

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.

1994-2001	annual average numbers	age-standardized rate ^a
	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

^aEuropean age-standardized rate per 100,000 persons per year.

^bEstimated 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%

^aAge-groups used for this cancer differ from those for other cancers in this report. ^bUnknown values shown as "X" for stage and other variables. ^cMV = 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%)

^aAge-groups used for this cancer differ from those for other cancers in this report.

^bUnknown 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.

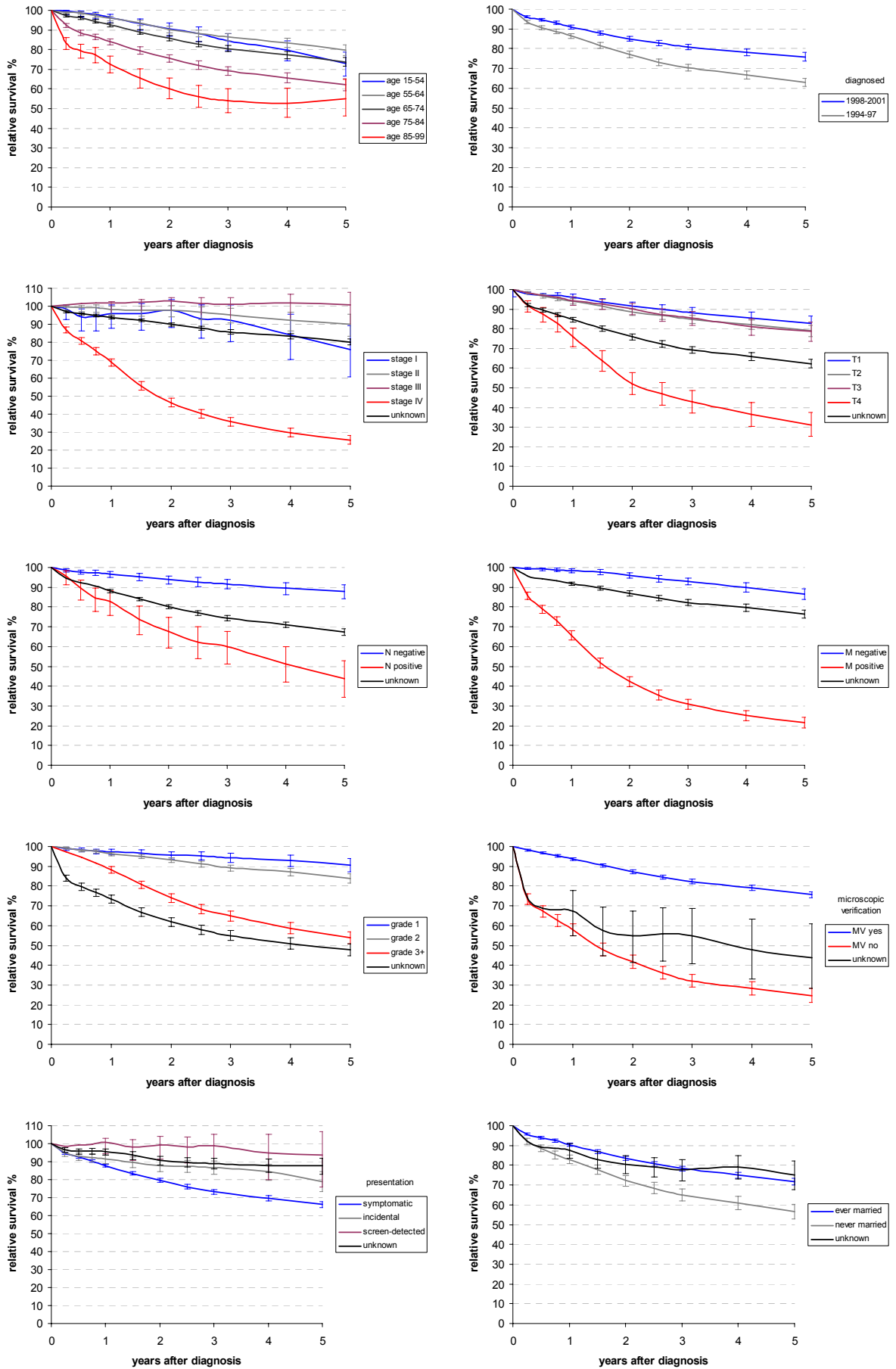


Figure 6.3.1 Relative survival up to five years after diagnosis for prostate cancer patients diagnosed during 1994-2001: variation by patient and tumour characteristics. 95% confidence intervals are shown.

