*31.0*	*31.7*	*34.6*	*34.7*	*39.7*	***	*30.4*	*33.2*	*

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated in hospitals of a given caseload.

Table 6.5.4 Summary of surgical caseloads by year of diagnosis and surgical consultant, based on prostate cancer patients having surgical treatment within six months of diagnosis (invasive cancers only). For this table, but not main treatment analyses, patients are counted once (for a given diagnosis year or diagnosis period) for *each* surgical consultant involved, excluding unknown consultants and those based outside the Republic of Ireland

	1994	1995	1996	1997	1998	1999	2000	2001		94-97	98-01	
consultants (1+ case)	53	48	49	47	60	51	47	53		75	94	
case average	10	12	14	14	11	12	14	14		8	7	
<10 cases/year[a]	34	28	27	25	39	28	23	26		57	71	
% of cases	*22.1*	*14.2*	*12.8*	*11.5*	*16.6*	*12.7*	*9.1*	*8.8*	***	*22.3*	*15.1*	***
<20 cases/year	46	40	36	34	47	44	35	41		66	81	
% of cases	*53.5*	*44.3*	*31.1*	*32.5*	*34.2*	*50.0*	*34.9*	*37.4*	***	*45.3*	*36.4*	***
<50 cases/year	52	47	47	45	58	48	44	50		74	92	
% of cases	*86.2*	*80.6*	*76.0*	*76.6*	*78.8*	*71.3*	*73.3*	*71.5*	***	*83.9*	*82.8*	
50+ cases/year	1	1	2	2	2	3	3	3		1	2	
% of cases	*13.8*	*19.4*	*24.0*	*23.4*	*21.2*	*28.7*	*26.7*	*28.5*	***	*16.1*	*17.2*	

[a]Surgical caseloads per year (individual years or averaged across four years – latter not equivalent to average of annual caseloads).
* P<0.05, ** P<0.01, *** P<0.001: significant trend (1994 to 2001, Mantel's trend test, 1 d.f.) or difference (1994-97 v. 1998-01, χ^2 test, 1 d.f.) in proportion of patients treated by surgical consultants of a given caseload.

6.5.6 Variation by patient and tumour characteristics

More detailed comparisons are made under the section covering logistic regression analysis (*section 6.6.1*). Basic tabulations of treatment for each category of patient or tumour are shown in *Table 6.5.5*. Note that these tabulations are based on unadjusted data – thus patients or tumours compared under a given variable may also differ in other characteristics, some of which may be more important determinants of treatment. See *Table 6.5.1* and *Figure 6.5.1* for treatments by age-group.

Table 6.5.5 Summary of treatment of prostate cancer cases, 1998-2001, by patient and tumour characteristics: unadjusted percentages receiving treatment within six months of diagnosis. See *Table 6.2.2* for sample sizes.

	Overall treatment	Surgery	Radiotherapy	Hormone
total cases	77.9%	43.1%	9.9%	41.4%
age 15-54[a]	82.6%	57.3%	14.2%	27.1%
age 55-64	82.7%	50.3%	19.6%	29.7%
age 65-74	78.9%	41.7%	12.1%	43.3%
age 75-84	75.3%	41.0%	2.2%	47.1%
age 85+	68.2%	32.5%	1.2%	46.1%
stage I	93.1%	31.0%	27.6%	48.3%
stage II	90.9%	59.1%	15.7%	31.7%
stage III	88.4%	68.1%	7.2%	24.6%
stage IV	83.8%	35.0%	10.7%	68.7%
stage X[a]	75.7%	43.8%	9.3%	36.1%
T1	72.0%	43.0%	11.1%	27.9%
T2	79.2%	40.1%	12.2%	40.6%
T3	90.7%	58.3%	5.3%	46.4%
T4	92.3%	52.9%	12.0%	70.7%
T X	75.2%	41.6%	8.6%	42.5%
N negative	90.9%	67.0%	11.2%	26.6%
N positive	96.0%	48.0%	8.0%	72.0%
N X	75.9%	39.7%	9.7%	43.0%
M negative	85.2%	49.9%	11.6%	42.3%
M positive	82.3%	30.3%	11.9%	69.7%
M X	73.3%	43.0%	8.5%	33.8%
grade 1	77.4%	52.6%	8.5%	27.7%
grade 2	79.6%	48.1%	11.4%	34.9%
grade 3+	85.4%	55.2%	9.3%	50.4%
grade X	68.4%	18.3%	8.5%	51.9%
MV yes	80.3%	48.5%	10.3%	39.7%
MV no	62.9%	1.4%	6.1%	58.3%
MV X	22.4%	0.0%	10.2%	12.2%
symptomatic	81.5%	44.6%	8.7%	48.0%
incidental	80.2%	43.9%	16.4%	28.3%
screen detected	73.5%	30.1%	18.1%	33.7%
presentation X	59.7%	36.6%	11.0%	17.2%
non-smoker	81.2%	46.6%	9.9%	44.0%
ex-smoker	83.8%	49.6%	7.5%	45.8%
smoker	81.0%	44.9%	6.6%	47.9%
smoking status X	70.3%	35.5%	12.7%	33.6%
ever married	78.8%	45.1%	10.1%	40.4%
never married	77.9%	39.0%	5.1%	50.6%
marital status X	64.8%	23.8%	19.8%	31.2%

[a]See *Table 6.5.1* for a further breakdown by age, for the overall period 1994-2001.

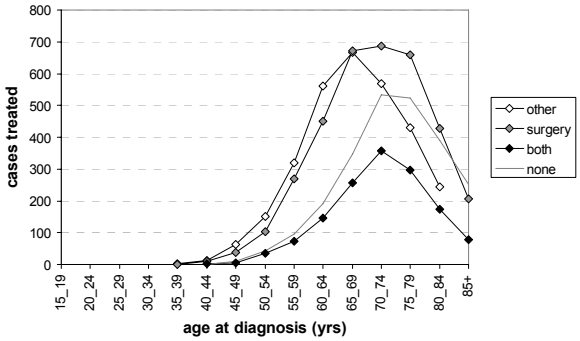

Figure 6.5.1 Age-profiles for tumour-directed treatments within six months of diagnosis for prostate cancer cases diagnosed 1994-2001: numbers of cases having surgery (only), other treatments (radiotherapy, chemotherapy or hormone therapy but not surgery), both surgery and other treatments, or no treatment.

6.5.7 National trends

See *section 6.5.2*.

6.5.8 Regional variation

Regional variations in treatment, unadjusted for patients or tumour characteristics, are summarized for the period 1998-2001 in *Figure 6.5.2*. Overall treatment varied quite markedly between regions (range 67-87% of regional cases). The use of specific modalities varied to a greater extent: from 18% of cases (North-Western region) to 57% (North-Eastern) for surgery, from 4% of cases (North-Eastern) to 17% (Southern) for radiotherapy, and from 30% of cases (Eastern) to 73% (North-Western) for hormonal therapy. More rigorous comparisons of treatments between regions, taking account of age and where possible other patient and tumour characteristics, are presented in *section 6.6.3* (additionally covering 1994-2001 as a whole and 1994-97).

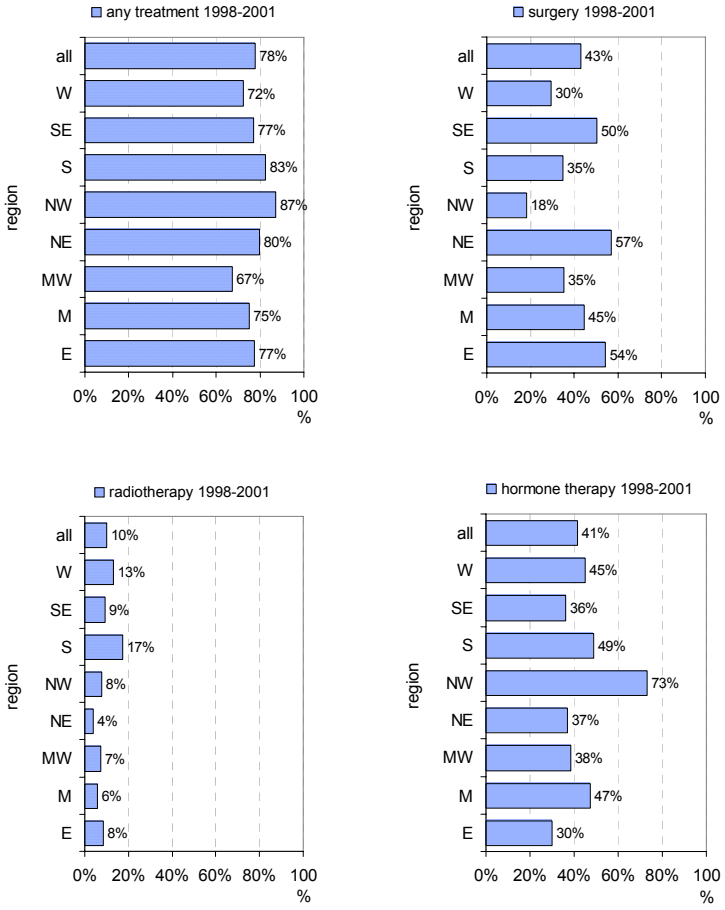

Figure 6.5.2 Percentage of prostate cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence, 1998-2001.

6.6 Treatment: logistic regression analysis

6.6.1 Variation by patient and tumour characteristics

Preliminary multivariate logistic regression models were used to assess variation in treatments in relation to patient and tumour characteristics other than region of residence and year of diagnosis (before examining those). Comparisons here are with baseline groups for relevant variables – diagnosis age 15-54 (for this cancer), tumour grade 1, T category 1 (smallest size/local extension), N negative (no nodal involvement), M negative (no distant metastasis), microscopically verified (MV), symptomatic method of presentation, non-smoker and ever married – having adjusted for all variables shown in the relevant table (*Tables 6.6.1-4*). The main comparisons are based on data for 1994-2001 as a whole. However, attention is drawn to any significant differences in patterns between the diagnosis periods 1994-97 and 1998-2001.

Overall treatment

No significant variation in overall treatment by age was seen, based on adjusted risk ratios (*Table 6.6.1*). Overall during 1994-2001, treatment was significantly more likely for cases that were grade 3+; or T categories 2-4 and unknown. Treatment was significantly less likely for cases of unknown grade, N category, M category, microscopic verification status or marital status, or lacking microscopically verification. Patterns were broadly similar for diagnosis periods 1994-97 and 1998-2001, but with significant changes in relative risk of treatment for cases that were coded T4, N unknown, and incidental or unknown method of presentation.

Surgical treatment

Surgical treatment was significantly more likely for cases that were T category 3-4 or unknown; M category unknown; or ex-smokers (*Table 6.6.2*). Surgery was significantly less likely for cases in age-group 65-74; or that were grade 2 or unknown; N positive or unknown; M positive; not microscopically verified or MV status unknown; screen-detected or unknown method of presentation; unknown smoking status; or among patients who were never married or whose marital status was unknown.

The relationship between T-category and surgery appeared to change significantly between cases diagnosed during 1994-97 and those during 1998-2001, with T2 tumours in the earlier period being significant more likely than T1 (clinically inapparent) tumours to have surgery, but T2 tumours in the later period significantly less likely to have surgery than T1 tumours (*Table 6.6.2*). Similarly, in the earlier (but not the later) period, tumours that presented incidentally were significantly more likely to have surgery than were symptomatic cases. RR estimates fell significantly between earlier and later years for cases whose grade, N-category, grade, method of presentation, or smoking status was unknown, compared with baseline groups for those variables, perhaps indicating a reduction in the quality of data available for non-surgical cases of prostate cancer.

Radiotherapy

Radiotherapy use was significantly more likely among cases that were grade 2 or grade unknown; N category unknown; M positive (metastatic); incidentally detected; or marital status unknown (*Table 6.6.3*). Treatment was significantly less likely for cases that were aged 65-74 or older; T category 3; M category unknown; smokers and ex-smokers; and never married. Patterns were broadly similar in periods 1994-97 and 1998-2001. Relative risks for radiotherapy use (compared with baseline groups) were significantly higher in the recent period for cases in age-group 55-64 or incidentally detected, and significantly lower for N positive cases.

Hormonal therapy

Hormonal therapy was significantly more likely for older patients (age 65-74 and above) and cases that were grade 2, 3+ or unknown; T category 2 or unknown; N positive or unknown; M positive (metastatic); or never married (*Table 6.6.4*). It was significantly less likely for cases of unknown M category, microscopic verification status, method of presentation or smoking status, and for incidentally detected cases. However, the relative risks for hormonal use (compared with baseline groups) changed significantly between periods 1994-97 and 1998-2001 for a number of groups – falling significantly for grade 2 and 3+, N unknown, M positive, and non-MV cases, but increasing for T2 and T4 cases and those of unknown smoking status.

Table 6.6.1 Risk ratios for overall treatment of prostate cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-54	1.000		1.000			1.000	
age 55-64	1.010 (0.951-1.056)	0.709	0.971 (0.849-1.052)	0.551		1.036 (0.967-1.089)	0.270
age 65-74	0.971 (0.907-1.023)	0.306	0.928 (0.798-1.021)	0.151		1.002 (0.926-1.061)	0.941
age 75-84	0.943 (0.873-1.001)	0.058	0.901 (0.763-1.003)	0.059		0.970 (0.885-1.037)	0.427
age 85+	0.941 (0.863-1.005)	0.076	0.908 (0.762-1.013)	0.096		0.955 (0.853-1.034)	0.301
grade 1	1.000		1.000			1.000	
grade 2	0.999 (0.965-1.029)	0.965	0.982 (0.933-1.026)	0.462		1.023 (0.975-1.065)	0.321
grade 3+	**1.044** (1.010-1.074)	0.012	1.025 (0.977-1.067)	0.286		**1.070** (1.020-1.112)	0.007
grade X	**0.934** (0.887-0.977)	0.002	**0.879** (0.805-0.946)	0.000		0.972 (0.907-1.030)	0.369
T1	1.000		1.000			1.000	
T2	**1.117** (1.081-1.149)	0.000	**1.136** (1.082-1.183)	0.000		**1.090** (1.036-1.137)	0.001
T3	**1.235** (1.194-1.269)	0.000	**1.227** (1.156-1.278)	0.000		**1.222** (1.161-1.269)	0.000
T4	**1.212** (1.154-1.258)	0.000	**1.142** (1.042-1.218)	0.008	*	**1.267** (1.189-1.316)	0.000
T X	**1.133** (1.102-1.161)	0.000	**1.121** (1.074-1.161)	0.000		**1.126** (1.079-1.167)	0.000
N negative	1.000		1.000			1.000	
N positive	1.000 (0.918-1.055)	0.988	0.999 (0.866-1.087)	0.988		1.041 (0.924-1.081)	0.357
N X	**0.921** (0.884-0.953)	0.000	0.976 (0.920-1.023)	0.350	*	**0.872** (0.815-0.919)	0.000
M negative	1.000		1.000			1.000	
M positive	1.020 (0.993-1.044)	0.128	1.038 (0.995-1.075)	0.078		1.012 (0.975-1.044)	0.474
M X	**0.959** (0.934-0.982)	0.000	0.970 (0.927-1.008)	0.130		**0.954** (0.922-0.983)	0.001
MV yes	1.000		1.000			1.000	
MV no	**0.783** (0.728-0.835)	0.000	**0.774** (0.692-0.851)	0.000		**0.816** (0.740-0.886)	0.000
MV X	**0.460** (0.310-0.632)	0.000	**0.349** (0.167-0.616)	0.000		**0.557** (0.350-0.780)	0.000
symptomatic	1.000		1.000			1.000	
incidental	1.031 (0.992-1.066)	0.107	**1.085** (1.018-1.139)	0.014	*	0.990 (0.939-1.034)	0.701
screen detected	0.900 (0.774-1.004)	0.063	0.866 (0.582-1.084)	0.275		**0.874** (0.730-0.989)	0.031
presentation X	**0.803** (0.758-0.847)	0.000	0.952 (0.856-1.034)	0.278	*	**0.758** (0.705-0.808)	0.000
non-smoker	1.000		1.000			1.000	
ex-smoker	1.018 (0.988-1.045)	0.229	0.999 (0.950-1.043)	0.991		1.036 (0.998-1.069)	0.057
smoker	0.990 (0.960-1.018)	0.504	0.987 (0.940-1.029)	0.567		1.001 (0.960-1.036)	0.944
smoking status X	**0.925** (0.893-0.954)	0.000	**0.925** (0.870-0.975)	0.003		**0.918** (0.878-0.955)	0.000
ever married	1.000		1.000			1.000	
never married	0.994 (0.964-1.023)	0.719	0.982 (0.933-1.025)	0.436		1.001 (0.960-1.038)	0.940
marital status X	0.955 (0.898-1.005)	0.084	0.925 (0.821-1.014)	0.108		0.971 (0.904-1.030)	0.363

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Unknown values shown as "X" for T category, N category, M category, grade, microscopic verification (MV), method of presentation, marital status and smoking status.
*Significant difference in RR between diagnosis periods.

