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CANCER OUTCOMES MONITORING

CANCER TREATMENT POLICIES & THEIR EFFECTS ON SURVIVAL

Central Nervous System

KEY SITES STUDY 1

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CANCER TREATMENT POLICIES & THEIR EFFECTS ON SURVIVAL

Central Nervous System

Report Produced by

NY CRIS *Northern and Yorkshire*
Cancer Registry and Information Service
within the Leeds Teaching Hospitals NHS Trust

CANCER OUTCOMES MONITORING

in collaboration with the
Research School of Medicine
University of Leeds

Key Sites Study Funded by the NHS R&D Program for Cancer

KEY SITES STUDY

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2 INTRODUCTION

2.1. FOREWORD

2.1.1. CNS Tumours

Tumours of the central nervous system (CNS) account for 1.3% of malignancies. The cumulative risk for an individual developing a CNS tumour from birth to the age of 74 is approximately 0.5%, or 1 in every 200. From a general practice perspective, CNS tumours are uncommon; a general practitioner will see, on average, one new case every 8.6 years. The diagnosis of a CNS tumour causes considerable distress to both the patient and the patient's family. Timely diagnosis and referral to a specialist centre for multi-disciplinary manage-ment are important, although difficulties may arise because early symptoms can be vague.

Recommended management of CNS tumours varies according to the histological type of the lesion. For example, it is accepted that a high proportion of meningiomas may be removed surgically, without the need for further therapy, whilst gliomas, the most common type of brain tumour, may require post-operative radiotherapy. Generally, radiotherapy is recommended for gliomas of high grade. There is, however, no randomised clinical trial evidence to support its use in the treatment of low grade gliomas and differences in opinion regarding the value of radiotherapy still exist today. In the past, this lack of consensus may have resulted in variation in the management of patients with low grade glioma, potentially having an impact on survival. The actual extent of such variation in practice and the influence on survival has never been assessed.

2.1.2. Key Sites Study

This report contains the results of a retrospective study of population-based data collected by the Northern and Yorkshire Cancer Registry and Information Service. The aim of this work was to investigate, as far as possible, the degree of variation in the management of patients with primary tumours of the CNS in the former Yorkshire Region between the years 1986 and 1994, and to determine the impact of any variation on survival. A combination of descriptive analysis of treatment patterns, along with survival and multivariate analyses have been performed.

The formation of NYCRIS and the integration of the Northern and Yorkshire Cancer Registries occurred in 1997 but only data collected by the former Yorkshire Cancer Registry have been analysed in this work. The CNS study forms part of a larger project, funded by the NHS R&D Programme for Cancer, which investigates variation in the management of a number of common cancers managed between 1986 and 1994. Long term follow-up (survival up to five years from diagnosis) was an important component of the analysis, and retrospective methodologies were essential. The results in this report should not, therefore, be viewed necessarily as a reflection of current practices.

2.1.3. Calman-Hine

The Calman-Hine report recommended a uniformly high standard of management for all patients with cancer, and the establishment of cancer centres and units requires evidence-based decision-making regarding the optimal structuring of cancer services. The results of a study such as this may provide both a valuable starting point for establishing standards to be achieved in a cancer centre, and may also provide important evidence in support of decision-making surrounding the provision of cancer services.

2.2. EXECUTIVE SUMMARY

2.2.1. Tumours of the Central Nervous System

During the period 1986-94, approximately 330 new patients with cancers of the central nervous system were diagnosed annually in Yorkshire (8.3 new patients per 100,000 population). The incidence rate has increased slightly in more recent years but this may be due to improved diagnosis. Of the 2948 cases diagnosed during the study period, 2245 (76%) have been considered for more detailed review: 651 meningiomas and nerve sheath tumours, 281 lower grade gliomas and 1313 higher grade gliomas. Data for each of these groups are presented separately in this report

Most patients (1911/2245, 85%) in the review group were treated at one of the three regional specialist neurosurgical centres, based in Leeds (LGI), Wakefield (Pinderfields) and Hull (Hull Royal Infirmary) and nearly all of these (1852/1911, 97%) were managed by a neurosurgeon. Patients not referred to one of the specialist centres were significantly older than those who were referred and most were managed by geriatricians or general physicians. Of the 1594 patients with glioma, 952 (60%) were referred to one of the two regional radiotherapy centres, based in Leeds (Cookridge) and Hull (Princess Royal). Data for each of the three specialist centres and the two radiotherapy centres are presented anonymously in this report.