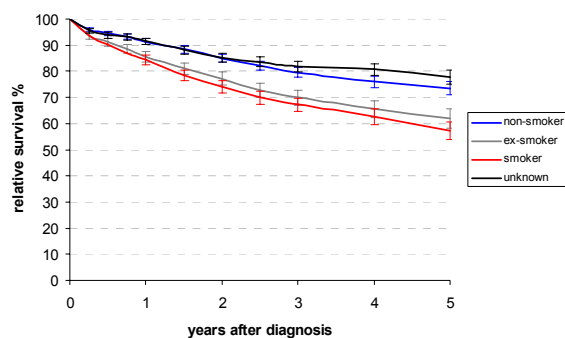


Figure 6.3.1 (continued)

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	
	^aEHR (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

^aEHR = 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.

^bSee Table 6.4.2 but region and diagnosis year excluded here.

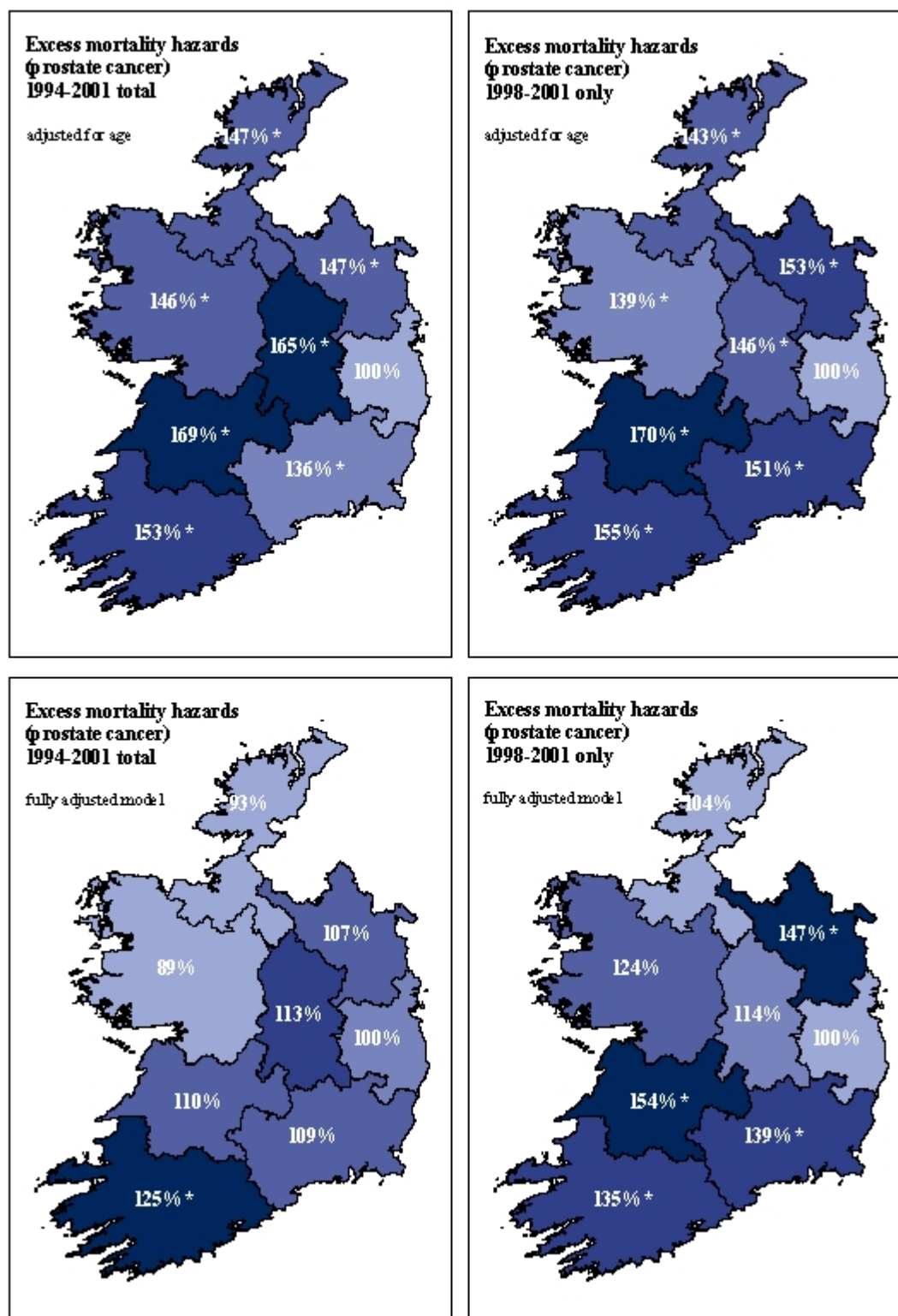


Figure 6.4.1 Regional variation in excess mortality hazards (based on relative survival) for prostate cancer, expressed in comparison with patients from the Eastern region (100%): 1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See Table 6.4.2 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 ^a EHR (95% CI)	P	1994-1997 EHR (95% CI)	P	1998-2001 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

^aEHR = 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.

^bModels 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.

^cAge-categories (specific to for prostate cancer): EURO CARE age-groups 15-54, 55-64, 65-74, 75-84, 85+.

^dStage-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.

^eFinal (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					total	1994-97	1998-2001	