Table 6.6.2 Risk ratios for surgical treatment of prostate cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-54	1.000		1.000			1.000	
age 55-64	0.912 (0.803-1.018)	0.106	0.946 (0.764-1.110)	0.542		0.904 (0.767-1.040)	0.171
age 65-74	**0.861** (0.757-0.965)	0.009	0.936 (0.762-1.095)	0.451		**0.809** (0.679-0.942)	0.005
age 75-84	0.908 (0.802-1.012)	0.086	0.904 (0.728-1.067)	0.264		0.889 (0.752-1.024)	0.111
age 85+	0.977 (0.849-1.098)	0.720	0.945 (0.747-1.122)	0.568		0.982 (0.808-1.147)	0.842
grade 1	1.000		1.000			1.000	
grade 2	**0.877** (0.826-0.927)	0.000	**0.911** (0.844-0.974)	0.006		0.939 (0.855-1.023)	0.162
grade 3+	0.982 (0.927-1.035)	0.519	0.961 (0.893-1.026)	0.249		1.073 (0.979-1.164)	0.125
grade X	**0.660** (0.599-0.724)	0.000	**0.761** (0.672-0.849)	0.000	*	**0.621** (0.532-0.717)	0.000
T1	1.000		1.000			1.000	
T2	1.011 (0.939-1.084)	0.755	**1.281** (1.184-1.371)	0.000	*	**0.875** (0.773-0.981)	0.022
T3	**1.299** (1.200-1.394)	0.000	**1.407** (1.273-1.522)	0.000		**1.222** (1.073-1.370)	0.003
T4	**1.322** (1.195-1.440)	0.000	**1.241** (1.076-1.390)	0.005		**1.409** (1.206-1.597)	0.000
T X	**1.308** (1.244-1.371)	0.000	**1.288** (1.207-1.364)	0.000		**1.288** (1.181-1.393)	0.000
N negative	1.000		1.000			1.000	
N positive	**0.706** (0.581-0.832)	0.000	**0.769** (0.601-0.926)	0.003		**0.630** (0.446-0.829)	0.000
N X	**0.648** (0.595-0.702)	0.000	**0.787** (0.705-0.867)	0.000	*	**0.559** (0.493-0.629)	0.000
M negative	1.000		1.000			1.000	
M positive	**0.782** (0.720-0.845)	0.000	**0.732** (0.653-0.812)	0.000		**0.7**97 (0.701-0.897)	0.000
M X	**1.058** (1.014-1.102)	0.010	1.018 (0.960-1.074)	0.523		**1.086** (1.019-1.153)	0.011
MV yes	1.000		1.000			1.000	
MV no	**0.074** (0.051-0.105)	0.000	**0.098** (0.063-0.150)	0.000		**0.045** (0.023-0.088)	0.000
MV X	**0.075** (0.018-0.274)	0.000	**0.102** (0.025-0.363)	0.000		-	
symptomatic	1.000		1.000			1.000	
incidental	1.048 (0.962-1.133)	0.270	**1.254** (1.120-1.375)	0.000	*	0.956 (0.843-1.073)	0.465
screen detected	**0.561** (0.400-0.756)	0.000	**0.485** (0.241-0.849)	0.007		**0.572** (0.379-0.820)	0.001
presentation X	**0.834** (0.761-0.908)	0.000	1.109 (0.948-1.260)	0.180	*	**0.833** (0.744-0.927)	0.001
non-smoker	1.000		1.000			1.000	
ex-smoker	**1.069** (1.006-1.132)	0.032	1.034 (0.947-1.120)	0.434		**1.105** (1.012-1.197)	0.026
smoker	0.981 (0.920-1.042)	0.556	0.941 (0.858-1.023)	0.163		1.001 (0.911-1.092)	0.970
smoking status X	**0.845** (0.790-0.900)	0.000	1.021 (0.933-1.107)	0.631	*	**0.754** (0.685-0.827)	0.000
ever married	1.000		1.000			1.000	
never married	**0.906** (0.838-0.976)	0.009	**0.871** (0.791-0.953)	0.002		0.964 (0.875-1.055)	0.438
marital status X	**0.706** (0.598-0.824)	0.000	0.840 (0.674-1.010)	0.066		**0.633** (0.507-0.776)	0.000

[a,b]See *Table 6.6.1*.
*Significant difference in RR between diagnosis periods.

Table 6.6.3 Risk ratios for radiotherapy of prostate cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
age 15-54	1.000		1.000			1.000	
age 55-64	1.102 (0.822-1.452)	0.507	0.667 (0.380-1.128)	0.135	*	1.335 (0.940-1.848)	0.104
age 65-74	**0.633** (0.465-0.853)	0.002	**0.434** (0.250-0.736)	0.002		0.771 (0.528-1.105)	0.161
age 75-84	**0.138** (0.093-0.202)	0.000	**0.138** (0.073-0.257)	0.000		**0.132** (0.079-0.218)	0.000
age 85+	**0.068** (0.033-0.138)	0.000	**0.070** (0.024-0.199)	0.000		**0.063** (0.023-0.169)	0.000
grade 1	1.000		1.000			1.000	
grade 2	**1.308** (1.044-1.631)	0.020	1.010 (0.667-1.518)	0.960		1.187 (0.897-1.557)	0.227
grade 3+	1.231 (0.958-1.575)	0.103	1.265 (0.834-1.901)	0.266		1.053 (0.764-1.438)	0.747
grade X	**1.529** (1.170-1.983)	0.002	**1.872** (1.191-2.896)	0.007		1.206 (0.860-1.671)	0.272
T1	1.000		1.000			1.000	
T2	1.084 (0.868-1.348)	0.471	1.006 (0.651-1.541)	0.975		0.991 (0.759-1.282)	0.947
T3	**0.462** (0.314-0.674)	0.000	0.606 (0.307-1.180)	0.143		**0.382** (0.239-0.606)	0.000
T4	1.014 (0.694-1.462)	0.940	1.051 (0.563-1.920)	0.874		0.971 (0.599-1.533)	0.906
T X	0.871 (0.698-1.082)	0.214	0.857 (0.582-1.253)	0.431		0.891 (0.679-1.160)	0.398
N negative	1.000		1.000			1.000	
N positive	1.323 (0.790-2.150)	0.281	**2.605** (1.209-5.297)	0.015	*	0.782 (0.331-1.726)	0.560
N X	**1.526** (1.222-1.892)	0.000	**2.131** (1.283-3.467)	0.004		**1.292** (1.006-1.642)	0.044
M negative	1.000		1.000			1.000	
M positive	**1.523** (1.249-1.845)	0.000	**1.599** (1.126-2.245)	0.009		**1.555** (1.208-1.975)	0.001
M X	**0.711** (0.599-0.843)	0.000	**0.628** (0.443-0.888)	0.008		**0.737** (0.604-0.896)	0.002
MV yes	1.000		1.000			1.000	
MV no	1.072 (0.788-1.445)	0.653	0.905 (0.556-1.455)	0.686		1.167 (0.776-1.715)	0.451
MV X	1.044 (0.418-2.414)	0.923	-			1.849 (0.741-3.895)	0.179
symptomatic	1.000		1.000			1.000	
incidental	**1.481** (1.184-1.842)	0.001	0.806 (0.436-1.465)	0.486	*	**1.561** (1.219-1.981)	0.000
screen detected	1.581 (0.948-2.554)	0.078	0.810 (0.108-4.817)	0.832		1.557 (0.910-2.550)	0.104
presentation X	0.984 (0.783-1.232)	0.894	0.740 (0.363-1.475)	0.399		0.888 (0.692-1.133)	0.345
non-smoker	1.000		1.000			1.000	
ex-smoker	**0.801** (0.641-0.997)	0.048	0.815 (0.554-1.189)	0.292		0.796 (0.604-1.041)	0.097
smoker	**0.680** (0.546-0.845)	0.000	0.799 (0.562-1.129)	0.205		**0.606** (0.454-0.803)	0.000
smoking status X	1.185 (1.000-1.400)	0.050	1.104 (0.777-1.555)	0.576		1.135 (0.932-1.376)	0.203
ever married	1.000		1.000			1.000	
never married	**0.644** (0.510-0.810)	0.000	0.857 (0.598-1.220)	0.396		**0.543** (0.398-0.737)	0.000
marital status X	**1.868** (1.449-2.383)	0.000	1.531 (0.824-2.748)	0.175		**1.972** (1.496-2.553)	0.000

[a,b]See *Table 6.6.1*.
*Significant difference in RR between diagnosis periods.

Table 6.6.4 Risk ratios for hormonal treatment of prostate cancer patients (within six months of diagnosis), by patient and tumour variables other than year of diagnosis and region of residence, for cases diagnosed 1994-2001: multivariate model.

Variable value[b]	1994-2001 [a]RR (95% CI)	P	1994-1997 RR (95% CI)	P		1998-2001 RR (95% CI)	P
age 15-54	1.000		1.000			1.000	
age 55-64	1.117 (0.907-1.352)	0.285	1.039 (0.701-1.457)	0.840		1.169 (0.906-1.467)	0.219
age 65-74	**1.375** (1.148-1.617)	0.001	1.089 (0.755-1.494)	0.629		**1.574** (1.278-1.885)	0.000
age 75-84	**1.341** (1.115-1.585)	0.002	1.105 (0.766-1.514)	0.573		**1.553** (1.253-1.869)	0.000
age 85+	**1.291** (1.044-1.562)	0.019	1.085 (0.724-1.529)	0.674		**1.472** (1.137-1.835)	0.004
grade 1	1.000		1.000			1.000	
grade 2	**1.565** (1.418-1.720)	0.000	**1.850** (1.570-2.159)	0.000	*	**1.251** (1.097-1.414)	0.001
grade 3+	**1.913** (1.741-2.090)	0.000	**2.366** (2.036-2.716)	0.000	*	**1.517** (1.335-1.705)	0.000
grade X	**1.836** (1.644-2.037)	0.000	**1.563** (1.247-1.929)	0.000		**1.679** (1.475-1.888)	0.000
T1	1.000		1.000			1.000	
T2	**1.380** (1.252-1.513)	0.000	1.032 (0.861-1.223)	0.723	*	**1.487** (1.313-1.667)	0.000
T3	**1.575** (1.394-1.761)	0.000	**1.307** (1.039-1.604)	0.023		**1.688** (1.451-1.930)	0.000
T4	**1.920** (1.683-2.156)	0.000	**1.732** (1.390-2.088)	0.000		**2.039** (1.709-2.353)	0.000
T X	**1.135** (1.028-1.249)	0.013	0.987 (0.843-1.146)	0.872	*	**1.251** (1.095-1.417)	0.001
N negative	1.000		1.000			1.000	
N positive	**1.896** (1.524-2.287)	0.000	**1.850** (1.260-2.564)	0.002		**2.235** (1.707-2.710)	0.000
N X	**1.793** (1.626-1.965)	0.000	**2.146** (1.789-2.532)	0.000	*	**1.561** (1.381-1.746)	0.000
M negative	1.000		1.000			1.000	
M positive	**1.426** (1.332-1.518)	0.000	**1.636** (1.453-1.823)	0.000	*	**1.401** (1.290-1.509)	0.000
M X	**0.793** (0.735-0.854)	0.000	**0.796** (0.690-0.914)	0.001		**0.802** (0.732-0.875)	0.000
MV yes	1.000		1.000			1.000	
MV no	**1.138** (1.021-1.258)	0.019	**1.496** (1.268-1.730)	0.000	*	1.021 (0.879-1.169)	0.775
MV X	**0.502** (0.274-0.855)	0.009	0.775 (0.293-1.629)	0.555		**0.435** (0.196-0.858)	0.013
symptomatic	1.000		1.000			1.000	
incidental	**0.775** (0.687-0.869)	0.000	0.895 (0.722-1.089)	0.279		**0.711** (0.613-0.816)	0.000
screen detected	0.979 (0.747-1.231)	0.873	1.285 (0.715-1.918)	0.362		0.856 (0.626-1.107)	0.259
presentation X	**0.492** (0.424-0.567)	0.000	**0.315** (0.183-0.525)	0.000		**0.461** (0.394-0.535)	0.000
non-smoker	1.000		1.000			1.000	
ex-smoker	1.002 (0.928-1.077)	0.948	1.032 (0.910-1.160)	0.611		0.991 (0.899-1.086)	0.862
smoker	1.054 (0.983-1.127)	0.133	1.092 (0.976-1.213)	0.121		1.069 (0.977-1.163)	0.140
smoking status X	**0.825** (0.762-0.891)	0.000	**0.563** (0.472-0.666)	0.000	*	**0.914** (0.836-0.994)	0.036
ever married	1.000		1.000			1.000	
never married	**1.143** (1.067-1.220)	0.000	**1.156** (1.029-1.289)	0.015		**1.124** (1.029-1.221)	0.010
marital status X	0.942 (0.803-1.092)	0.445	0.814 (0.559-1.135)	0.240		1.010 (0.848-1.180)	0.905

[a,b]See *Table 6.6.1*.
*Significant difference in RR between diagnosis periods.

6.6.2 National and regional trends

These are summarized for the period 1996 to 2001, highlighting significant changes in the age-adjusted risk of treatment, nationally and regionally.

Overall treatment

Nationally, there was a small but significant reduction in overall treatment between 1996 and 2001, equivalent to about a 1.4% lower (relative) likelihood of treatment in successive years (*Table 6.6.5*). Incorporation of stage-related variables in the model had little effect. Five of the eight regions of residence also showed significant reductions in age-adjusted risk of treatment, by about 2-4% annually in relative terms.

Table 6.6.5 Average annual changes in the proportion of prostate cancer patients having any tumour-directed treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 annual [a]RR (95% CI)	P
age-adjusted		
total	**0.986** (0.979-0.992)	0.000
E	**0.982** (0.970-0.993)	0.002
M	0.992 (0.971-1.012)	0.472
MW	**0.958** (0.938-0.978)	0.000
NE	1.017 (0.990-1.042)	0.195
NW	**0.975** (0.955-0.993)	0.005
S	1.003 (0.990-1.016)	0.583
SE	**0.978** (0.957-0.997)	0.029
W	**0.978** (0.956-0.998)	0.036
age-, stage-adjusted[b]		
total	**0.984** (0.977-0.990)	0.000

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown; grade 1, 2, 3+, unknown.

Surgical treatment

National surgery usage fell significantly between 1996 and 2001, by about 8% annually (*Table 6.6.6*). This reduction was also significant after adjustment for stage-related variables. Seven of the eight regions also showed significant annual reductions in surgery, by 5%-20% annually.

Table 6.6.6 Average annual changes in the proportion of prostate cancer patients having surgical treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 RR (95% CI)	P
age-adjusted		
total	**0.924** (0.913-0.935)	0.000
E	**0.952** (0.937-0.967)	0.000
M	**0.920** (0.887-0.953)	0.000
MW	**0.901** (0.862-0.939)	0.000
NE	0.985 (0.950-1.020)	0.430
NW	**0.802** (0.738-0.870)	0.000
S	**0.905** (0.876-0.935)	0.000
SE	**0.921** (0.892-0.951)	0.000
W	**0.932** (0.878-0.989)	0.021
age-, stage-adjusted		
total	**0.907** (0.894-0.919)	0.000

Radiotherapy

Use of radiotherapy increased significantly between 1996 and 2001, by about 13% annually based on national data, also significant after stage-adjustment (*Table 6.6.7*). Much of this increase appeared to be concentrated in three regions (North-Western, Southern and South-Eastern) where significant increases by 25%-34% annually were seen.

Table 6.6.7 Average annual changes in the proportion of prostate cancer patients having radiotherapy (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 RR (95% CI)	P
age-adjusted		
total	**1.132** (1.083-1.183)	0.000
E	1.058 (0.971-1.153)	0.193
M	1.032 (0.833-1.274)	0.771
MW	0.870 (0.743-1.014)	0.076
NE	1.045 (0.816-1.336)	0.723
NW	**1.342** (1.086-1.653)	0.006
S	**1.328** (1.201-1.468)	0.000
SE	**1.246** (1.083-1.431)	0.002
W	1.067 (0.964-1.179)	0.206
age-, stage-adjusted		
total	**1.158** (1.106-1.212)	0.000

Hormonal therapy

There was a small but significant increase in relative use of hormonal therapy between 1996 and 2001, by about 3.3% per year at national scale (*Table 6.6.8*). This remained significant after stage-adjustment. Significant increases were also seen for patients from two regions (Midland and Southern, by 9%-20% annually), but a decrease for Western region (by about 4.4% annually).