2.2.2. Meningiomas & Nerve Sheath Tumours (M&N)

Most patients (87%) were treated with definitive surgery (which is defined as either surgery with curative intent, or the maximum safe macroscopic resection possible), although there was some decrease in the use of surgery over the age of 60 years. There was no tendency for the surgical rates to change over time or to vary between the specialist centres. The proportion of patients receiving no treatment was slightly higher at Centre 1 (7%) compared with Centres 2 (4%) or 3 (2%) but patients at Centre 1 were also significantly older than those at the other two centres. Radiotherapy was used in less than 2% of these patients.

The overall survival of patients, diagnosed in the period 1986-90, was 74% at five years. There was a highly significant five-year survival difference between patients who received definitive surgery (77%) and those who received no surgery (17%). The survival of patients managed at Centre 1 was significantly poorer than those managed at the other two centres. This was still the case after adjusting for patient age and other case mix factors. However information regarding performance status and precise details of tumour site were unavailable for analysis. It is possible that factors such as these could contribute to the differences observed in survival by centre.

2.2.3. Glioma Grades I & II (GL)

Over half of all patients (56%) were treated with definitive surgery and a further third (33%) had a brain tumour biopsy. The proportion of untreated patients increased over the age of 60 years. More patients at Centre 1 were treated with definitive surgery (77%) compared to Centres 2 (52%) or 3 (51%) while less had a biopsy (13% compared with 40 and 44% respectively). Over half of all patients (58%) received radiotherapy, nearly always in combination with surgery (either definitive or biopsy). Substantially less patients treated at Centre 1 received radiotherapy (36%) compared with patients treated at Centres 2 (75%) or 3 (71%). This difference between centres in the use of radiotherapy did not appear to be due to differences in the age distribution of patients and it was evident over the entire study period, although less marked in more recent years. During the study period, the overall use of radiotherapy increased from 51% to 61% of patients while the proportion receiving no treatment decreased from 13% to 4%.

The overall survival of patients, diagnosed in the period 1986-90, was 42% at five years. Those patients having received radiotherapy (with or without definitive surgery) displayed improved survival at two years by about 25% but showed no advantage by five years. Two-year survival

at Centre 1, which had the lowest radiotherapy referral rate, was 25% lower than at the other two centres although, by five years, there was no significant difference between the centres. After allowing for case mix factors, survival was found to be significantly better for those patients who received definitive surgery in combination with radiotherapy, compared with all other treatment combinations. After adjusting for casemix and post operative mortality, there was no difference in survival of patients who were given definitive surgery with radiotherapy and those who received definitive surgery alone. Clinical trial evidence has also proved inconclusive in assessing the optimal management of this group.

2.2.4. Glioma Grades III & IV (GH)

Fifty percent and 27% of this group of patients had definitive surgery or a tumour biopsy respectively and 48% received radiotherapy, nearly always in combination with surgery. A substantial proportion (32%) of patients over the age of 60 years received no treatment.

There was less variation in management policies between the three centres in comparison with the lower grade tumours. A smaller proportion of patients received definitive surgery at Centre 2 (55% compared with 63 and 68%) and less biopsy procedures were used in Centre 1 (17% compared with 31 and 34%) but a very similar proportion of patients at all three centres received radiotherapy. Over the study period the proportion of patients receiving radiotherapy increased from 42% to 55% while the proportion of untreated patients decreased from 28% to 12%. The differences in rates of surgery and biopsy procedures between centres were reduced over time but whereas patients treated at Centres 2 or 3 were more likely to be treated with radiotherapy towards the end of the study period, this increase was not seen at Centre 1.

The overall survival of patients, diagnosed in the period 1986-90, was 10% at five years. Radiotherapy (with or without definitive surgery) improved survival at one year by about 20% and at two years by 5-10% but showed no advantage by five years. There were no significant differences in survival between patients managed at each of the three neurosurgical centres.