	age 15-54	55-64	65-74	75-84	85+		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%	*

^aSurgery 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 where treated	Region of residence																		
	1994-2001 total										1998-2001 subtotal								
	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	*

^aSurgical 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	

^aSurgical 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%

^aSee *Table 6.5.1* for a further breakdown by age, for the overall period 1994-2001.

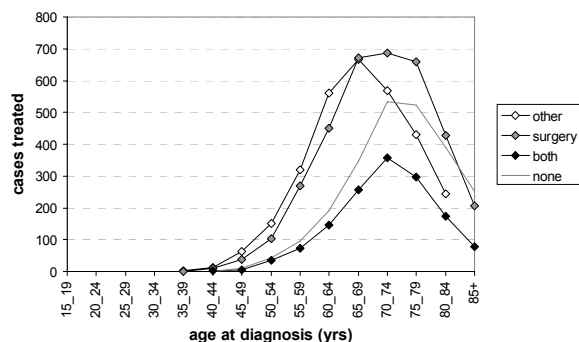


Figure 6.5.1 Age-profiles for tumour-directed treatments within six months of diagnosis for prostate cancer cases diagnosed 1994-2001: numbers of cases having surgery (only), other treatments (radiotherapy, chemotherapy or hormone therapy but not surgery), both surgery and other treatments, or no treatment.

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).

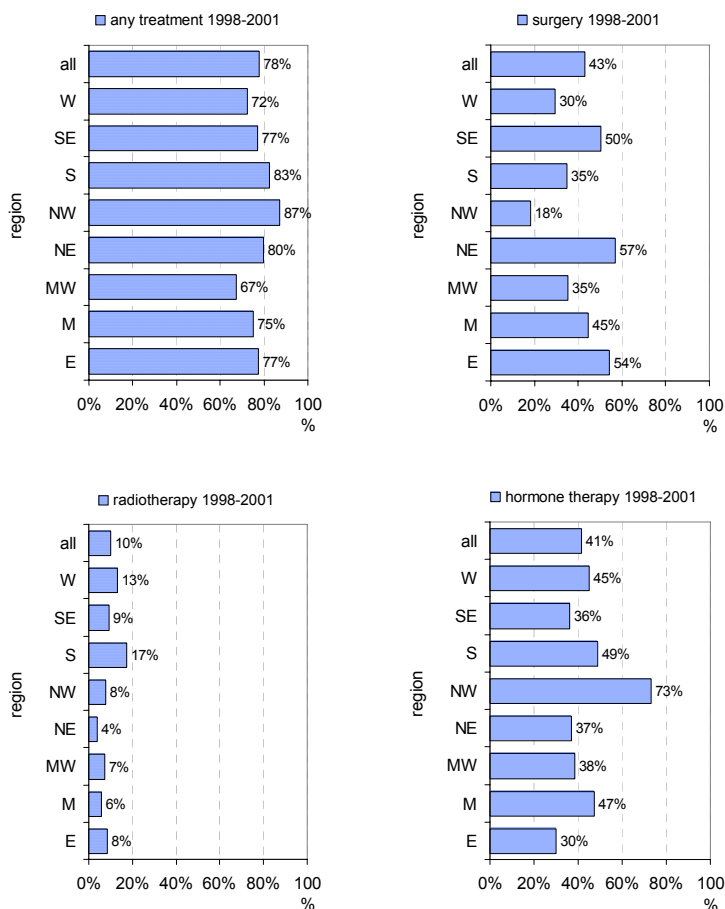


Figure 6.5.2 Percentage of prostate cancer cases having tumour-directed treatment within six months of diagnosis, by region of residence, 1998-2001.