Table 6.6.8 Average annual changes in the proportion of prostate cancer patients having hormonal treatment (within six months of diagnosis), overall and by region of residence, 1996-2001.

	1996-2001 RR (95% CI)	P
age-adjusted		
total	**1.033** (1.015-1.050)	0.000
E	1.037 (0.996-1.079)	0.072
M	**1.200** (1.103-1.304)	0.000
MW	1.017 (0.947-1.091)	0.625
NE	1.012 (0.951-1.075)	0.697
NW	0.972 (0.942-1.000)	0.055
S	**1.091** (1.046-1.137)	0.000
SE	1.038 (0.984-1.093)	0.161
W	**0.956** (0.922-0.990)	0.011
age-, stage-adjusted		
total	**1.042** (1.023-1.061)	0.000

6.6.3 Regional variation

Regional variations in treatment use (relative risks compared with the Eastern region) are summarized in *Figures 6.6.1-3* for the overall period 1994-2001 and for the most recent diagnosis period, 1998-2001. Results of age-adjusted and fully adjusted models are presented for overall treatment, surgical treatment, radiotherapy and hormonal therapy. More detailed summaries, overall and for the periods 1994-97 and 1998-2001, are presented in *Tables 6.6.9-12*.

Overall treatment

As for other cancers in this report, overall treatment varied less between regions than did individual treatment modalities. Age-adjusted analyses for 1994-2001 indicated that patients from two regions (North-Western and Southern) were significantly more likely to receive treatment than those from the Eastern region (*Table 6.6.9*). Patients from the Western region were slightly less likely to be treated. However, only the higher treatment usage for the North-Western region was seen in both the 1994-97 and 1998-2001 diagnosis periods, and relative risk values (RRs) differed significantly between periods for the Mid-Western and North-Eastern regions.

Adjustment for stage-related variables modified, and to some extent moderated, the patterns of regional variability, as did fuller adjustment for patient and tumour characteristics. Based on the final model, patients from three regions (Mid-Western, North-Western and Southern) were more likely to receive treatment than those from the Eastern region. As in the basic model, however, geographic patterns were not wholly consistent across the two diagnosis periods examined. In particular, RRs differed significantly between periods for the Mid-Western region (treatment use high relative to Eastern region during 1994-97 but low during 1998-2001).

Table 6.6.9 Risk ratios for overall treatment of prostate cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.974 (0.923-1.020)	0.282	0.955 (0.870-1.029)	0.254		0.984 (0.919-1.041)	0.613
MW	0.999 (0.954-1.040)	0.973	**1.134** (1.076-1.180)	0.000	*	**0.877** (0.808-0.940)	0.000
NE	0.989 (0.944-1.030)	0.623	**0.924** (0.848-0.993)	0.031	*	1.037 (0.982-1.085)	0.174
NW	**1.140** (1.105-1.169)	0.000	**1.139** (1.077-1.188)	0.000		**1.137** (1.094-1.173)	0.000
S	**1.052** (1.021-1.081)	0.001	1.019 (0.964-1.067)	0.476		**1.073** (1.035-1.106)	0.000
SE	0.998 (0.960-1.033)	0.932	0.990 (0.929-1.044)	0.741		1.004 (0.955-1.048)	0.855
W	**0.960** (0.919-0.998)	0.040	0.981 (0.919-1.036)	0.525		**0.943** (0.888-0.993)	0.027
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.982 (0.931-1.029)	0.489	0.971 (0.884-1.046)	0.476		0.984 (0.917-1.043)	0.632
MW	**1.071** (1.032-1.106)	0.001	**1.187** (1.140-1.223)	0.000	*	0.965 (0.901-1.022)	0.255
NE	1.003 (0.957-1.044)	0.891	0.959 (0.882-1.027)	0.254		1.047 (0.990-1.094)	0.097
NW	**1.186** (1.158-1.209)	0.000	**1.183** (1.130-1.223)	0.000		**1.177** (1.141-1.205)	0.000
S	**1.072 (**1.042-1.100)	0.000	**1.058** (1.004-1.105)	0.034		**1.088** (1.050-1.121)	0.000
SE	1.001 (0.962-1.037)	0.939	1.011 (0.949-1.066)	0.691		0.999 (0.947-1.045)	0.985
W	1.009 (0.971-1.044)	0.616	1.033 (0.974-1.085)	0.252		0.991 (0.938-1.038)	0.738
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.972 (0.918-1.021)	0.285	0.989 (0.901-1.063)	0.790		0.959 (0.887-1.023)	0.227
MW	**1.073** (1.032-1.110)	0.001	**1.212** (1.169-1.244)	0.000	*	**0.935** (0.864-0.999)	0.046
NE	0.992 (0.944-1.036)	0.757	0.955 (0.875-1.025)	0.226		1.032 (0.971-1.083)	0.284
NW	**1.161** (1.127-1.189)	0.000	**1.200** (1.149-1.237)	0.000		**1.131** (1.082-1.170)	0.000
S	**1.061** (1.027-1.092)	0.001	**1.076** (1.021-1.123)	0.008		**1.055** (1.009-1.095)	0.018
SE	0.994 (0.952-1.032)	0.767	1.025 (0.962-1.080)	0.418		0.975 (0.917-1.026)	0.354
W	0.996 (0.955-1.034)	0.873	1.017 (0.953-1.073)	0.569		0.993 (0.939-1.042)	0.818

[a]Risk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).
[b]Age-group 15-54, 55-64, 65-74, 75-84, or 85+.
[c]Grade 1, 2, 3+, unknown [grade is an integral part of TNM staging for prostate cancer]; T categories 1-4 & unknown; N category negative, positive, unknown; M category negative, positive, unknown.
[d]Age-group; grade; T, N and M categories; microscopic verification yes, no, or unknown; method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); individual year of diagnosis. [Marital status did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

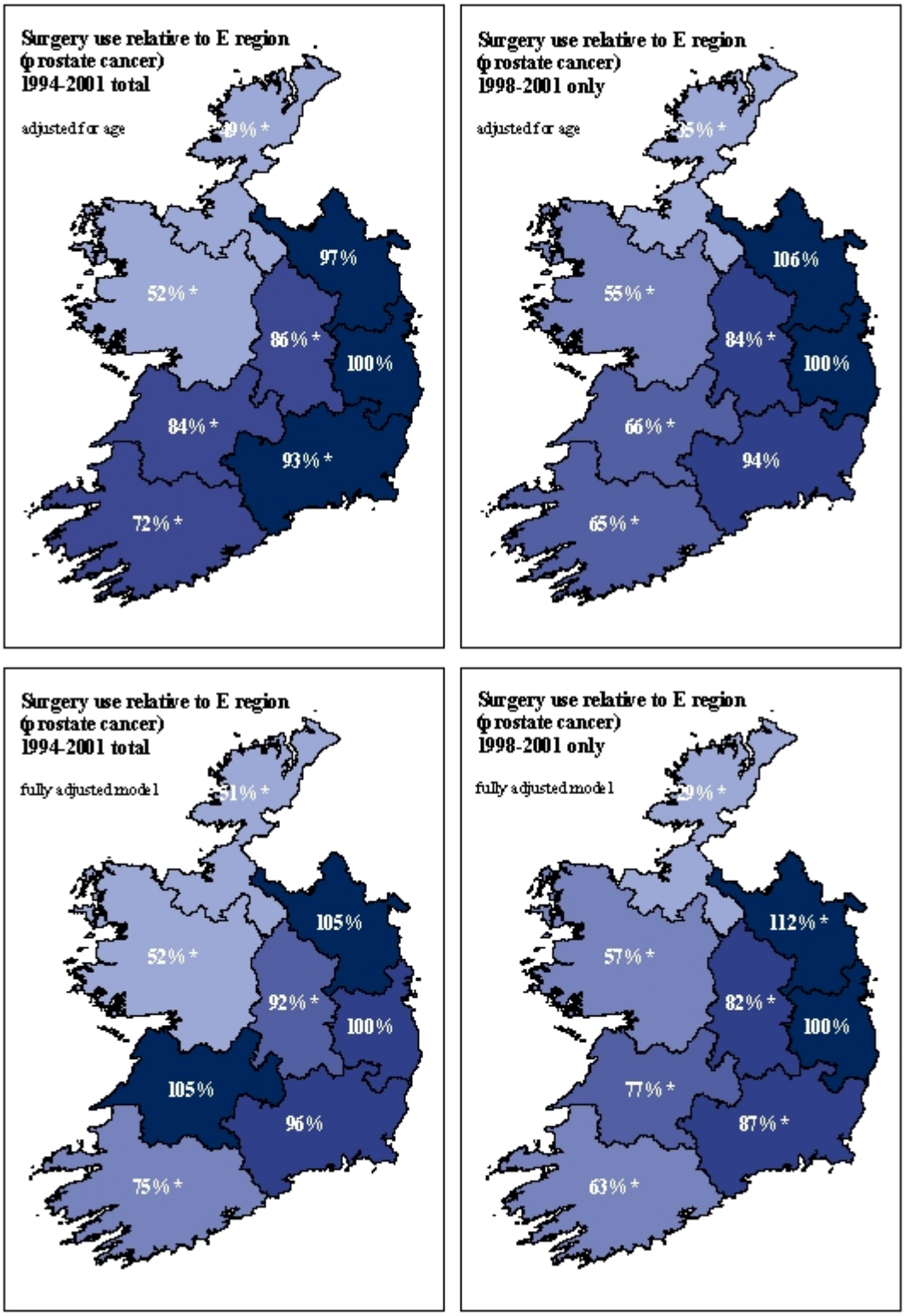

Figure 6.6.1 Regional variation in surgical treatment for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.10* for further details. * = significantly high or low values (P<0.05).

Surgical treatment

The use of surgery was significantly lower among patients from six regions (Midland, Mid-Western, Southern, South-Eastern and, most markedly, North-Western and Western) compared with the Eastern region (*Figure 6.6.1*, *Table 6.6.10*), based on an age-adjusted model for 1994-2001 as a whole. This also applied to five regions during 1994-97 and 1998-2001. However, relative risk values (RRs) differed significantly between diagnosis periods for four regions (Mid-Western, North-Eastern, North-Western and Southern).

For 1994-2001 as a whole, adjustment for a wider range of variables moderated regional discrepancies somewhat (though not for some regions). The final model indicated significantly low use of surgery in four regions (Midland, Southern and, again most markedly, North-Western and Western). Again, the pattern differed substantially between diagnosis periods, and full adjustment appeared to have a greater moderating effect on the pattern for the earlier period. For 1994-97, the full model indicated low use of surgery in two regions but high use of surgery in the Mid-Western relative to the Eastern region. For 1998-2001, use of surgery was significantly low in six regions (and significantly high in the North-Eastern region). RRs differed significantly between periods for five regions (Midland, Mid-Western, North-Western, Southern and South-Eastern), involving lower RRs (compared with Eastern region) in the more recent period i.e. a widening of regional variation.

Table 6.6.10 Risk ratios for surgical treatment of prostate cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	**0.862** (0.789-0.936)	0.000	**0.893** (0.786-0.996)	0.043		**0.843** (0.742-0.946)	0.003
MW	**0.839** (0.772-0.907)	0.000	0.987 (0.896-1.072)	0.775	*	**0.658** (0.567-0.755)	0.000
NE	0.974 (0.908-1.039)	0.450	**0.876** (0.782-0.968)	0.008	*	1.060 (0.965-1.151)	0.210
NW	**0.491** (0.433-0.554)	0.000	**0.694** (0.596-0.794)	0.000	*	**0.348** (0.283-0.424)	0.000
S	**0.715** (0.665-0.766)	0.000	**0.803** (0.729-0.877)	0.000	*	**0.649** (0.584-0.718)	0.000
SE	**0.929** (0.872-0.985)	0.013	**0.917** (0.837-0.994)	0.036		0.937 (0.856-1.017)	0.127
W	**0.520** (0.469-0.574)	0.000	**0.483** (0.413-0.559)	0.000		**0.549** (0.477-0.628)	0.000
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**0.886** (0.807-0.965)	0.005	0.960 (0.844-1.069)	0.485		**0.830** (0.723-0.940)	0.002
MW	0.986 (0.912-1.058)	0.714	**1.147** (1.056-1.227)	0.002	*	**0.762** (0.656-0.872)	0.000
NE	1.025 (0.954-1.094)	0.479	0.960 (0.857-1.057)	0.434		1.089 (0.988-1.185)	0.081
NW	**0.583** (0.514-0.656)	0.000	**0.785** (0.675-0.895)	0.000	*	**0.404** (0.326-0.495)	0.000
S	**0.735** (0.680-0.790)	0.000	**0.856** (0.772-0.938)	0.001	*	**0.641** (0.570-0.715)	0.000
SE	**0.911** (0.850-0.972)	0.004	0.960 (0.872-1.043)	0.358		**0.863** (0.777-0.949)	0.002
W	**0.561** (0.504-0.621)	0.000	**0.532** (0.453-0.618)	0.000		**0.584** (0.504-0.670)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**0.916** (0.833-0.999)	0.047	1.017 (0.898-1.126)	0.767	*	**0.815** (0.703-0.930)	0.002
MW	1.052 (0.972-1.129)	0.198	**1.284** (1.198-1.354)	0.000	*	**0.770** (0.655-0.889)	0.000
NE	1.054 (0.979-1.126)	0.154	0.990 (0.883-1.090)	0.856		**1.116** (1.010-1.218)	0.032
NW	**0.509** (0.443-0.582)	0.000	**0.861** (0.742-0.978)	0.019	*	**0.288** (0.227-0.363)	0.000
S	**0.754** (0.695-0.815)	0.000	0.933 (0.845-1.019)	0.130	*	**0.631** (0.555-0.711)	0.000
SE	0.955 (0.890-1.020)	0.179	1.034 (0.944-1.118)	0.442	*	**0.870** (0.778-0.963)	0.006
W	**0.523** (0.466-0.584)	0.000	**0.539** (0.457-0.628)	0.000		**0.565** (0.482-0.655)	0.000

[a,b,c]See *Table 6.6.9*.
[d]Age-group; grade; T, N and M categories; microscopic verification yes, no, or unknown; method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever married, never married, unknown); individual year of diagnosis.
*Significant difference in RR between diagnosis periods.

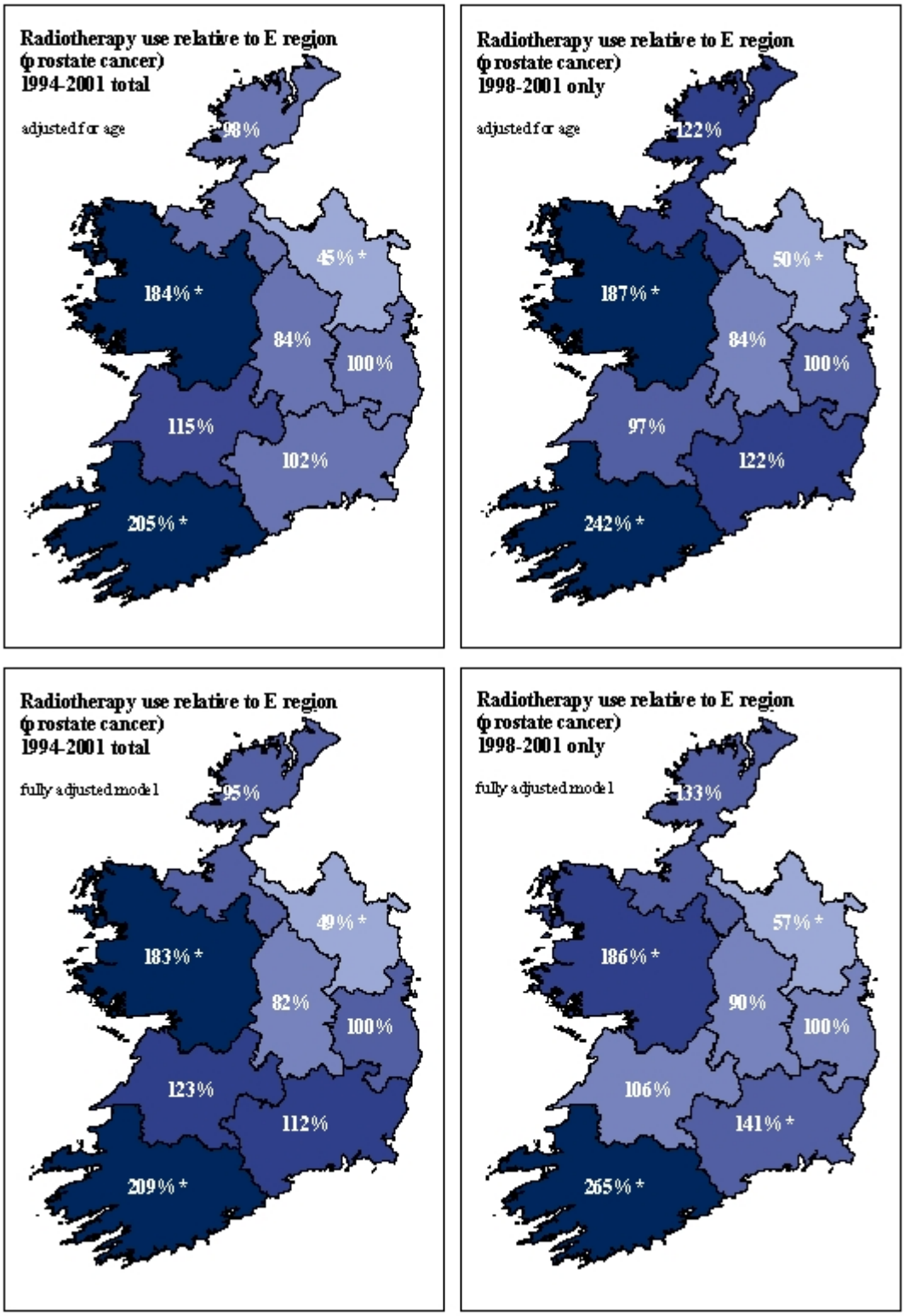

Figure 6.6.2 Regional variation in radiotherapy for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.11* for further details. * = significantly high or low values (P<0.05).