2.2.5. Referral Times

Almost fifty percent of patients were treated (or had a decision not to treat) within one month of their GP's referral, varying from 34.3% for patients with meningiomas or nerve sheath tumours to 60.7% for those with high grade gliomas and declined from 55.5% in 1986-88 to 34.7% in 1992-94. Over 7% of all patients (11% by 1992-94) had not been treated within 6 months of referral.

Overall, 61% of glioma patients referred for radiotherapy, received it within the recommended time interval of 4 weeks after surgery , varying from 78% in Centre 1 to 46% in Centre 3 and from 49% in Radiotherapy Centre A to 85% in Radiotherapy Centre B. Just over seven percent of patients received radiotherapy more than two months after surgery.

2.2.6. Recommendations for Future Work

i. Investigate the reasons for the identified differences in survival across neurosurgical centres for the meningiomas/nerve sheath tumours, given the similarity of treatment practices, exploring the relative contribution of casemix and the possibility of variation in other aspects of management.

ii. Determine, by means of a randomised clinical trial, whether survival is improved in low grade glioma patients treated by definitive surgery in combination with radiotherapy, as compared to those treated by definitive surgery alone.

iii. In the low grade gliomas, examine whether treatment differences across the neurosurgical centres are still evident within current practice today, developing more robust methods for addressing variations in casemix.

2.3. ACKNOWLEDGEMENTS

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2.3.2. Other Acknowledgements

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POPULATION DESCRIPTION 3

3.1. ALL CNS TUMOURS

3.1.1. New Registrations

During the study period, 1986-94, a total of 2948 patients were registered with tumours of the central nervous system (ICD9 Codes: 191-2, 225) in the former Yorkshire region, averaging approximately 328 new cases per annum.

There was a broadly similar proportion of males (51.5%) and females (48.5%), and the median age group at diagnosis was 50-59. In terms of incidence, the age-standardised rate over the whole study period was 8.3 cases per 100,000 population.

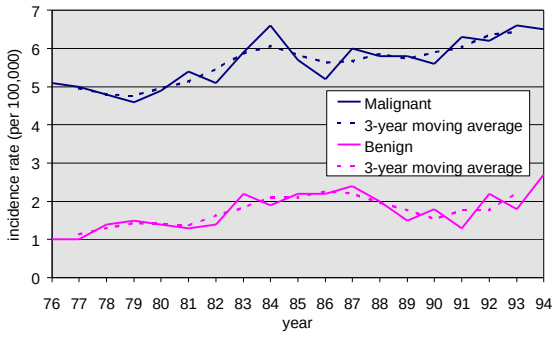
By 1994, there had been a 20% increase in malignant CNS tumours, and in particular a sharp rise was observed from 1983 onwards. It was initially suggested that this may reflect the introduction of CT scanning but, on further investigation, it was found that this diagnostic facility had been introduced into the three neurosurgical centres in the region between 1977 and 1981. Other possible explanations include improvements in registration practice, particularly during the earlier years, where there was an increase in the number of pathology reports being submitted to the registry.

Some variation in age-standardised incidence was observed according to district of residence, with the highest rate (9.7%) being seen in Harrogate and the lowest (6.9%) in Grimsby.

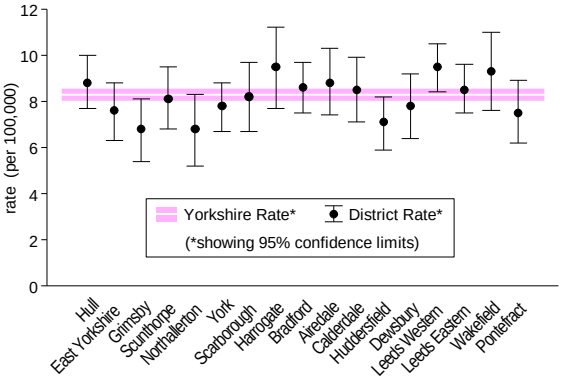
▼ Characteristics of All CNS Tumour Patients