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

^aRisk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).

^bUnknown 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	0.797 (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		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	1.117 (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 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

^aRisk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).

^bT 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 ^a RR (95% CI)	P	1994-1997 RR (95% CI)	P	1998-2001 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

^aRisk ratios derived from adjusted odds ratios using the method of Zhang & Yu (1998).

^bAge-group 15-54, 55-64, 65-74, 75-84, or 85+.

^cGrade 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.

^dAge-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.

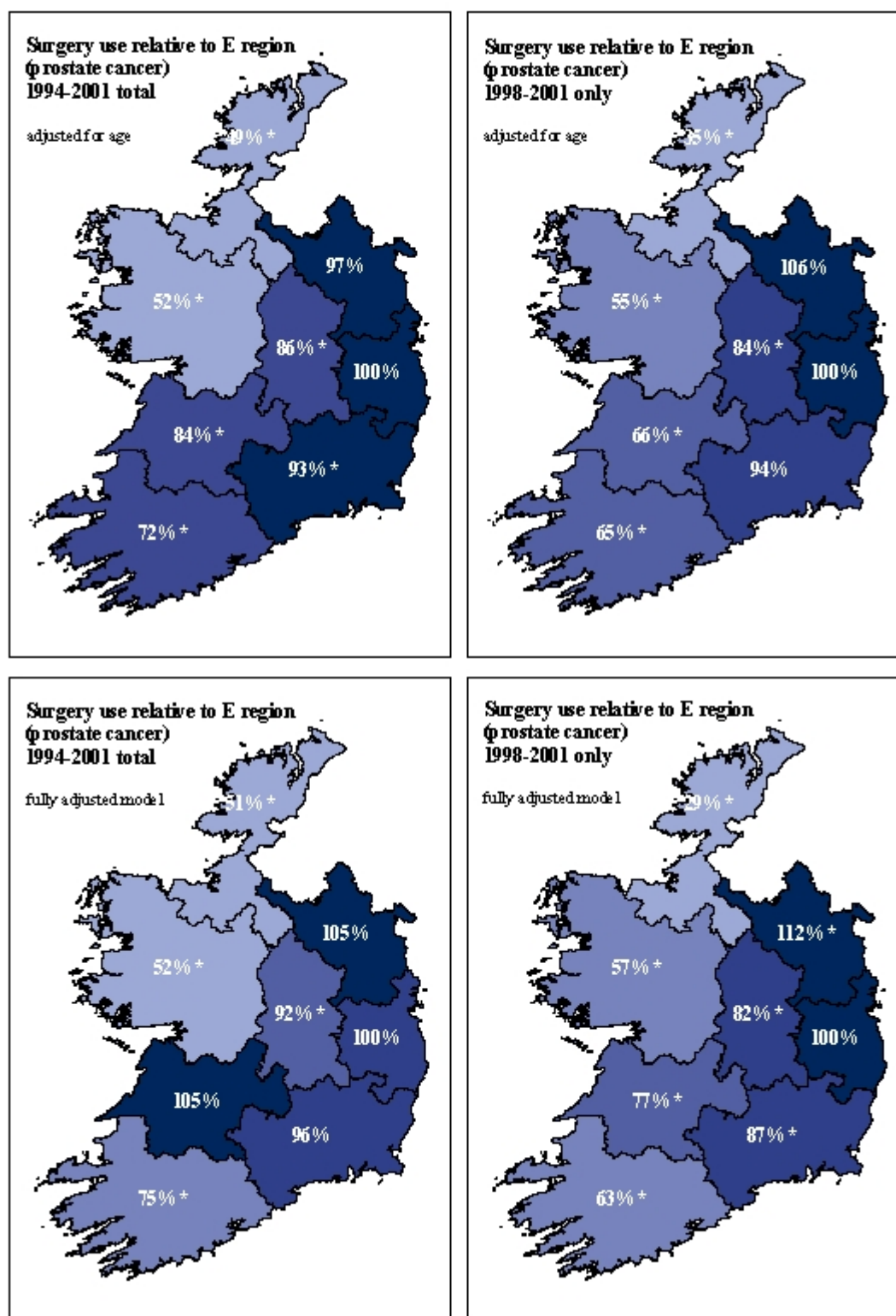


Figure 6.6.1 Regional variation in surgical treatment for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%): 1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.10* for further details. * = 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 ^a RR (95% CI)	P	1994-1997 RR (95% CI)	P	1998-2001 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*.