Radiotherapy

Regional patterns were less complex than for surgical treatment. For 1994-2001 as a whole, the basic and fully adjusted models indicated significantly (and substantially) greater use of radiotherapy in patients from the Southern and Western regions, and lower use in patients from the North-Eastern region, compared with the Eastern region (*Figure 6.6.2*, *Table 6.6.11*). Essentially the same pattern was seen for the 1998-2001 diagnosis period, but radiotherapy use was also significantly high among patients from South-Eastern region, based on the final model. Relative risk values differed significantly between diagnosis periods for three regions (North-Western, Southern and South-Eastern), in each instance reflecting an increase (or larger increase) in radiotherapy use compared with the Eastern region (cf. *section 6.6.2*).

Table 6.6.11 Risk ratios for radiotherapy of prostate cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	0.839 (0.584-1.196)	0.338	0.823 (0.437-1.521)	0.541		0.840 (0.538-1.290)	0.432
MW	1.149 (0.869-1.508)	0.325	1.435 (0.948-2.141)	0.086		0.968 (0.657-1.409)	0.870
NE	**0.452** (0.299-0.680)	0.000	**0.370** (0.170-0.796)	0.011		**0.497** (0.304-0.802)	0.004
NW	0.983 (0.716-1.339)	0.918	0.480 (0.221-1.027)	0.059	*	1.215 (0.857-1.699)	0.269
S	**2.049** (1.720-2.428)	0.000	1.250 (0.866-1.785)	0.230	*	**2.420** (1.987-2.921)	0.000
SE	1.021 (0.798-1.300)	0.865	0.648 (0.391-1.064)	0.087	*	1.222 (0.921-1.607)	0.163
W	**1.836** (1.491-2.246)	0.000	**1.778** (1.241-2.511)	0.002		**1.873** (1.450-2.390)	0.000
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	0.807 (0.559-1.156)	0.247	0.647 (0.337-1.225)	0.184		0.844 (0.539-1.303)	0.452
MW	1.116 (0.837-1.477)	0.450	1.242 (0.802-1.897)	0.328		0.979 (0.657-1.437)	0.916
NE	**0.464** (0.306-0.699)	0.000	**0.326** (0.148-0.707)	0.004		**0.535** (0.327-0.864)	0.010
NW	0.900 (0.650-1.237)	0.523	**0.402** (0.183-0.871)	0.021	*	1.188 (0.825-1.686)	0.348
S	**2.060** (1.718-2.456)	0.000	1.161 (0.789-1.691)	0.445	*	**2.575** (2.101-3.123)	0.000
SE	1.065 (0.830-1.360)	0.616	0.624 (0.372-1.035)	0.068	*	1.287 (0.966-1.697)	0.084
W	**1.761** (1.423-2.165)	0.000	**1.505** (1.033-2.165)	0.033		**1.901** (1.465-2.436)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	0.821 (0.567-1.179)	0.289	0.658 (0.341-1.247)	0.203		0.895 (0.569-1.386)	0.627
MW	1.229 (0.918-1.631)	0.163	1.260 (0.810-1.933)	0.302		1.064 (0.710-1.568)	0.760
NE	**0.491** (0.323-0.742)	0.001	**0.337** (0.153-0.732)	0.006		**0.573** (0.349-0.929)	0.024
NW	0.953 (0.684-1.319)	0.778	**0.414** (0.187-0.901)	0.026	*	1.329 (0.918-1.891)	0.129
S	**2.093** (1.730-2.516)	0.000	1.217 (0.817-1.791)	0.330	*	**2.647** (2.133-3.244)	0.000
SE	1.117 (0.868-1.430)	0.384	0.607 (0.361-1.010)	0.055	*	**1.410** (1.056-1.864)	0.020
W	**1.831** (1.472-2.262)	0.000	**1.568** (1.067-2.272)	0.022		**1.859** (1.417-2.408)	0.000

[a,b,c]See *Table 6.6.9*.
[d]Age-group; grade; T, N and M categories; method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever married, never married, unknown); individual year of diagnosis. [Microscopic verification status did not significantly improve model-fit and was excluded from the final model.]
*Significant difference in RR between diagnosis periods.

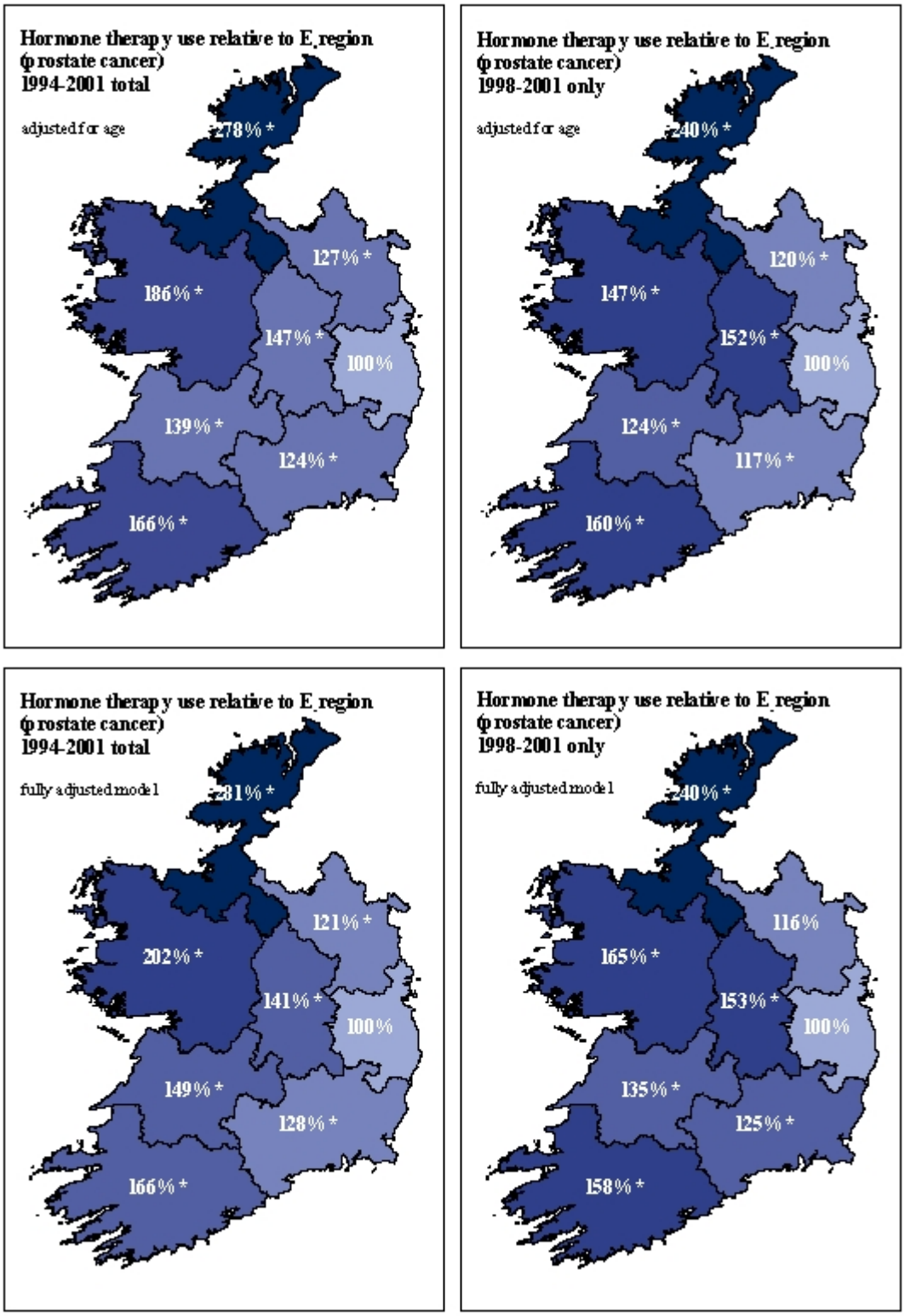

Figure 6.6.3 Regional variation in hormonal therapy for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%):
1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.12* for further details. * = significantly high or low values (P<0.05).

Hormonal therapy

Use of hormonal therapy was substantially lower for patients from the Eastern region, compared with all other regions, during 1994-2001. The magnitude of this variation was essentially the same whether based on an age-adjusted or a more fully adjusted model (*Figure 6.6.3*, *Table 6.6.12*). The basic pattern and regional rankings were similar for the 1994-97 and 1998-2001 diagnosis periods, but hormonal use was generally closer to that in the Eastern region in the more recent period. For the two regions with highest use of hormonal therapy during 1994-97 (North-Western and Western), relative risk values (RRs) fell significantly between these periods. RRs also differed significantly between periods for the Midland and Mid-Western regions, based on some models.

Table 6.6.12 Risk ratios for hormonal treatment of prostate cancer patients (within six months of diagnosis), by region of residence, for cases diagnosed 1994-2001. Relative risks in bold = significant difference from Eastern region (RR <1 = lower use of treatment than in Eastern region, RR >1 = higher use).

	1994-2001		1994-1997			1998-2001	
	[a]RR (95% CI)	P	RR (95% CI)	P		RR (95% CI)	P
basic model: age-adjusted[b]							
E	1.000		1.000			1.000	
M	**1.474** (1.314-1.642)	0.000	**1.309** (1.030-1.634)	0.028		**1.520** (1.335-1.708)	0.000
MW	**1.385** (1.241-1.537)	0.000	**1.703** (1.429-2.002)	0.000	*	**1.242** (1.073-1.421)	0.004
NE	**1.268** (1.130-1.415)	0.000	**1.412** (1.154-1.703)	0.001		**1.204** (1.044-1.373)	0.011
NW	**2.777** (2.630-2.913)	0.000	**3.532** (3.208-3.825)	0.000	*	**2.398** (2.239-2.542)	0.000
S	**1.662** (1.543-1.783)	0.000	**1.754** (1.522-2.001)	0.000		**1.598** (1.466-1.732)	0.000
SE	**1.236** (1.118-1.361)	0.000	**1.371** (1.150-1.618)	0.001		**1.174** (1.038-1.318)	0.011
W	**1.859** (1.722-1.997)	0.000	**2.644** (2.363-2.923)	0.000	*	**1.471** (1.318-1.627)	0.000
fuller model: age-, stage-adjusted[b,c]							
E	1.000		1.000			1.000	
M	**1.498** (1.325-1.678)	0.000	1.200 (0.920-1.535)	0.172	*	**1.608** (1.408-1.809)	0.000
MW	**1.573** (1.407-1.745)	0.000	**1.878** (1.563-2.217)	0.000	*	**1.455** (1.260-1.656)	0.000
NE	**1.283** (1.135-1.441)	0.000	**1.425** (1.147-1.741)	0.002		**1.242** (1.069-1.426)	0.005
NW	**2.930** (2.785-3.061)	0.000	**3.678** (3.347-3.970)	0.000	*	**2.522** (2.364-2.662)	0.000
S	**1.776** (1.644-1.910)	0.000	**1.846** (1.583-2.126)	0.000		**1.711** (1.566-1.856)	0.000
SE	**1.372** (1.238-1.512)	0.000	**1.420** (1.177-1.692)	0.000		**1.362** (1.205-1.524)	0.000
W	**1.983** (1.835-2.130)	0.000	**2.734** (2.430-3.035)	0.000	*	**1.595** (1.428-1.762)	0.000
final multivariate model[d]							
E	1.000		1.000			1.000	
M	**1.407** (1.235-1.589)	0.000	1.146 (0.869-1.480)	0.324	*	**1.525** (1.323-1.730)	0.000
MW	**1.488** (1.321-1.664)	0.000	**1.723** (1.413-2.064)	0.000		**1.350** (1.155-1.555)	0.000
NE	**1.209** (1.061-1.367)	0.005	**1.283** (1.018-1.591)	0.035		1.163 (0.992-1.347)	0.061
NW	**2.814** (2.654-2.960)	0.000	**3.525** (3.163-3.849)	0.000	*	**2.397** (2.220-2.556)	0.000
S	**1.658** (1.523-1.797)	0.000	**1.683** (1.423-1.966)	0.000		**1.577** (1.426-1.729)	0.000
SE	**1.279** (1.146-1.420)	0.000	**1.333** (1.093-1.604)	0.005		**1.250** (1.096-1.413)	0.001
W	**2.015** (1.860-2.169)	0.000	**2.556** (2.241-2.871)	0.000	*	**1.649** (1.475-1.824)	0.000

[a,b,c]See *Table 6.6.9*.
[d]Age-group; grade; T, N and M categories; microscopic verification yes, no, or unknown; method of presentation (symptomatic, incidental, screen-detected, unknown); smoking status (non, ex, smoker, unknown); marital status (ever married, never married, unknown); individual year of diagnosis.
*Significant difference in RR between diagnosis periods.

6.7 Discussion: prostate cancer

The major findings here are:

- significant increases in relative survival of patients between the periods 1994-97 and 1998-2001, nationally and in seven out of eight regions;
- significant regional variation in relative survival throughout 1994-2001, involving lower survival of patients in all regions outside of the Eastern region (and all but one during 1994-97);
- significant decreases in the use of surgical treatment between 1996 and 2001, nationally and in seven regions;
- significant increases in radiotherapy, nationally and in three regions;
- significant increases in hormonal therapy, nationally and in two regions;
- significant regional variation in treatments, notably involving lower use of surgical treatment for patients from four regions, higher use of hormone therapy for all regions and higher use of radiotherapy for up to three regions, compared with the Eastern region.

Survival trends

Apparent marked improvements in relative survival of prostate cancers, whether basic survival estimates or assessed by statistical modelling, were seen at national and regional scales between diagnosis periods 1994-97 and 1998-2001. Patients from almost all regions also showed significant improvements in survival. But a substantial proportion of the improvements seen could involve lead-time bias, whereby earlier detection of cases extends recorded survival time, in addition to or even in the absence of any true survival benefit. This particularly applies to a cancer, such as prostate cancer, for which earlier detection through screening (in this case, by Prostate Specific Antigen testing) is not yet proven to reduce mortality from that cancer.

It is clear from changes in the numbers and age-distribution of cases that detection - but not necessarily the true underlying incidence - of prostate cancer has increased substantially within the period covered. This seems most likely to reflect increasing use of the PSA test to help identify cases. It is not yet clear how much of this PSA testing has been done in men with symptoms of prostate problems (not necessarily prostate cancer), and how much in wholly asymptomatic individuals (i.e. as "screening" for prostate cancer). The apparent use of PSA testing for screening, outside of any formal screening programme in Ireland, is the subject of a current National Cancer Registry project funded by the Health Research Board.