Factor		Registrations	
Sex	Male	1517	***51.5%***
	Female	1431	***48.5%***
Age group	0-9	125	***4.2%***
	10-19	92	***3.1%***
	20-29	142	***4.8%***
	30-39	249	***8.4%***
	40-49	359	***12.2%***
	50-59	558	***18.9%***
	60-69	777	***26.4%***
	70-79	492	***16.7%***
	80-89	141	***4.8%***
	90+	13	***0.4%***
Total	All ages	2948	***100%***

▼ Age-Standardised Rate - CNS in Yorkshire 1976-94



▼ ASR by District of Residence 1986-94



3.2. STUDY POPULATION

3.2.1. Exclusions

A total of 2948 patients were registered with tumours of the central nervous system over the study period 1986-94. Several exclusions were made, including those groups for which data was generally incomplete : patients primarily managed outside of the region, patients managed privately, and death certificate only (DCO) registrations*. Histological tumour types considered either to be relatively rare or to require particularly unusual/specialist management were also excluded, leaving a total of 2245 cases for inclusion in the study dataset. Details of the exclusions are given below.

▼ Exclusions

Exclusions	Number
Primarily managed extra-regionally	185
Private cases	142
Death certificate only registrations* (DCO rate=2.7%)	80
Rarer tumour types (see table to right for details)	296
Total Exclusions	703

Excluded Types	Number
Medulloblastoma	61
Unspecified types	210
Ganglioglioma	6
Astroblastoma	1
Paraganglioma	2
Rhabdomyosarcoma	1
Teratoma	1
Haemangiopericytoma	1
Pineocytoma	1
Chordoma	3
Neuroblastoma	2
Neuroepithelioma	7
Total	296

* Death certificate only (DCO) registrations :
Patients for whom the only available information was that given on the death certificate.

3.2.2. Definition of Study Groups

The behaviour and prognosis of central nervous system tumours varies greatly, and a combined study of all cases was not considered meaningful. Different histological types were therefore grouped together, on the basis of likely common management and of similar behaviour/ prognosis, to form the three study groups described on the next page. The three groups studied throughout this report are: the meningioma and nerve sheath tumours (M&N), low grade gliomas (GL) and high grade gliomas (GH).

This categorisation of tumour types involved the retrospective review of the pathology reports by a single neuropathologist in order to address any variation in reporting. It is recognised however that, whilst such a review can ensure the consistent classification of cases according to the recorded details, it cannot overcome the problems associated with differences in the interpretation of histological specimens.

▼ Study Groups by Time Period

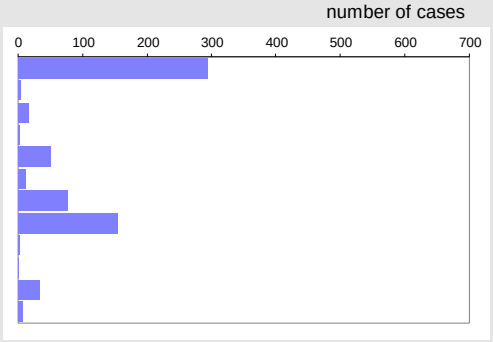
Study Group	1986-88		1989-91		1992-94	
Meningiomas & Nerve Sheath Tumours	231	***32.2%***	171	***24.7%***	249	***29.7%***
Glioma Grades I&II	110	***15.3%***	99	***14.3%***	72	***8.6%***
Glioma Grades III&IV	376	***52.4%***	421	***60.9%***	516	***61.6%***

There was a 10% increase in the proportion of high grade gliomas over the study period, which may represent a true increase in the incidence of these tumours or may be due to changes in histopathological classification, as mentioned above.

1. Meningiomas & Nerve Sheath Tumours (M&N)

Depending upon location, complete surgical removal is possible for the majority of the these tumours. In a small number of cases, where resection is incomplete, radiotherapy may be necessary.