^dAge-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.

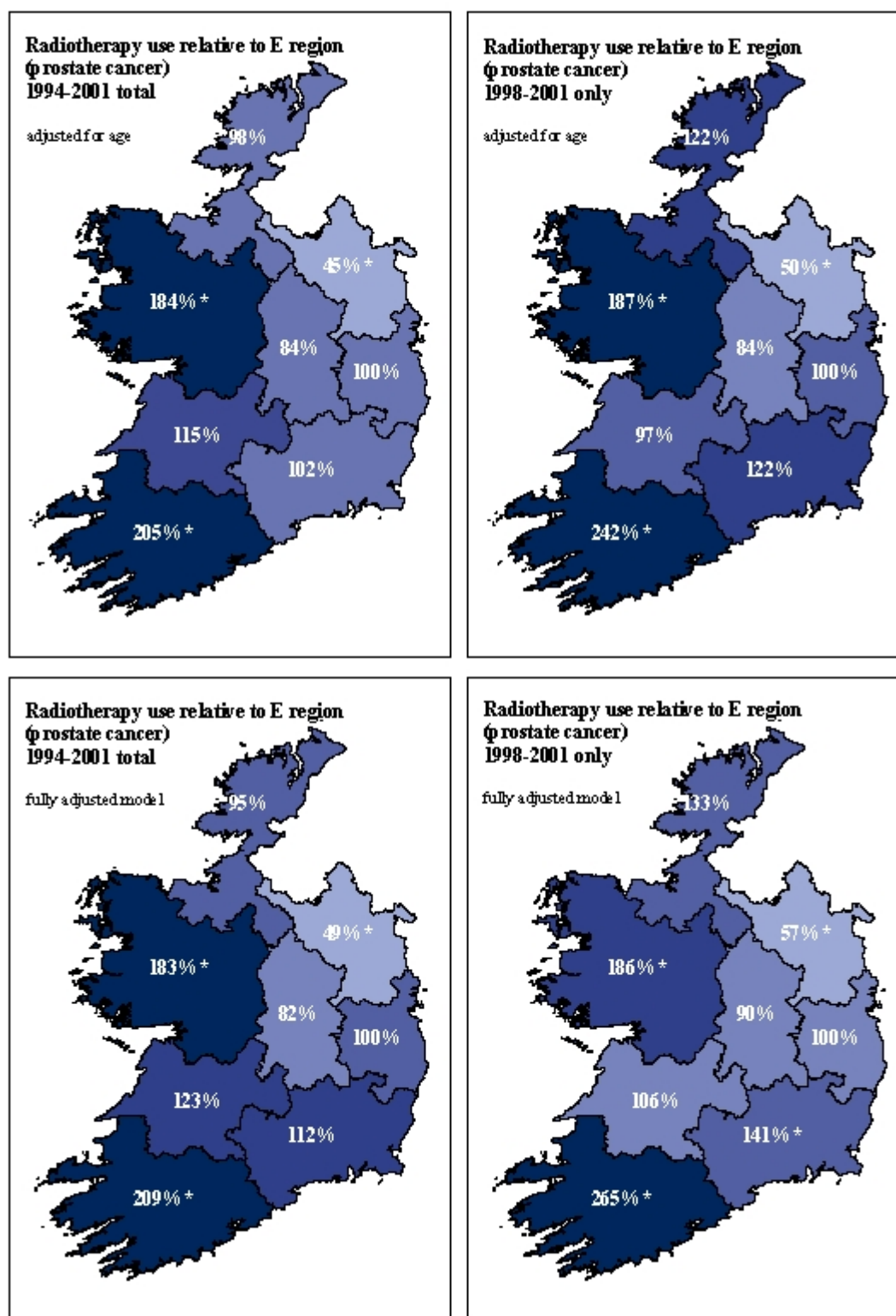


Figure 6.6.2 Regional variation in radiotherapy for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%): 1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.11* for further details. * = significantly 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 ^a RR (95% CI)	P	1994-1997 RR (95% CI)	P	1998-2001 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.

^dAge-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.