Improvements in survival between the diagnosis periods 1994-97 and 1998-2001 were seen in patients below age 75 but not in older patients. Possible reasons for this might include the disease being more readily treatable in younger patients, or earlier improvements in treatment in younger patients. But the age-discrepancy would also be consistent with increasingly earlier diagnosis (e.g. through screening) among younger patients, in particular.

Regional variation in survival

Regional disparities in survival, assessed by relative survival modelling, were evident for both the 1994-97 and 1998-2001 diagnosis periods. However, while adjustment for stage-related and other variables 'removed' most of the regional variation for 1994-97, those variables appeared to 'explain' less of the variation for 1998-2001. It is not clear why, but one possibility may be that apparent trends towards earlier detection of prostate cancer are not fully captured by the patient and tumour variables available. For example, although the proportion of cases reported as 'symptomatic' fell between 1994-97 and 1998-2001, there was a corresponding rise in the proportion of cases whose method of presentation was unknown. Difficulties, changes over time or regional differences in recording or interpreting stage-related variables for this cancer might also be involved.

Staging of cases may have been complicated by changes in investigative and diagnostic practice, or difficulty in agreeing a definition of 'symptomatic' cases. For example, an increase in PSA testing might be expected to lead to an increase in T1 tumours ("clinically inapparent tumour not palpable nor visible by imaging", Fleming *et al*. 1997), especially T1c ("tumour identified by needle biopsy e.g., because of elevated PSA"). But numbers and proportions of T1 prostate tumours as recorded by the National Cancer Registry have actually fallen. The main increase seems to be in T2 tumours ("confined within the prostate"). Possibly this is a coding artifact and some T2 tumours might better be coded as T1c. If so, this further complicates interpretation of time-trends and regional variation in survival of prostate cancer patients. In addition to this, a substantial increase in the proportion of cases without full TNM staging has occurred. This may reflect an increase in the proportion of early-stage (including sub-clinical) cases, which may not receive full investigations or staging. Grade, an important part of staging for this cancer, was known for 76% of cases during 1998-2001, but completeness for other components of stage ranged from 87% for the N category to

only 55% for the T category and 43% for M category in the same period.

Survival: international context

Directly comparable European data are not available for the same periods, but the most recent Europe-wide results (from EUROCARE-3) are summarized in *Table 6.7.1*. The five-year relative survival of Irish patients diagnosed during 1994-97 (63%) was similar to or slightly lower than the European average based on for 1990-94 diagnoses.

Table 6.7.1 Comparison of five-year relative survival for prostate cancer patients, Ireland 1994-97 and 1998-2001, and Europe 1990-94, age-adjusted to the EUROCARE-3 standard patient population for this cancer.[a]

	Ireland 1994-97 5-yr survival (95% CI)		Ireland 1998-2001 survival (95% CI)		Europe 1990-94[b] survival (95% CI)		[range][c]
male	63.1%	(60.7%-65.4%)	73.0%	(70.4%-75.6%)	65.4%	(64.4%-66.4%)	[38.6%-83.6%]

[a]Capocaccia *et al*. (2003) and unpublished. [b]EUROCARE-3: Sant *et al*. (2003). [c]Range of national figures: highest Austria.

Standard treatment modalities for prostate cancer

Evidence-based summaries of standard treatment options, by stage or other prognostic grouping, are available as part of the US National Cancer Institute's PDQ Cancer Information Summaries: (http://www.cancer.gov/cancertopics/pdq/cancerdatabase).

A brief summary is provided below, by broad modality (see also *Appendix 1*).

Surgery: Curative (as single modality or in combination with adjuvant radiotherapy) for stage I; curative (single or in combination with adjuvant hormonal therapy) for stage II; curative or palliative for stage III; palliative for stage IV.

Radiotherapy: Curative or adjuvant for stage I; adjuvant for some stage II cases; curative [or survival-prolonging], adjuvant or palliative for stages III-IV.

Hormonal therapy: Adjuvant for stage II; curative, adjuvant or palliative for stages III; curative or adjuvant for stage IV.

Treatment trends

The most obvious trends were declines in the use of surgery nationally and in all regions, and increases in radiotherapy nationally and in some regions. Moderate increases in hormonal therapy were seen at national scale, but trends varied between regions. The factors influencing these trends, and the implications of these trends in terms of appropriateness of treatment, are unclear, without further exploration of the data e.g. trends stratified further by patient and tumour characteristics. At national scale, the basic trends were the same whether assessed using an age-adjusted model or a more complex model adjusting for age and for stage-related variables. Only age-adjusted models were attempted for regional time-trends. But for radiotherapy and hormone therapy, there was some evidence that the (univariate) relationship between treatment and age changed over time. This involved an apparent shift towards greater (relative) use of radiotherapy for age-group 55-64 and of hormone therapy for age-groups 65-64 and over during 1998-2001 compared with 1994-97. Some changes in the relationship between treatment and stage-related variables were also apparent, for all three modalities. It is thus possible that the age-adjusted or stage-adjusted models examined here do not adequately describe treatment trends for this cancer, even at the scale of broad modalities.

Regional variation in treatment

There were stronger indications for this cancer than for others considered in this report (breast, colorectal and lung cancers) that low usage of a given treatment modality in a region may have been balanced, to some extent, by higher use of another modality. This was particularly apparent for the two most frequent modalities for this cancer (surgery and hormone therapy). However, in the absence of comprehensive data on factors that might have influenced treatment decisions, and against a likely background of unorganized and poorly documented screening, it is difficult to confirm this apparent finding. These difficulties also apply to potential comparisons of the quality or appropriateness of treatment decisions between regions.

For this cancer, treatment comparisons are also complicated by the lack of comprehensive data on 'watchful waiting' as initial choice of therapy. If the use of watchful waiting has reflected regional or institutional factors, or varied over time within some or all regions, it is likely to have influenced the geographic and temporal patterns seen for other treatments.

The regional patterns for radiotherapy, and how

they differed between diagnosis periods, provided a good example of the interplay between regional variation and time-trends in treatment. Radiotherapy use varied more substantially (relative to patients from the Eastern region) during 1998-2001 than during 1994-97. This appeared to be consistent with significant increases in radiotherapy use between 1996 and 2001 for three regions (North-Western, Southern and South-Eastern), compared with slower increases for the Eastern region.

Treatment: international context

Comparisons are made here with first-course treatments reported for cancers in the USA as part of the National Cancer Data Base (http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm). Data have been extracted from the latter for cases diagnosed during 1998-2001, to provide nearest-equivalent data on treatments of prostate cancer.

Based on the data used in this report, Irish patients were significantly less likely to receive treatment than in the USA (*Table 6.7.2*). This largely involved significantly lower use of radiotherapy in Ireland. Overall use of surgery was similar in both populations. The use of hormonal therapy appeared to be higher in Ireland, although it may not have been completely reported for US patients. Of the specific single or multi-modal treatments reported, Irish patients were significantly less likely to have surgery only, radiotherapy only or surgery plus radiotherapy, but significantly more likely to have hormonal therapy only or surgery plus hormonal therapy.

If Irish data are expanded to include all recorded treatments within 12 months (rather than 6 months) of diagnosis, the differences noted remain significant. The proportion of Irish patients having radiotherapy increases from 9.9% (within 6 months) to 18.6% (within 12 months), but this is still much lower than the US figure. For other modalities, and for overall treatment, use of a 12-month period increases the proportions recorded as treated only slightly.

Table 6.7.2 Comparison of main treatment modalities and combinations for patients with invasive prostate cancer, Ireland and USA, in diagnosis period 1998-2001. US data were not specified in detail for some treatments.

	Ireland 1998-2001		**USA[a]© 1998-2001**
any treatment	77.9%	***	91.0%
no treatment	22.1%	***	9.0%
any surgery[a]	43.1%	ns	44.0%
any hormonal therapy	41.4%	-	[c]≥29.9%
any radiotherapy	9.9%	***	≥40.6%
surgery only	29.9%	***	36.4%
hormone only	25.7%	***	5.7%
surgery + hormone	11.2%	***	3.9%
radiotherapy only	5.2%	***	20.2%
hormone + radio	2.6%	***	20.4%
surgery + radio	1.3%	-	-
others	2.1%	-	4.5%

- = data not available or statistical comparison not possible.
[a]Source of US data: National Cancer Data Base of first-course treatments reported by hospitals approved by the American College of Surgeons Commission on Cancer; see http://web.facs.org/ncdbbmr/ncdbbenchmarks7.cfm.
© Commission on Cancer, American College of Surgeons. NCDB Benchmark Reports, v1.1. Chicago, IL, 2002. The content reproduced from the applications remains the full and exclusive copyrighted property of the American College of Surgeons. The American College of Surgeons is not responsible for any ancillary or derivative works based on the original Text, Tables, or Figures.
[b]US surgical data are for surgery of primary site only.
[c]≥ indicates that overall use of these treatments among patients in the USA may be higher than shown, as figures for less frequent combinations of modalities are not quoted on the NCDB website.

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Chapter 7. GENERAL DISCUSSION

7.1 Main conclusions

Improvements in survival for breast, colorectal and prostate cancers, but not lung cancers, were seen at national scale between the earlier (1994-1997) and later (1998-2001) parts of the period examined. Improvements in treatment or in early diagnosis are presumably involved, but exaggeration of true survival improvements by lead-time bias cannot be ruled out, especially for prostate cancer.

Regional variation in survival is still apparent, as noted in our previous report (NicAmhlaoibh *et al*. 2004), with survival generally lowest for patients resident outside the Eastern region, except for lung cancer. This variation is partly but not wholly explained by variation in patient or tumour characteristics.

Trends in treatment appeared to be broadly in line with expectations of greater or better-targeted use of radiotherapy and chemotherapy, although no increase in radiotherapy use was seen for breast cancer. An apparent major fall in use of hormonal treatment for breast cancer may also be in line with expectations of improved targeting of appropriate treatment. This may also apply to increased use of hormone therapy and reduced use of surgery for prostate cancer.

At regional scales, there is still substantial variation in the use of particular treatment modalities. These variations are largely unexplained by patient and tumour characteristics, suggesting that geographic and institutional influences on treatment may be critical. Evidence of increased specialization or centralization of services is limited, although further analysis is required.

7.2 Cautions on use and interpretation of multivariate analyses

Analyses presented in this report are, in general terms, aimed at:

1. Identifying and quantifying differences in survival and treatment between years and regions.
2. Assessing if such differences can be 'explained' statistically by other patient and tumour characteristics, e.g. age, stage – i.e. are annual or regional differences still evident after adjustment for possible annual or regional variation in relevant patient and tumour characteristics?

However, the explanatory power of the analyses presented is potentially limited by a number of factors. These include:

1. Incomplete data for some variables.
2. Simplicity of assumptions, e.g. that the relationship between age and treatment, or stage and treatment, is similar in different regions or different years.
3. Related to the latter point, possible variation between patient groups in the 'meaning' of particular variable values. This includes the concept of 'stage migration', whereby patients diagnosed in more recent years (or in some hospitals) may be more likely to be assigned to a correct, higher category of stage because more thorough investigations are made.
4. Lack of information on other potentially relevant variables, e.g. reasons for non-treatment of some cases.

Standard statistical methods, e.g. logistic regression of treatment data, and Cox regression or other modelling of survival data, can only partly allow for such factors, for example:

1. By including missing variable values as 'unknown' (rather than blank). But the meaning of 'unknown' may vary between patient groups. Also, a high proportion of 'unknowns' among one patient group might statistically explain poorer treatment or survival, but might itself be an indicator of poor-quality investigation or care.
2. By introducing interaction terms between, or stratifying for, variables considered likely to have a complex inter-relationship. This can, however, produce over-complex models, and it may not be practicable to include or check for interaction terms for other than age and stage-related variables.
3. By including all potentially relevant available variables, in the hope that some of these may act as proxies for unmeasured factors. But there may be too many variables in the model, and variation in unmeasured factors may still be missed.

For regression-based comparisons of survival, a particular problem is posed by non-proportional hazards. This involves variables for which mortality differences between patient groups are not constant throughout follow-up. This can be allowed for statistically by either stratifying analyses if Cox regression is used or by introducing interaction terms for relevant variables if relative survival modelling is used (as in this report).

For some purposes, analyses adjusted for age and sex only may be the most informative, given the high proportion of 'unknown' data and uncertainty about the consistency of recording for most other variables. For assessment of regional variation and

of time-trends in treatment and survival, we have thus presented age-adjusted (and where relevant sex-adjusted) risk ratios and hazard ratios as the basic summary measures. In some respects, arguably, these are the most important measures.

For more complex models, dropping 'unknown' values was not a realistic option, as a high proportion of cases would have been excluded. Trends or regional differences based on only cases with high-quality data would be unlikely to be representative overall. But caution is obviously required in interpreting the results of models incorporating variables that may be substantially incomplete, or for which temporal or regional variation in coding is a possibility.

It is clear from the data analyzed here that lack of microscopic verification, or of information on stage or grade, tends to be associated with poor survival and lack of treatment of cancer patients. Inclusion of these variables in models of regional variation in survival or treatment may reduce (and in a statistical sense explain) some of the regional variation seen. However, such 'explanation' could imply under-investigation and resultant under-treatment, not necessarily related to patients' fitness for treatment. Thus to say that survival among patients from region B is poor in part because microscopic verification levels there are below-average would not necessarily be an adequate 'explanation', as equivalent patients from a different region might have been investigated and treated more thoroughly.

In some instances, inclusion of further variables actually increased the apparent magnitude of regional or year effects. In some instances this may reflect unrecognized interactions between those variables and year or region, or interactions which models could not reasonably be expected to allow for. Inclusion of extra variables in a model can also have the effect of increasing the random 'noise' in the data, at the expense of clarity.

Further planned analyses will attempt to incorporate measures of patients' condition or comorbidity (based on case-matching against hospital in-patient data from HIPE) and of patients' socioeconomic status (area-based deprivation measures). These may provide further clues to observed regional variations in survival or treatment of Irish cancer patients. Interpretation may still be difficult. For example, general patient status, and relevant non-cancer conditions, may not be sufficiently well-documented in hospital records to explain why particular patients fared badly or did not receive particular treatments. When using deprivation measures, there is also the issue of whether variation in socioeconomic status 'explains' variation in survival or treatment in any non-statistical sense. To some extent, socioeconomic status may provide a proxy for the general health or stage at diagnosis of patients. But there is also often an implication that patients of higher socioeconomic status are more likely to receive high-quality treatment. Inclusion of deprivation measures in a model might appear to reduce or 'explain' regional variations in survival or treatment, even though the underlying factor might be under-treatment of patients from poorer backgrounds.

7.3 Time-trends in relative survival

In general, results presented here show good evidence of improvements in relative survival for the more treatable cancers (breast, colorectal and prostate cancers) when comparing the 1994-97 and 1998-2001 diagnosis periods. But there was only limited evidence of improved survival for lung cancers, the most fatal of the cancers considered. Regionally, results for the other cancers were generally consistent with improvements. Apparent changes were not always statistically significant, in part reflecting small sample sizes at regional scales.

Possible changes in patient or tumour characteristics over time appeared to provide only a partial explanation of trends in survival. Improvements in treatment are likely to account, in part, for the survival improvements seen. But changes in unmeasured or poorly measured factors could also be involved.

For cancers amenable to earlier detection through screening (organized or unorganized), a further caveat is that increases in average survival time (from date of diagnosis) are <u>not necessarily</u> always associated with true reductions in mortality for those cancers. Earlier detection through screening is generally expected to improve outcomes as a result of cancer being detected, on average, at a less advanced and more treatable stage. There is currently good international evidence of this for breast and colorectal cancers but not for lung or prostate cancers (see *section 7.5*). Even for cancers where there is a proven or well-supported benefit of screening – as measured by actual reductions in cancer mortality rates – *lead-time bias* can exaggerate the benefits if average individual survival (rather than the population-based mortality rate) is measured.

There is good preliminary evidence (not presented here) that the introduction of the BreastCheck screening programme in some regions during 2000-01 is already producing a 'stage-shift' towards less advanced, more treatable breast cancers. However, lead-time bias alone will quite likely lead to substantial further improvements in apparent survival (for the age-range 50-64), before real

benefits in terms of mortality reductions become apparent. Within the period covered by this report, it is unlikely that such bias will have had any major influence. The survival improvements seen for breast cancer are thus likely to be largely genuine.

For prostate cancer, very marked improvements in apparent survival are already evident here, even in the absence of organized screening. Available data on tumour grade and other tumour and patient tumour characteristics do not seem to 'explain' the improvements very well. The coincidence of these improvements with very rapid recent increases in case-numbers (by on average 8% per year since 1994), suggests that lead-time bias is likely to be a substantial contributor. This seems to reflect widespread, albeit unorganized use of the Prostate Specific Antigen test for screening purposes. Real benefits of improvements in prostate cancer treatment – notably increased use of hormone therapy – may also be occurring.