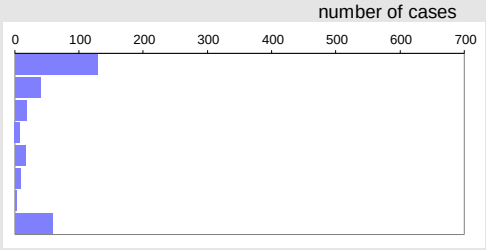
Tumour Type Registered (M&N)	N (1986-94)
Meningioma NOS	294
Meningioma angiomatous	4
Meningioma fibrous	16
Meningioma haemangioblastic	3
Meningioma meningotheliomatous	49
Meningioma psammomatous	11
Meningioma transitional	76
Neurilemmoma	154
Neurofibroma	3
Neurofibroma flexiform	1
Haemangioblastoma	33
Choroid plexus papilloma benign	7
Total	651



2. Glioma Grades I & II (GL)

Primary management of the low grade gliomas involves the surgical removal of as much of the tumour as is safe, although complete resection is frequently not possible. Optimal practice with respect to the use of radiotherapy has not been clearly established by means of randomised controlled trials.

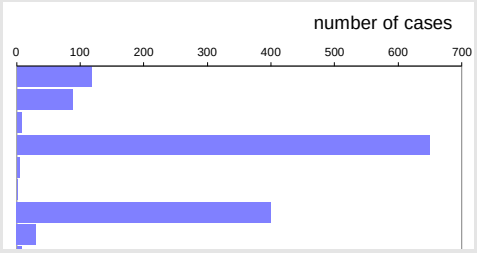
Tumour Type Registered (GL)	N (1986-94)
Astrocytoma NOS (grade I & II)	129
Astrocytoma fibrillary	40
Astrocytoma gemistocytic type	18
Astrocytoma protoplasmic	8
Ependymoma (grade I & II)	16
Ependymoma myxopapillary	9
Ependymoma papillary	2
Oligodendroglioma (grade I & II)	59
Total	281



3. Glioma Grades III & IV (GH)

The majority of high grade glioma patients relapse and die, even following maximal surgery and radical radiotherapy. Debulking may be used to relieve the rapidly progressive symptoms generally associated with these tumours. Radiotherapy also provides useful palliation, usually employed as a radical course over four to six weeks, or as a short course of one to two weeks for patients with a poor performance status. At the time of relapse, a small number of selective patients may be treated with chemotherapy but response rates are low (20-30%). The provision of effective support care, to the patient and family, is of particular importance.

Tumour Type Registered (GH)	N (1986-94)
Astrocytoma NOS (grade III & IV)	153
Astrocytoma anaplastic	77
Ependymoma NOS (grade III & IV)	11
Glioblastoma	626
Glioblastoma giant cell	5
Glioblastoma with sarcomatous component	2
Glioma malignant	400
Glioma mixed	31
Oligodendroglioma (grade III & IV)	8
Total	1313