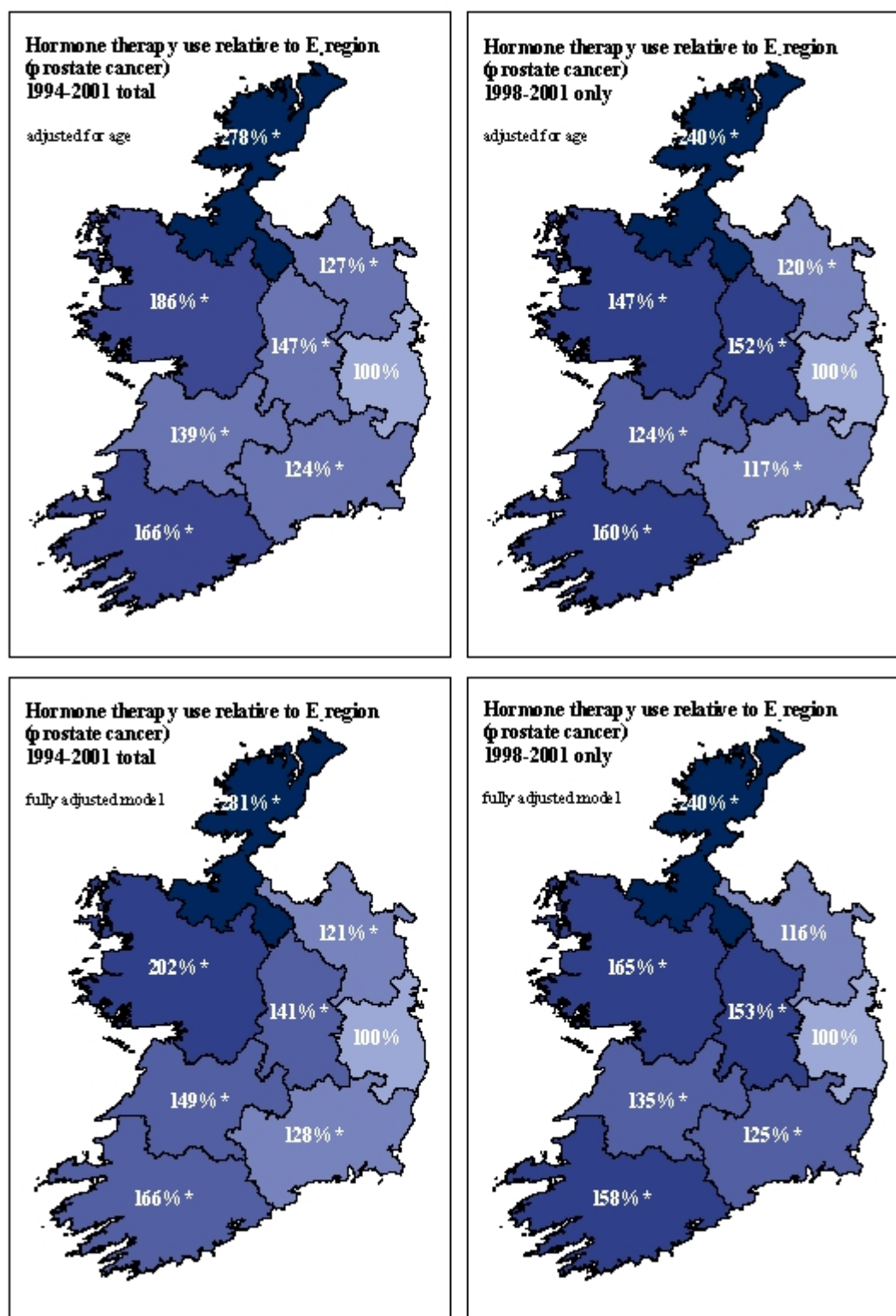


Figure 6.6.3 Regional variation in hormonal therapy for prostate cancer, expressed as risk ratios compared with patients from the Eastern region (100%): 1994-2001 total (left), 1998-2001 (right); basic age-adjusted model (top), fully-adjusted model (bottom). See *Table 6.6.12* for further details. * = 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	
	^aRR (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.

^dAge-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		Ireland 1998-2001		Europe 1990-94 ^b	
	5-yr survival (95% CI)		survival (95% CI)		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%]

^aCapocaccia *et al.* (2003) and unpublished. ^bEUROCARE-3: Sant *et al.* (2003). ^cRange 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,c} 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%	-	≥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.

^aSource 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>.

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^bUS 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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