7.4 Regional variation in relative survival

Regional variation was most evident from unadjusted data, and from basic multivariate models adjusted for age and sex only (plus cell-type for lung cancer). But the variation seen in the basic model is in one sense a 'true' measure of regional variation in cancer-related survival. This reflects or integrates variation in a range of relevant factors likely to influence survival, directly or indirectly. Such factors may include early detection, thoroughness of diagnostic and prognostic investigations, quality or appropriateness of treatment, and socioeconomic, marital and smoking status. Apart from age and sex (or perhaps even including age), it is arguable that regional disparities in all the important factors influencing survival are themselves part of wider societal disparities relevant to health.

Fuller adjustment for stage and other tumour and patient variables modified and, in general, substantially reduced regional discrepancies. In statistical terms, these variables appeared to 'explain' some of the differences. This applied particularly to prostate cancer, for which little regional variation was apparent in the full model – significantly higher excess mortality (lower relative survival) among patients from the Southern region only. For breast cancer, full adjustment reduced the number of regions with significantly low survival from seven to four (Midland, Southern, South-Eastern and Western regions). For colorectal cancer, survival was significantly low among patients from the Mid-Western, Southern and South-Eastern regions. In contrast, survival of lung cancer patients was significantly high among patients from three regions (Mid-Western, North-Western and Western), although absolute differences were small for this high-fatality cancer.

In theory, after adjusting for available patient and tumour variables, the remaining variation should reflect variation in treatment or in unmeasured factors. But prognostic and demographic variables were often substantially incomplete, and may have been correlated with the quality of diagnostic or prognostic investigations. Unrecognized or over-complex interactions between variables may also cloud interpretation. Thus the full explanatory power of the models is difficult to assess. Even a 'perfect' model would require cautious interpretation as the factors adjusted for may be crucial influences on survival and may also merit action to reduce disparities.

It is worth noting that no region had significantly poorer survival for all four cancers. Patients from the Southern region did have significantly poorer survival than the reference Eastern region for breast, colorectal and prostate cancers during 1994-2001 as a whole. In the most recent diagnosis period, 1998-2001, only two of those cancers had significantly low survival in the Southern region (and also in the Mid-Western and South-Eastern regions).

7.5 Factors influencing survival

Factors relevant to assessment of regional and temporal survival patterns are discussed further below. These can be considered as potential explanatory factors accounting in part for the patterns seen, or as potential confounders for which adjustment may be needed in order to reveal patterns reflecting quality of treatment. However, the individual factors, and how they influence survival, may also be also of interest in themselves.

Findings for the period 1994-2001 as a whole are summarized. Particular weight is given to results of multivariate analyses (also summarized in *Table 7.1*). For age, stage-related variables and tumour grade, multivariate results quoted refer mainly to the first year after diagnosis. This is because it was generally found necessary to allow for interactions between these variables and time after diagnosis, thus age-related and stage-related patterns could not readily be summarized beyond the first year. A number of factors (e.g. comorbidity) not examined in the present study are also discussed.

We have provided brief references to other published studies but have not attempted a detailed review, given the scale of the relevant literature. (see Gospodarowicz *et al*. 2001 for fuller details).

Early detection and screening; method of detection

As noted above, earlier detection, reflecting

organized screening, unorganized screening or other public health initiatives or trends, can be expected to result in improved survival. Some of the improvements are likely to be genuine, but lead-time bias may exaggerate the true benefits. Data on patient and tumour characteristics from this report are consistent with trends towards earlier detection for breast cancer, but there is little or no evidence of this for colorectal and lung cancers. For prostate cancer, the data are more difficult to interpret, but major increases in numbers of cases diagnosed among younger men, in particular, suggest that earlier detection is occurring. During 1994-2001, patients whose breast cancer was screen-detected cases had significantly better relative survival than symptomatically-presenting patients. This applied even after adjustment for other variables (including stage). Survival was also higher for screen-detected than for symptomatic cases of colorectal and prostate cancer. However, for prostate cancer this was not statistically significant after adjustment for other variables. Insufficient data were available for screen-detected lung cancers.

Lung and prostate cancers which presented incidentally, i.e. during examination for other conditions, were also significantly associated with higher survival (compared with symptomatic cases). In contrast, breast cancers which presented incidentally showed the opposite pattern. The reason for this discrepancy is unclear.

An earlier analysis of 1994-98 data (NicAmhlaoibh *et al*. 2004) did not examine the influence of method of detection on survival, in part because the vast majority of cases were recorded as having presented symptomatically. In particular, the percentages of cases noted as screen-detected in that period were extremely small – 1.8% for breast, 0.6% for prostate and only 0.2% for colorectal and lung cancer. (Percentages screen-detected during 1994-2001 as a whole were 4.1% for breast, 1.0% for prostate and 0.3% for colorectal and lung cancer.)

Published studies aimed at assessing the benefits of screening broadly agree that properly-organized screening reduces mortality from breast cancer (see review by Vainio & Bianchini 2001). However, even based on results of screening trials, this conclusion is not universally accepted (Olsen & Gøtzsche 2001). For prostate cancer, the benefits of screening are much more controversial, with the general consensus being that there is not yet sufficient evidence that screening reduces mortality from this cancer (see *Box* below). Likewise, for lung cancer there is not yet sufficient evidence that screening saves lives. For colorectal cancer, however, there is good evidence that screening reduces cancer-specific mortality. Note that, for proper evaluation of screening, the outcome measures assessed are mortality rates among screened compared with non-screened populations, not among patients whose cancers were screen-detected compared with other patients.

Screening for breast, colorectal, lung and prostate cancers

Evidence-based summaries are available as part of the US National Cancer Institute's PDQ Cancer Information Summaries: (http://www.cancer.gov/cancertopics/pdq/cancerdatabase).

Brief extracts are provided below.

Breast cancer: "Based on fair evidence, screening mammography in women aged 40 to 70 years decreases breast cancer mortality. The benefit is higher for older women, in part because their breast cancer risk is higher."

Colorectal cancer: "Based on solid evidence, screening for colorectal cancer reduces colorectal cancer mortality, but there is little evidence that it reduces all cause mortality."

Lung cancer: "Based on fair evidence, screening does not reduce mortality from lung cancer."

Prostate cancer: "Using the PSA test to screen men for prostate cancer is controversial because it is not yet known if this test actually saves lives."

Treatment

Trends or regional variations in survival shown in this report are likely to reflect, in part, the provision of appropriate treatments aimed at a cure or at prolonging life. Explicitly or convincingly demonstrating this link is difficult, however, especially against a background of increased earlier detection for some cancers. One possible approach is to include treatment status within statistical models of survival. This has not been attempted here, in part because patients receiving and not receiving particular treatments are likely to differ in unmeasured characteristics e.g. their general health. Further analyses are planned, to take into account available information on comorbidity (other health conditions in the same patients).

Basic summaries of survival data, stratified by treatment status, are presented earlier in this report. As noted, the survival of treated and untreated patients is likely to reflect other differences between the patient groups involved, rather than their actual treatment. More generally, this caution applies to any attempts to assess the influence of treatment on survival, other than as part of a randomized clinical trial. To an extent, patients' receipt or non-receipt of a particular treatment might provide no more than a proxy variable for unmeasured factors influencing patients' suitability for that treatment. Standard treatment recommendations, stratified by relevant prognostic

or predictive factors, are primarily based on results of randomized trials (cf. *Appendix 1*).

Interactions between treatment and other variables potentially contribute to temporal, regional or wider geographic patterns in the survival of cancer patients. If treatment decisions are not always objectively evidence-based, for example if there are geographic biases in the treatment of older patients unrelated to other clinical factors, under-treatment may contribute to the survival patterns seen.

Age

For all four cancers, analyses unadjusted for other actors indicated significantly poorer relative survival among older patients. This is additional to underlying (non-cancer-related) age effects on survival. The pattern and strength of age-related variation varied between cancers. For lung cancer, there was significantly reduced survival for all patients aged 45 years or more, compared with age-group 15-44. For other cancers, lower survival was mainly evident for patients aged at least 65 or 75 years. Based on the first year after diagnosis, statistical models adjusted for other patient and tumour variables confirmed and provided further detail on these patterns. Significantly low relative survival (high excess mortality) was seen for lung cancer patients aged 45 or more (just over two-fold variation between the youngest and oldest age-groups); for breast and colorectal cancer patients aged 55 or more (three-fold variation between age-groups); and for prostate cancer patients aged 65 or more (three- or four-fold variation between age-groups).

In an earlier analysis of 1994-98 data for the same cancers (NicAmhlaoibh *et al*. 2004), multivariate models of cancer-specific survival were stratified by age, and age effects on survival were not reported for most cancers. However, lung cancer mortality in males was significantly higher in all age-groups over 50 years compared to the under-50 group, with about two-fold variation overall. This was similar to the pattern seen for relative survival during 1994-2001.

For breast cancer, Fitzgibbons (2001) noted a lack of consensus from published studies regarding the prognostic value of age. This reflected differences in study design and the potential confounding effects of factors such as differences in treatment of patients of different ages. Again, no clear prognostic role for age was noted for colorectal cancer by Hobday & Erlichman (2001) after adjustment for other prognostic factors, especially stage. For lung cancer, age was noted as a prognostic factor for non-small-cell carcinoma by Brundage & Mackillop (2001), but particularly in advanced cases. For prostate cancer, Denis & Murphy (2001) noted that age was a "reliable prognostic factor … for survival in patients with localized or advanced disease."

Across a range of cancers, under-treatment and under-investigation of cancers in older patients have been noted as potential contributors to poorer average prognosis among older patients (O'Connell *et al*. 2001, Ng *et al*. 2005). However, it may not be straightforward to establish if this reflects a true bias against older patients, as opposed to reflecting age-related variation in other prognostic factors, especially if those are poorly quantified. For example, in Ireland older patients with lung cancer are less likely to receive treatment but Mahmud *et al*. (2003) considered that adequate adjustment for stage and comorbidity was not possible.

Cancers among younger age-groups are sometimes associated with poorer survival. We found only limited evidence of younger age being associated with poorer survival in this study, for breast and prostate cancers only. Very much the opposite was seen for lung cancer. For breast cancer, some but not all studies have found survival in younger women to be poorer than in older women, reflecting tumours that are more advanced, more aggressive or more likely to recur (Klauber-DeMore 2005-2006). For colorectal cancer, cancers in patients under 40 years of age tend to be more aggressive and to present at a later stage, although early-stage survival may be higher in younger patients (O'Connell *et al*. 2004).

Sex

Unadjusted analyses indicated significantly poorer five-year survival for male compared with female patients with lung cancer. This also appeared to be the case for colorectal cancer. Significant differences were confirmed by multivariate analyses, which estimated mortality risks among female patients as 8% lower for lung cancer and 6% lower for colorectal cancer.

An earlier multivariate analysis of 1994-98 data also noted significantly lower (cancer-specific) mortality among female patients with those cancers – 11% lower for lung cancer and 14% lower for surgically treated colorectal cancer (NicAmhlaoibh *et al*. 2004).

Female lung cancer patients are known from other studies to survive longer, on average, than male patients. Gritz *et al*. (2005) suggested that one factor involved may be smoking, given that, across studies, women consistently have a shorter history of tobacco exposure. Among patients with limited-stage small-cell lung cancer, however, Videtic *et al*. (2005) noted better survival in female than male patients, among both smokers and non-smokers.

For patients diagnosed with incurable cancer, a review by Hauser *et al*. (2006) noted that patients' gender was not associated with survival duration, except for longer survival of female lung cancer patients.

For colorectal cancer, Hobday & Erlichman (2001) did not consider gender a significant prognostic factor, after adjustment for other factors.

Tumour stage and grade

The T, N and M categories of stage were strongly associated with survival, both in univariate analyses and in analyses adjusted for other variables. Based on fully adjusted analyses covering the first year after diagnosis, the T category of stage was associated with a five-fold variation in excess mortality (between categories T1 and T4) for breast cancer, almost four-fold variation for colorectal cancer, and two-fold variation for lung and prostate cancers. Tumour involvement of regional nodes (N category) accounted for an approximate doubling of mortality risk for all four cancers. Most strikingly, distant metastatic involvement (M category) was associated with a ten-fold increased risk for breast cancer, eight-fold for prostate cancer, four-fold for colorectal cancer and two-fold for lung cancer.

Tumour grade is an important component of stage for prostate cancer, and accounted for almost a three-fold variation in mortality. Grade was also an important determinant of survival for breast and colorectal cancers (almost two-fold variation between lowest and highest categories), but had only a small influence on survival for lung cancer.

Overall stage, derived from a combination of T, N and M categories (plus grade for prostate cancer), was not included in statistical models. However, unadjusted analyses indicated substantially poorer survival for stage IV for breast, colorectal and prostate cancers, and stages III, IV and unknown for lung cancer.

Earlier analyses for these cancers during 1994-98 found broadly similar effects of stage and grade on cancer-specific survival (NicAmhlaoibh *et al*. 2004). However, most of the reported stage/grade effects cannot be directly compared between these studies, as the more recent figures mainly refer to the first year following diagnosis. In some instances, notably T category for breast cancer and M category for prostate cancer, this apparently accounts for more marked gradients in survival seen in the present analysis. The other patient and tumour variables included in multivariate analyses also differed somewhat between studies (see also *section 7.6* below).

A caution is also needed on comparisons between hazard ratios based on cause-specific mortality and those based on excess mortality assessed in relative survival terms. Both cause-specific and excess mortality risks aim to measure the 'extra' mortality risk associated with a cancer diagnosis, modified by other variables. However, cause-specific mortality is based on the cause of death attributed for death-certification purposes, thus is potentially open to error. If the severity (e.g. stage) of a cancer influences the likelihood of a patient's death being attributed to their cancer, over and above 'real' effects on mortality risk, hazard ratios assessed by cause-specific analyses could be biased. Further exploration of the data analyzed here, running cause-specific and relative survival analyses on the same data and adjusted for the same variables, might help identify such biases.

Tumour morphology (cell-type)

For breast cancer, carcinomas and cancers of unspecified type were associated with higher mortality risk (2.5-fold higher for non-specific cancer compared with breast-specific adenocarcinoma morphologies). Variation between the other, specific cell-types was comparatively minor, and not statistically significant after adjustment for other variables. An earlier, cause-specific analysis of 1994-98 data (NicAmhlaoibh *et al*. 2004) was stratified by tumour morphology but did not present hazard ratios by cell-type.

Fitzgibbons (2001) noted that "special-type" carcinomas of the breast – including tubular, mucinous, medullary and papillary carcinomas – had a more favourable prognosis, overall or adjusted for stage, than ductal and lobular carcinomas. We did not explicitly examine this but we found no significant survival difference between "other specified carcinoma types" (including papillary and medullary carcinomas) and ductal or lobular adenocarcinomas.

For lung cancer, the fully adjusted mortality risk was 1.4 times higher for cancers of unspecified or rarer cell-types, compared with non-small-cell carcinomas. Unadjusted relative survival was about twice as high for non-small-cell as for non-small-cell carcinomas, but the difference was not significant after adjustment for other variables including stage. The earlier analysis did not report adjusted hazard ratios by cell-type, but unadjusted survival at five years was, again, about twice as high for non-small cell as for small-cell carcinomas (NicAmhlaoibh *et al*. 2004). Brundage & Mackillop (2001) noted the importance of histology for lung cancer, but that "while, strictly speaking, the use of tumor histology to define these two entities is itself an application of a prognostic factor, the distinction between groups is so widely accepted that the

analysis and application of prognostic factors generally now occurs within each group."

Classification of colorectal and prostate cancers by histological type is less complex, for the majority of patients, and is not considered to be important prognostically (Hobday & Erlichman 2001; Denis & Murphy 2001).

Microscopic verification status

Based on univariate analyses, cancer patients lacking microscopic verification (MV) of their diagnosis had among the lowest survival of any category of patient. For example, five-year relative survival for patients diagnosed during 1994-2001 averaged 20% for breast cancer patients lacking MV (compared to 77% for those with MV); 8% (v. 53%) for colorectal cancer; 5% (v. 10%) for lung cancer; and 25% (v. 76%) for prostate cancer. Multivariate analyses confirmed these patterns for colorectal and prostate cancers, with two-fold or greater variation in excess mortality between patients of different MV status. For breast and lung cancers, the independent effect of MV status was not measured as this variable did not contribute significantly to model-fit.