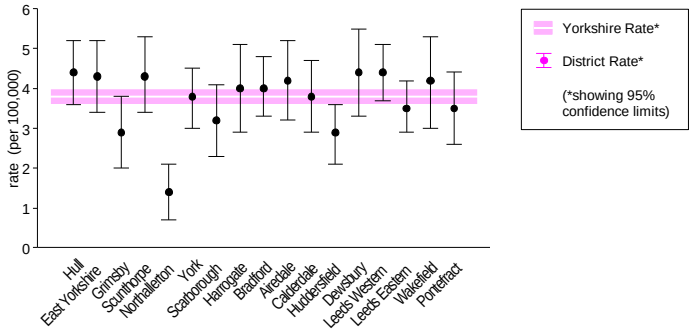


3.2.3. Characteristics of Each Study Group

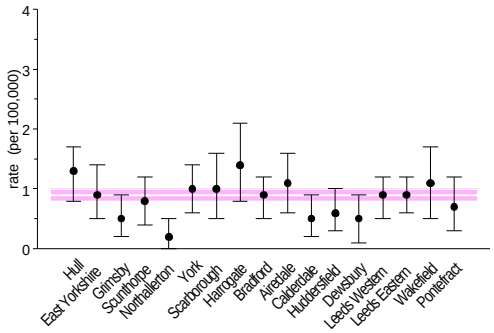
▼ Characteristics of Each Study Group

Factor		Overall		M&N		GL		GH	
Sex	Male	**1163**	**51.8%**	242	**37.2%**	159	**56.6%**	762	**58.0%**
	Female	**1082**	**48.2%**	409	**62.8%**	122	**43.4%**	551	**42.0%**
Age Group	0-9	**37**	***1.6%***	4	***0.6%***	15	***5.3%***	18	***1.4%***
	10-19	**40**	***1.8%***	5	***0.8%***	16	***5.7%***	19	***1.4%***
	20-29	**99**	***4.4%***	26	***4.0%***	36	***12.8%***	37	***2.8%***
	30-39	**197**	***8.8%***	64	***9.8%***	52	***18.5%***	81	***6.2%***
	40-49	**289**	***12.9%***	90	***13.8%***	57	***20.3%***	142	***10.8%***
	50-59	**468**	***20.8%***	131	***20.1%***	43	***15.3%***	294	***22.4%***
	60-69	**652**	***29.0%***	183	***28.1%***	40	***14.2%***	429	***32.7%***
	70-79	**368**	***16.4%***	111	***17.1%***	16	***5.7%***	241	***18.4%***
	80-89	**91**	***4.1%***	34	***5.2%***	5	***1.8%***	52	***4.0%***
	90+	**4**	***0.2%***	3	***0.5%***	1	***0.4%***	0	***0.0%***
Overall		**2245**	***100%***	651	***100%***	281	***100%***	1313	***100%***

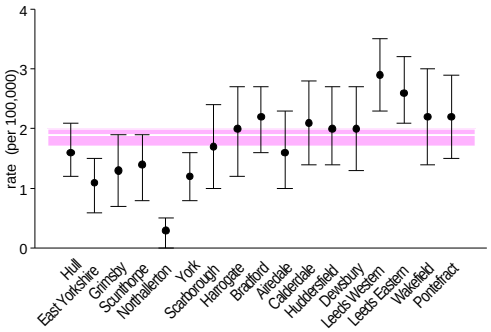
▼ Age-Standardised Rate by District of Residence 1986-94, Meningiomas & Nerve Sheath Tumours (M&N)



▼ Age-Standardised Rate by District of Residence 1986-94, Glioma Grades I & II (GL)



▼ Age-Standardised Rate by District of Residence 1986-94, Glioma Grades III & IV (GH)



Nearly twice as many females as males were diagnosed as having a meningioma/nerve sheath tumour during the study period 1986-94. A very different split was seen amongst the gliomas (both low and high grade), where the majority (57.8%) were male. The median age group at diagnosis was 40-49 in the low grade gliomas but was somewhat older (median age group 60-69) in the other two study groups.

Incidence in the Northallerton district was consistently low but it should be noted that this is due to the exclusion of the cases primarily managed outside of the region. Northallerton lies close to the Northern border of the former Yorkshire Region, and many of the residents of this area, diagnosed with a brain tumour, would have been referred and treated outside the region.

MANAGEMENT & TREATMENT 4

The hospital of primary management (whether this be a neurosurgical centre or a district general hospital) was available for all patients, as was information about attendance at a radiotherapy centre. Hospitals were not recorded if a patient was referred for example, for a specialist assessment at a neurosurgical centre, if management of the patient was not formally transferred. This was also true of the recorded managing consultants. A consultant would only be recorded by NYCRIS if management of a patient was actually transferred to that consultant.

With respect to treatment, it should be noted that, until 1994, only *definitive* treatment administered within nine weeks of the first episode would have been routinely recorded. Definitive surgery is defined as either surgery with curative intent, or the maximum safe macroscopic resection possible. For patients where no definitive surgical procedure was recorded, supplementary details of any biopsies performed were obtained from the registration paper records. Biopsy information was not obtained for patients if a definitive surgical procedure had been recorded. There was minimal usage of chemotherapy for the CNS tumour patients in the study, and analyses of this treatment modality have therefore not been included. Data regarding other supportive care, such as dexamethasone, was not available.

Attention is also drawn to the fact that the information contained within this report relates to the period 1986-94, and that current management practices are *not* described. This time period was selected on the basis of the most recent year for which the NYCRIS dataset was available at the outset of the study, and to provide a cohort of patients with sufficient follow-up to enable an analysis of survival.

4.1. TREATMENT OVERVIEW FOR YORKSHIRE

4.1.1. Treatment Practices by Study Group

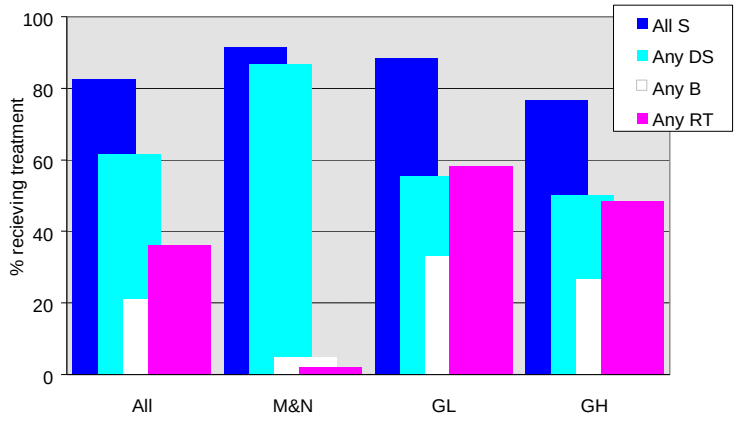
▼ Overall Treatment Practices by Study Group

Modality	Overall		M&N		GL		GH	
DS	**841**	***37.5%***	555	***85.3%***	65	***23.1%***	221	***16.8%***
DS+RT	**540**	***24.1%***	10	***1.5%***	91	***32.4%***	439	***33.4%***
B	**238**	***10.6%***	30	***4.6%***	25	***8.9%***	183	***13.9%***
B+RT	**235**	***10.5%***	1	***0.2%***	68	***24.2%***	166	***12.6%***
RT	**37**	***1.6%***	1	***0.2%***	5	***1.8%***	31	***2.4%***
None	**354**	***15.8%***	54	***8.3%***	27	***9.6%***	273	***20.8%***
Any DS	**1381**	***61.5%***	565	***86.8%***	156	***55.5%***	660	***50.3%***
Any B	**473**	***21.1%***	31	***4.8%***	93	***33.1%***	349	***26.6%***
All S	**1854**	***82.5%***	596	***91.5%***	249	***88.6%***	1009	***76.8%***
Any RT	**812**	***36.2%***	12	***1.8%***	164	***58.4%***	636	***48.4%***
Total	**2245**	***100%***	651	***100%***	281	***100%***	1313	***100%***

DS	=	Definitive surgery
B	=	Biopsy
RT	=	Radiotherapy
All S	=	Definitive Surgery or Biopsy

As outlined below, the treatment modalities employed were broadly as expected, with high surgery rates across all three study groups. The relatively high radiotherapy rate (58.4%) for the low grade gliomas was of particular interest since evidence from randomised controlled trials, demonstrating the benefit of this therapy, is currently unclear.

▼ Treatment Practices by Study Group



- **Meningiomas & Nerve Sheath Tumours (M&N) :** The majority (86.8%) of patients underwent definitive surgery, and this was followed by radiotherapy in only a handful of cases. A review of the registration paper records enabled an investigation of the appropriateness of the decision not to operate, with the following reasons being given:

▼ Reasons Given for Decision not to Operate

Reason Found	% of non-surgical M&N cases
Patient too old/unfit (all over the age of 60)	***68%***
Patient refused surgery	***12%***
Not known	***8%***
Tumour "inoperable"	***6%***
Tumour observed over a period of time	***6%***

- **Glioma Grades I & II (GL) :** Surgery followed by radiotherapy was used in over 56.6% of cases, with 32.4% having definitive surgery and 24.2% having biopsy before their radiotherapy. A further quarter of patients underwent a definitive operation, without subsequent use of radiotherapy.
- **Glioma Grades III & IV (GH) :** A range of treatment practices was seen within the high grade gliomas; the most common modality being definitive surgery in combination with radiotherapy (33.4%). Similar rates of definitive surgery alone (16.8%), biopsy alone (13.9%), and biopsy followed by radiotherapy (12.6%) were also demonstrated. A relatively high number of patients, one in five, received no treatment.