For the period 1994-98, multivariate analyses by NicAmhlaoibh *et al*. (2004) also found that cancer-specific mortality was twice as high among colorectal and prostate cancer cases lacking MV. This variable did not contribute significantly to model-fit for breast cancer, and analyses for lung cancer required stratification by MV status. Its influence on survival was not directly measured for those cancers.

These findings are not unexpected, as patients with more advanced cancer, or in poorer general health, are less likely to undergo thorough diagnostic investigations.

Smoking status

For all four cancers, patients recorded as current smokers at the time of their diagnosis had a slightly, but significantly, higher excess mortality risk than non-smokers, after adjustment for other characteristics. Excess risks among smokers were 15% higher than among non-smokers for lung cancer, 19% higher for colorectal cancer, 24% higher for breast cancer, but 50% higher for prostate cancer. Significantly elevated risk (lower survival) was also seen among ex-smokers for colorectal cancer (12% higher than among non-smokers) and prostate cancer (54% higher).

Interpreting these findings requires caution, given that the influence of smoking status on survival may also be mediated through other health conditions. The mortality risks assessed here are 'excess risks' among cancer patients compared with the general population, thus in theory should (mainly) reflect the influence of the cancer. However, smoking prevalence in the general population is (by definition) lower than among cancer patients who smoke. Thus some of the excess risk among the latter group may reflect a direct influence of smoking on survival (not just cancer-related survival). In this instance, there seem to be good theoretical grounds for suggesting that relative survival (for cancer patients who smoke) may not necessarily give a good approximation to cancer-specific survival. However, findings here are supported by a previous of 1994-98 data (NicAmhlaoibh *et al*. 2004), which noted significantly elevated cancer-specific mortality risks (18-23% higher) among breast, colorectal, lung and prostate cancer patients who were smokers.

There is evidence from many other studies for a negative influence of smoking on survival of cancer patients. This applies both to overall survival and to survival associated with cancer and its treatment (e.g., Yu *et al*. 1997; review by Gritz *et al*. 2005). Smoking has been found to increase the risk of progression to metastatic disease among patients with localized prostate cancer treated by radiotherapy, both among current smokers (five-fold increased risk) and previous smokers (three-fold increase) (Pantarotto *et al*. 2006). Smoking has also been associated with lower survival among lung cancer patients, independently of the effects of tobacco-related comorbidities (Tammemagi *et al*. 2004). In particular, pulmonary complications following surgery for lung cancer are more likely among smokers (e.g. Vaporciyan *et al*. 2002). Smoking has also been found to reduce wound-healing after surgery in breast cancer and other patients; and to reduce the effectiveness of, or increase complications following, radiotherapy. Less well-studied are possible reduced effectiveness of chemotherapy, and exacerbation of treatment-related weight loss, in patients who smoke during treatment (Gritz *et al*. 2005).

Marital status

For colorectal, lung and prostate cancers, adjusted excess mortality risks among patients who were never married were slightly but significantly higher than among those who were ever married, by 12%, 20% and 29% respectively. Marital status was not included in the multivariate model for breast cancer, thus its independent effect on survival could not be assessed for this cancer. However, unadjusted relative survival was significantly low for breast cancer patients who were never married.

For 1994-98 cases (NicAmhlaoibh *et al*. 2004),

cancer-specific mortality was also significantly higher (by 15-20%) among unmarried colorectal and prostate cancer patients. Again, marital status was not included in the multivariate model for breast cancer (as it did not significantly improve model-fit). For lung cancer the influence of marital status was not directly measured as analyses were stratified by this variable.

Based on US data, Lai *et al*. (1999) noted that, "after controlling for age, race, and treatment, married patients with cancers of all major primary sites had significantly better survival than single, separated, divorced, or widowed patients." Single patients appeared to have the most consistently poor survival across cancers, and the influence of marital status was more marked for men than for women. Differences in provision or receipt of treatment had been controlled for, and general health status, access to healthcare, and socioeconomic status were suggested as possible factors mediating the influence of marital status.

The influence of marital status on treatment has also been noted as a likely factor influencing survival. For example, Osborne *et al*. (2006) noted that, in the US, unmarried women with stage I or stage II breast cancer were less likely to receive definitive treatment than married women. But, even after adjusting for treatment, tumour stage, comorbidity and socioeconomic status, unmarried women had poorer cancer-related survival. A role for "increased social support and social networks" was proposed. Villingshoj *et al*. (2006) noted significantly higher mortality among colorectal patients who had lost their partner before surgery, compared to patients co-habiting with the same partner as before their surgery. They suggested that the quality or effect of treatment somehow differed between these groups.

Missing or unknown data

Cases flagged as 'unknown' or unspecified for a given patient or tumour characteristic generally had higher cancer-associated mortality (poorer relative survival) compared with the baseline/reference groups for this variable. Fully adjusted models confirmed this for:

- T, N and M categories and grade for all four cancers examined;
- tumour morphology (cell-type) for breast and lung cancers;
- smoking status for breast, colorectal and lung cancers;
- microscopic verification status for colorectal and prostate cancers.

However, cases with method of presentation unknown had lower mortality (higher survival) than known symptomatic cases for all four cancers examined. This perhaps suggests this category included some screen-detected or other asymptomatically-presenting cases that were not explicitly identified as such.

Hospital and consultant caseloads or specialization

There are good reasons to expect better outcomes among patients treated by surgeons or other consultants with greater experience of treating those cancers, or in hospitals which treat larger numbers of those cancers. We have not examined the potential influence of these factors in the current report, but further analyses are planned. This may be important, as data summarized in this report indicate that substantial proportions of surgical patients are treated by hospitals or consultants having low annual caseloads.

However, published studies relating cancer outcomes to measures of caseload or specialization do not provide unequivocal results. The outcome measures used also vary somewhat, generally involving either crude (all-cause) or cancer-specific mortality. Some examples are discussed below.

Sainsbury *et al*. (1995) compared survival of breast cancer patients between surgeons in Yorkshire (1979-88). Mortality among patients treated by surgeons treating more than 30 new cases of breast cancer per year was significantly lower (by about 15%) than among patients treated by surgeons treating fewer than 10 cases per year. Higher survival was also found for patients treated by surgeons whose patients had higher rates of chemotherapy and hormone therapy. The authors noted "Had the practice of the surgeons with the better outcomes been used by all treating clinicians, 5-year survival would have increased by about 4-5%." They recommended "that patients with breast cancer be dealt with only by clinicians who see more than 30 new cases per year and who have a full range of treatment options available within a multidisciplinary setting." A further study by these authors, covering Yorkshire patients during 1989-94, found a similar influence of workload on survival of breast cancer patients (Mikeljevic *et al*. 2003).

At hospital level, Hebert-Croteau *et al*. (2005) found that overall (all-cause) mortality among lymph node-negative breast cancer patients in Quebec, Canada was significantly higher in hospitals with fewer than 50 new cases per year, compared with those with at least 100 cases per year. This was after adjusting for case mix and physician variables. However, the caseload effect disappeared after adjustment for the type of hospital, i.e. better outcomes in large hospitals reflected factors such as teaching status, research activity and availability of on-site radiotherapy facilities.

For colorectal cancer, a review by Hodgson *et al*. (2001) noted that surgeon expertise and hospital caseload were not associated consistently with long-term survival or with peri-operative mortality.

Likewise, hospital volume and surgeon experience have been found to influence post-operative outcomes for non-small-cell lung cancer, but not consistently across studies (Birim *et al*. 2005).

Comorbidity and general patient health

The influence of comorbidity on cancer-related survival was not examined in this report, but further analysis is planned. Cancer patients having other significant health conditions are less likely to be offered or given appropriate treatment for their cancer, and may have more complications following treatment. Their overall survival prospects, unrelated to their cancer, are also likely to be reduced, although analysis of cause-specific survival should be able to allow for this.

A previous analysis of Irish data from 1994-98 (NicAmhlaoibh *et al*. 2004) did attempt to incorporate comorbidity data obtained through matching of patients to the Hospital In-Patient Enquiry system (HIPE), covering public hospitals mainly. Unadjusted analyses suggested that comorbidity was associated with poorer cause-specific survival of colorectal and prostate cancer at five years. There was no apparent association with lung cancer survival at one year after diagnosis. Inclusion of available data on comorbidity significantly improved the fit of multivariate models of regional variation in survival for breast, prostate and male colorectal cancers. However, the independent influence of comorbidity on survival was not directly measured, as it proved necessary to stratify the analyses by comorbidity status. Comorbidity did not improve model-fit for lung and female colorectal cancers in that analysis.

Many published studies indicate that cancer patients with comorbid conditions have worse outcomes. For example, Hauser *et al*. (2006) reviewed studies of patients diagnosed with advanced-stage cancers, and found that comorbidity was "consistently associated with shorter survival." Nevertheless, based on comparisons across cancer types differing in their average fatality, Read *et al*. (2004) concluded that "concurrent comorbidities had the greatest prognostic impact among groups with the highest survival rate and the least impact in groups with the lowest survival rate."

It should be noted, however, that clinically-based studies often use all-cause mortality as the measured outcome, whether short-term (immediate post-operative) or longer-term. It is not always clear to what extent comorbidity influences or mediates cancer-specific survival (e.g. by influencing treatment choice or post-treatment complications).

Assessment of comorbidity, for the purposes of assessing patients' eligibility for specific treatments, can be somewhat subjective. Singh & Read (2004) reviewed available methods of objectively assessing "comorbid risk" in patients with localized prostate cancer, noting the potential for "personal bias" in treatment decisions unless such objective measures were used.

Socioeconomic factors

The potential influence on survival of material deprivation or other measures of socioeconomic status was not examined in this report. However, a previous analysis (NicAmhlaoibh *et al*. 2004) incorporated deprivation categories assigned to Irish cancer patients diagnosed during 1994-98. Those categories were based on a deprivation index assigned to small areas of residence (district electoral divisions or DEDs), using Population Census data (Small Area Health Research Unit 1997). Survival comparisons were made between patients from 'affluent', 'intermediate'; and 'deprived' areas. Deprived areas accounted for 21% of breast cancers, 22% of colorectal cancers, 31% of lung cancers and 19% of prostate cancers during 1994-98.

Having adjusted for other variables, the 1994-98 analysis found that cancer-specific mortality was 25% higher among breast cancer patients from deprived compared to affluent areas, and 15% higher among lung cancer patients from deprived areas. For colorectal and prostate cancers, deprivation did not significantly improve the fit of multivariate models, thus its influence on survival was not examined in detail. Unadjusted analyses of cancer-specific survival did provide some evidence of poorer survival among colorectal and prostate cancer patients from deprived areas.

Kogevinas & Porta (1997) reviewed 42 studies of social class differences in cancer survival, mainly from Europe and North America. They found that "patients in low social classes had consistently poorer survival than those in high social classes", regardless of the precise socioeconomic measures used. Mortality among patients of low versus high socioeconomic status was generally up to 50% higher. The widest differences were for cancers having a fairly good prognosis, such as cancers of the breast, corpus uteri, bladder and colon.

That review noted that lead-time bias could exaggerate the differences seen. Stage-specific comparisons would not necessarily be a solution, if

staging effort was influenced by socioeconomic factors. Length bias, whereby slower-growing tumours are more likely to be detected early, could also be relevant, if the aggressiveness of cancers differed between socioeconomic groups. Another potential bias considered was that causes of death might be less reliable for disadvantaged cancer patients. The latter group would also tend to be subject to more "competing causes" of death, but cause-specific analyses generally supported findings based on crude survival. Further research to quantify these potential biases was recommended.

Auvinen & Karjalainen (1997) provided a further review of potential explanations (including artifactual ones) for social class differences in cancer patient survival. They noted that, overall, "stage of disease at diagnosis appears to be the most important factor". Despite this, published studies did not provide clear-cut evidence that diagnostic delay was responsible for stage differences between social classes, nor that such delays necessarily influenced prognosis. The extent to which differences in stage explained survival differences also differed between cancers or studies. The role of treatment was also reviewed. Again, there was conflicting evidence from different studies as to the influence of treatment choice on social class differences in survival. The potential roles of treatment quality, and patients' compliance with treatment, were even more difficult to assess. Variations between social classes in the biology (e.g. aggressiveness) of tumours, in "host susceptibility" (of the patient) and in psychosocial factors were also considered, but no broad conclusions could be drawn. These authors concluded that social class differences in cancer survival were still only understood at a superficial level.

Potential problems in interpreting analyses of socioeconomic effects on both crude and cause specific mortality have been raised by various authors. Auvinen & Karjalainen (1997) suggested that the use of relative survival measures might improve comparisons between social groups, although it was noted that social-class-specific mortality data were not widely available.

One of the most detailed studies in this area examined relative survival of cancer patients in England and Wales (Coleman *et al*. 1999). Five deprivation categories were defined using the area-based Carstairs index of material deprivation. For correct comparison on relative survival between patients in different deprivation categories, deprivation-specific life tables were first constructed. The observed survival of patients from each category was compared with the expected survival of the general population in the same category; few previous studies had done this. Relative survival of cancer patients from affluent groups was found to be significantly higher for many cancers, compared with deprived groups. For the period 1981-90, for example, relative survival of patients from the most affluent compared to the most deprived group was 8-9 % points higher for breast cancer, 4-7 % points higher for colon and rectal cancers, 1 % point higher for lung cancer and 3-6 % points higher for prostate cancer. The factors involved were not directly assessed, but suggested possible explanations were: "longer delay in diagnosis or more advanced disease at diagnosis, worse general health or resistance to malignancy, different histological type or more aggressive disease, poorer access to optimal care, and lower compliance with treatment."

It was noted, however, that a number of other British studies of common cancers, including breast cancer, had found that stage of disease did not account for observed survival differences between deprivation categories (Carnon *et al*. 1994, Schrijvers *et al*. 1995).

Other prognostic factors

A range of other prognostic factors have been identified (Gospodarowicz *et al*. 2001), many reflecting molecular or other aspects of tumour biology. Such factors are increasingly being recorded as a routine part of diagnostic and prognostic investigations. Oestrogen and progesterone receptor status for breast cancer is one of the better-known examples, though was not available for most of the years considered in this report.

Table 7.1 Summary of the influence of patient and tumour characteristics on relative survival of cancer patients diagnosed during 1994-2001: significantly better (↑) or poorer (↓) survival, or no difference (=), compared with baseline group for each characteristic. Findings here are based on multivariate analyses that also included region of residence and year of diagnosis, and indicate the independent effect of each variable after adjustment for other variables.

	Breast cancer	**Colorectal cancer**	**Lung cancer**		**Prostate cancer**
age 15-44 [a]	.	.	.	age 15-54 [a]	.
age 45-54	=	=	↓	age 55-64	=
age 55-64	↓	↓	↓	age 65-74	↓
age 65-74	↓	↓	↓	age 75-84	↓
age 75+	↓	↓	↓	age 85+	↓
male	.	.	.		.
female	.	↑	↑		.
T1 [a]	.	.	.	T1	.
T2	↓	=	↓	T2	=
T3	↓	↓	↓	T3	=
T4	↓	↓	↓	T4	↓
T X	↓	↓	↓	T X	↓
N negative [a]	.	.	.	N negative	.
N positive	↓	↓	↓	N positive	↓
N X	↓	↓	↓	N X	↓
M negative [a]	.	.	.		.
M positive	↓	↓	↓		↓
M X	↓	↓	↓		↓
grade 1 [a]	.	.	.		.
grade 2	=	=	=		=
grade 3+	↓	↓	↓		↓
grade X	↓	↓	↓		↓
ductal/lobular	.	.	.		.
other adenocarc	=	.	.		.
other carcinoma	=	.	.		.
carcinoma NOS	↓	.	.		.
cancer NOS	↓	.	.		.
other cancer	=	.	.		.
non-small-cell	.	.	.		.
small-cell	.	.	=		.
other/NOS	.	.	↓		.
MV yes	.	.	.		.
MV no	.	↓	.		↓
MV X	.	↓	.		↓
symptomatic	.	.	.		.
incidental	↓	=	↑		↑
screen detected	↑	↑	↑		=
presentation X	↑	↑	↑		↑
non-smoker	.	.	.		.
ex-smoker	=	↓			↓
smoker	↓	↓	↓		↓
smoking status X	↓	↓	↓		
ever married	.	.	.		.
never married	.	↓	↓		↓
marital status X	.	=	=		=

[a]For these variables and cancers, results are based on the first year of follow-up only, as longer-term patterns are too complex to summarize.
. Reference (baseline) group, or no comparison available for this variable (or specific category).

7.6 Comparison of final multivariate models for regional variation in survival between this report and NicAmhlaoibh *et al*. (2004)

The geographic patterns of relative survival found for the period 1994-97 in the current report, based on relative survival modelling adjusted for tumour and patient characteristics, were broadly consistent with those found in a previous NCR analysis (NicAmhlaoibh *et al*. 2004), which covered a similar period. Apparent differences in 'fully adjusted' regional patterns between the current and earlier report (*Tables 7.2-7.5* below) may reflect a number of factors.

These include (to a lesser or greater extent):

- Differences in precise diagnosis years covered; the closest comparison is between the previous report and diagnosis period 1994-97 in the current report.
- Differences in completeness of follow up; cases diagnosed during 1994-98 had follow-up to 31 December 2001 in the previous report (incorrectly stated there as 1 January 2000), i.e. some cases had less than 4 years of follow-up available; cases diagnosed during 1994-97 had follow-up to 31 December 2003 in the current report (i.e. a full five years of follow-up for all cases).
- Differences in patient characteristics considered for inclusion in the statistical models used; most notably, the potential influences on survival of comorbidity (derived from hospital in-patient data) and area-based deprivation measures examined in the previous analysis for some cancers but not here.
- Differences in the precise mortality parameters included in models; cause-specific mortality was used in the previous report, excess mortality assessed by comparison with background mortality in the current report, although these are in essence alternative approaches to measuring the same basic parameter (i.e. the extra mortality among cancer patients attributable to their cancer).
- Differences in inclusion criteria between reports; although these were largely the same, the previous report excluded all patients who had more than one serious cancer, whereas the current report, for consistency with EUROCARE criteria, includes those patients (but only for their first serious cancer).
- Differences in age-groups used for adjustment of models; the previous report used age-groups $\leq$40, 41-50, 51-60, 61-70, 71-80 and 80+ years); the current report uses age-groups 15-44, 45-54, 55-64, 65-74 and 75+ years for breast, colorectal and lung cancers, and 15-54, 55-64, 65-74, 75-84 and 85+ years for prostate cancer (EUROCARE age-groups).
- Differences in coding for other variables; for example, the previous report distinguished N categories 0, 1, 2, 3 and unknown for breast cancer, but the current report simplified this to N negative, N positive or unknown, to minimize the complexity of models.
- Random or unpredictable differences, resulting less directly from the above factors or other minor differences in datasets.
- Differences in presentation of results for colorectal cancer; specifically, the previous report did not report results of a combined model for both sexes, thus direct comparison between reports is not possible.

However, for most cancer/region combinations the cause-specific and excess mortality hazard ratios, compared to patients from the Eastern region, differ mainly in magnitude or statistical significance, rather than qualitatively. In no instance for the most directly comparable years (1994-98 / 1994-97) were cause-specific and excess hazard ratios both contradictory and significant. Overall (except for colorectal cancer as far as can be judged), there was a tendency for the previous reports' analyses to 'explain' more of the regional variation during comparable diagnosis periods. Possibly this reflects adjustment for comorbidity or deprivation measures in the previous analysis, although other factors such as those listed cannot be ruled out. Nor does it follow that one or other analysis necessarily allows the 'correct' explanation or interpretation of geographic patterns seen. As noted earlier, there potential additional problems posed by, for example, incomplete availability of data for some variables, or inconsistency of data-definitions between patient groups.

A fuller analysis of the data is planned, incorporating more complete information on comorbidity and deprivation than was possible previously. However, we would reiterate a caution made earlier regarding deprivation. A patient's socioeconomic background may 'predict' or explain their survival to some extent, but it is arguable that this is an inadequate explanation that does not capture the underlying factors influencing survival.

Table 7.2 Comparison of regional patterns of mortality risk among breast cancer patients between this report (relative survival) and a previous analysis of 1994-98 data (cause-specific survival). Hazard ratios shown are from 'full' models adjusted for patient and tumour characteristics; statistically significant hazard ratios are shown in bold.

Region	[a]CSHR (95% CI) 1994-98 NicAmhlaoibh *et al*. 2004	[b]EHR (95% CI) 1994-97 this report	EHR (95% CI) 1998-2001 this report	EHR (95% CI) 1994-2001 this report
E	1.000	1.000	1.000	1.000
M	1.076 (0.836-1.384)	1.171 (0.908-1.510)	**1.379** (1.068-1.780)	**1.277** (1.068-1.527)
MW	1.122 (0.885-1.421)	0.986 (0.800-1.216)	1.240 (0.979-1.570)	1.069 (0.914-1.250)
NE	1.144 (0.915-1.431)	**1.240** (1.000-1.537)	1.015 (0.796-1.293)	1.139 (0.971-1.336)
NW	0.960 (0.751-1.226)	1.134 (0.897-1.434)	0.973 (0.742-1.277)	1.066 (0.894-1.271)
S	**1.332** (1.123-1.581)	**1.242** (1.052-1.466)	1.067 (0.878-1.297)	**1.162** (1.025-1.317)
SE	0.955 (0.774-1.179)	1.146 (0.944-1.392)	**1.407** (1.142-1.735)	**1.222** (1.061-1.407)
W	1.127 (0.915-1.387)	**1.239** (1.022-1.503)	**1.332** (1.067-1.662)	**1.262** (1.093-1.457)

[a]CSHR = cause-specific hazard ratio. [b]EHR = excess hazard ratio (based on relative survival).

Table 7.3 Comparison of regional patterns of mortality risk among colorectal cancer patients between this report (relative survival) and a previous analysis of 1994-98 data (cause-specific survival). Hazard ratios shown are from 'full' models adjusted for patient and tumour characteristics.

Region	CSHR (95% CI) 1994-98 NicAmhlaoibh *et al*. 2004		EHR (95% CI) 1994-97 this report	EHR (95% CI) 1998-2001 this report	EHR (95% CI) 1994-2001 this report
	female	male	sexes combined	sexes combined	sexes combined
E	1.000	1.000	1.000	1.000	1.000
M	0.884 (0.678-1.153)	**1.357** (1.086-1.693)	1.036 (0.870-1.233)	1.111 (0.922-1.338)	1.066 (0.939-1.210)
MW	**1.306** (1.023-1.667)	**1.238** (1.024-1.497)	1.069 (0.906-1.261)	**1.269** (1.092-1.474)	**1.152** (1.032-1.286)
NE	0.918 (0.732-1.149)	0.952 (0.786-1.153)	0.873 (0.747-1.020)	0.995 (0.860-1.151)	0.917 (0.825-1.020)
NW	1.065 (0.850-1.333)	1.144 (0.945-1.386)	1.015 (0.873-1.179)	1.093 (0.926-1.291)	1.038 (0.929-1.160)
S	1.028 (0.872-1.213)	**1.305** (1.133-1.504)	**1.327** (1.188-1.483)	**1.145** (1.019-1.286)	**1.240** (1.145-1.343)
SE	1.004 (0.825-1.221)	**1.214** (1.035-1.425)	1.125 (0.991-1.276)	1.071 (0.935-1.227)	**1.100** (1.003-1.206)
W	1.133 (0.931-1.379)	1.073 (0.916-1.257)	1.114 (0.978-1.269)	0.955 (0.832-1.096)	1.027 (0.935-1.129)

Table 7.4 Comparison of regional patterns of mortality risk among lung cancer patients between this report (relative survival) and a previous analysis of 1994-98 data (cause-specific survival). Hazard ratios shown are from 'full' models adjusted for patient and tumour characteristics.

Region	CSHR* 1994-98 NicAmhlaoibh *et al*. 2004	EHR (95% CI) 1994-97 this report	EHR (95% CI) 1998-2001 this report	EHR (95% CI) 1994-2001 this report
E	1.000	1.000	1.000	1.000
M	0.935	0.903 (0.786-1.037)	0.931 (0.818-1.059)	0.924 (0.841-1.015)
MW	0.963	**0.856** (0.762-0.961)	**0.868** (0.777-0.969)	**0.871** (0.804-0.943)
NE	0.947	**0.857** (0.764-0.960)	1.104 (0.991-1.229)	0.976 (0.903-1.055)
NW	0.914	**0.835** (0.739-0.944)	**0.872** (0.773-0.983)	**0.855** (0.785-0.931)
S	0.954	0.969 (0.888-1.058)	0.973 (0.892-1.061)	0.978 (0.919-1.039)
SE	1.082	0.968 (0.877-1.069)	**1.119** (1.014-1.235)	1.035 (0.966-1.109)
W	**0.874**	**0.785** (0.705-0.875)	**0.894** (0.804-0.994)	**0.839** (0.779-0.905)

* 95% CIs for 1994-98 analysis were incorrectly shown in the previous report and are not repeated here.

Table 7.5 Comparison of regional patterns of mortality risk among prostate cancer patients between this report (relative survival) and a previous analysis of 1994-98 data (cause-specific survival). Hazard ratios shown are from 'full' models adjusted for patient and tumour characteristics.

Region	CSHR (95% CI) 1994-98 NicAmhlaoibh *et al*. 2004	EHR (95% CI) 1994-97 this report	EHR (95% CI) 1998-2001 this report	EHR (95% CI) 1994-2001 this report
E	1.000	1.000	1.000	1.000
M	1.063 (0.859-1.316)	1.098 (0.843-1.429)	1.139 (0.827-1.569)	1.128 (0.923-1.377)
MW	1.108 (0.903-1.360)	0.934 (0.728-1.198)	**1.544** (1.152-2.069)	1.104 (0.913-1.335)
NE	0.915 (0.744-1.125)	0.845 (0.655-1.090)	**1.472** (1.111-1.949)	1.072 (0.889-1.292)
NW	1.064 (0.868-1.305)	0.869 (0.670-1.126)	1.038 (0.777-1.386)	0.934 (0.772-1.129)
S	1.128 (0.955-1.332)	**1.231** (1.003-1.511)	**1.350** (1.075-1.696)	**1.248** (1.073-1.450)
SE	0.950 (0.794-1.137)	0.921 (0.738-1.151)	**1.387** (1.072-1.794)	1.086 (0.919-1.284)
W	0.916 (0.768-1.093)	**0.725** (0.580-0.908)	1.239 (0.958-1.604)	0.894 (0.755-1.057)

7.7 Time-trends in treatment

The proportion of patients receiving any tumour-directed treatment showed no significant trend for breast cancer during 1996-2001, increased for lung and to a lesser extent colorectal cancer, and fell slightly for prostate cancer. Use of surgical treatment increased slightly for breast cancer, fell slightly for lung and to a lesser extent colorectal cancers, and fell more markedly for prostate cancer. Radiotherapy use increased markedly for prostate and colorectal (especially rectal) cancers, and to a lesser extent for lung cancer, but showed no trend for breast cancer. For breast cancer, the recorded use of hormonal treatment fell substantially, nationally and in all regions of residence, at the same time as a significant increase in the use of chemotherapy. Chemotherapy use also increased substantially for colorectal and lung cancers, and use of hormonal treatment increased moderately for prostate cancer.

Trends in treatment appeared to be broadly in line with expectations of greater or better-targeted use of radiotherapy and chemotherapy. A notable exception was the lack of an increase in radiotherapy use for breast cancer. Reduced use of hormonal treatment for breast cancer may also be in line with expectations of improved targeting of appropriate treatment. This may also apply to increased use of hormone therapy and reduced use of surgery for prostate cancer.

In many instances, the trends during 1994-2001 as a whole are consistent with those during the shorter period 1996-2001. However, we have focused on trends during the latter period, to minimize biases resulting from possible under-recording of treatments in earlier years. Such bias might have arisen as, in the first year or two of National Cancer Registry operation, collection of treatment data largely targeted the first four months after diagnosis, although in practice many later treatments were also recorded.

7.8 Regional variation in treatment

As noted in an earlier report (NicAmhlaoibh *et al*. 2004), there was clear regional variation within Ireland in the proportions of patients receiving particular treatment modalities. This applied both overall (1994-2001) and during earlier (1994-97) and more recent (1998-2001) diagnosis periods. For a given cancer type, regional variations were not necessarily the same for different treatment modalities. In general, there patients from a given region were relatively more likely to receive particular treatment modalities compared with others. To some extent, such regional variations may have been 'compensatory', if different treatment modalities or combinations of modalities of broadly equivalent effectiveness were used. Thus overall treatment varied less between regions than did individual treatment modalities. Nevertheless, given the range of variation seen for some cancers and modalities, it is likely that patients from some regions received, on average, more appropriate or less appropriate treatment compared with other regions.

Objectively comparing the 'quality' of treatment, in relation to best international practices and national or international recommendations, however, will require further work – not least to agree the standards for comparisons. Ireland's involvement in the European Cancer Health Indicators Project (EUROCHIP) should provide a good basis for such comparisons (cf. http://www.tumori.net/eurochip/).

The data available for this analysis did not allow direct assessment of the reasons why particular patients did or did not receive particular treatment modalities. However, it was possible to model and adjust for the effects of a number of relevant patient and tumour variables, but note the cautions expressed earlier. For most of the regional

comparisons presented, adjustment for the available 'explanatory' and prognostic data did not fully remove the regional variation seen. In part, this may be because a high proportion of cases were missing data for given variables. Another possible explanation is that unmeasured factors relating to patient's condition or comorbidity, or their willingness to accept treatment, may have varied regionally. Regional variation in the 'choice' of treatments preferred or offered by clinicians – whether related to local availability of services or otherwise – could also be involved.

It may be relevant that case with "unknown" values for a given tumour or patient variable tended to be less likely to receive treatment than cases with known values. Among other possibilities, this could indicate that many such patients were considered too ill or too old for treatment or detailed investigations. The interplay between treatment and the completeness or quality of diagnostic or prognostic information also complicates interpretation of 'adjusted' analyses.

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Appendix 1 Standard treatments for breast, colorectal, lung and prostate cancer, adapted from the US National Cancer Institute's PDQ Cancer Information Summaries.* Non-standard treatments that are subject to further evaluation in clinical trials are not shown.

Cancer site	Prognostic group[a]	Surgery	Radiotherapy	Chemotherapy	Hormone	combinations[b]
Breast	*stages I-IIIA ,operable IIIC:*					
	local-regional, node negative, low risk	cur, cur'	adj		adj	s, sr, sh, srh
	local-regional, node negative, intermediate risk	cur, cur'	adj	adj	adj	s, sr, sh, sch, srh, srch
	local-regional, node negative, high risk	cur, cur'	adj	adj	adj	s, sr, sc, sh, sch, src, srh, srch
	local-regional, node positive	cur, cur'	adj	adj	adj	s, sr, sc, sh, sch, src, srh, srch
	IIIB, inoperable IIIC, IV:					
	IIIB, IIIC or inflammatory	cur'	adj	adj	adj	scr, schr
	IV	pal	pal	pal	pal	c, h, ch, cr, cs, hs, chr, chs
Colon	stage I	cur				s
	stage II	cur				s
	stage III	cur'		adj		sc
	stage IV	(pal), (cur)	(pal)	pal		s, r, c
Rectum	stage I	cur, cur'	(cur), adj	adj		s, r, src
	stage II	cur'	adj	adj		src
	stage III	cur'	adj, pal	adj, pal		rc, src
	stage IV	pal, (cur)	pal	pal, adj		s, c, sc, cr
Lung	*non-small-cell:*					
	stage I	cur, cur'	cur	adj		s, r, sc
	stage II	cur, cur'	cur	adj		s, r, sc
	stage IIIA	cur, cur'	cur, adj	adj		s, r, cr, sr, scr
	stage IIIB	cur'	cur, adj, (pal)	cur, adj		c, r, cr, scr
	stage IV		pal	cur		c, r
	small-cell:					
	limited stage	cur'	adj	cur, adj		c, cr, sc, scr
	extensive stage		adj, pal	cur, adj		c, r, cr
Prostate[c]	stage I	cur, cur'	cur, adj			s, r, sr
	stage II	cur, cur'	(adj)		adj	s, r, sh, rh
	stage III	cur, pal	cur, adj, pal		cur, adj, pal	s, r, h, rh
	stage IV	pal	cur, adj, pal		cur, adj	s, r, h, sr, rh, srh

cur = curative (as single modality); cur' = curative surgery in combination with other treatment modalities;
adj = adjuvant (curative or prophylactic, in combination with surgery or other treatment modalities);
pal = palliative (primarily for symptom relief, as single modality or in combination); ( ) = in selected patients.
aStage groupings are based on the 6th edition of the TNM staging scheme.
[b]Main combinations (or single-modality treatments): surgery etc (s), radiotherapy (r), chemotherapy etc (c), hormone therapy (h); combinations shown are not necessarily complete lists.
[a] For prostate cancer, "careful observation without further immediate treatment" is also standard for stage I.
*http://www.cancer.gov/cancertopics/pdq/cancerdatabase