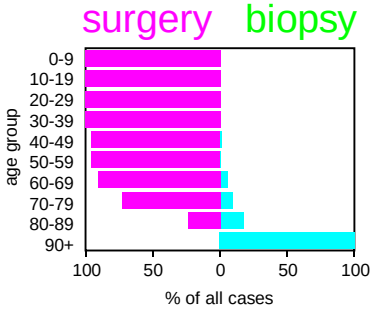
4.1.2. Treatment Practices by Age Group

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Surgery by Age Group

Age	N	DS		B		No Surgery	
0-9	**4**	4	***100%***	0	***0.0%***	0	***0.0%***
10-19	**5**	5	***100%***	0	***0.0%***	0	***0.0%***
20-29	**26**	26	***100%***	0	***0.0%***	0	***0.0%***
30-39	**64**	64	***100%***	0	***0.0%***	0	***0.0%***
40-49	**90**	86	***95.6%***	1	***1.1%***	3	***3.3%***
50-59	**131**	125	***95.4%***	1	***0.8%***	5	***3.8%***
60-69	**183**	166	***90.7%***	10	***5.5%***	7	***3.8%***
70-79	**111**	81	***73.0%***	10	***9.0%***	20	***18.0%***
80-89	**34**	8	***23.5%***	6	***17.6%***	20	***58.8%***
90+	**3**	0	***0.0%***	3	***100%***	0	***0.0%***
Total	**651**	565	***86.8%***	31	***4.8%***	55	***8.4%***

DS = Definitive surgery B = Biopsy



High rates of definitive surgery were seen up to the age of 70; rates then fell in the older age groups, with a corresponding rise in the use of biopsy and in the numbers receiving no treatment.

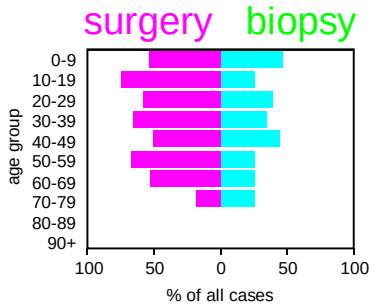
Glioma Grades I & II (GL)

▼ Surgery by Age Group

Age	N		DS		B		RT		No Treatment
0-9	**15**	8	***53.3%***	7	***46.7%***	5	***33.3%***	0	***0.0***
10-19	**16**	12	***75.0%***	4	***25.0%***	9	***56.3%***	0	***0.0***
20-29	**36**	21	***58.3%***	14	***38.9%***	28	***77.8%***	0	***0.0***
30-39	**52**	33	***65.5%***	18	***34.6%***	41	***78.8%***	0	***0.0***
40-49	**57**	29	***50.9%***	25	***43.9%***	36	***63.2%***	3	***5.3***
50-59	**43**	29	***67.4%***	11	***25.6%***	24	***55.8%***	2	***4.7***
60-69	**40**	21	***52.5%***	10	***25.0%***	19	***47.5%***	8	***20.0***
70-79	**16**	3	***18.8%***	4	***25.0%***	2	***12.5%***	8	***50.0***
80-89	**5**	0	***0.0%***	0	***0.0%***	0	***0.0%***	5	***100.0***
90+	**1**	0	***0.0%***	0	***0.0%***	0	***0.0%***	1	***100.0***
Total	**281**	156	***55.5%***	93	***33.1%***	164	***58.4%***	27	***9.6***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy

Surgery rates (both definitive and biopsy) were broadly stable up to the age of 70, at approximately 59% and 34% respectively. In the older age groups, the proportion undergoing an operation was somewhat lower, at about a third in total, but it should be noted that few patients over the age of 70 were diagnosed with low grade glioma. In relation to radiotherapy, rates increased to a maximum of 78.8% in the 30-39 age group, and then fell steadily with age.



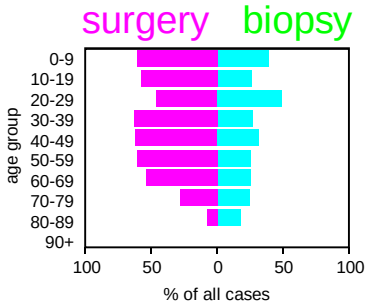
Glioma Grades III & IV (GH)

▼ Surgery by Age Group

Age	N		DS		B		RT		No Treatment
0-9	**18**	11	***61.1%***	7	***38.9%***	9	***50.0%***	0	***0.0***
10-19	**19**	11	***57.9%***	5	***26.3%***	17	***89.5%***	0	***0.0***
20-29	**37**	17	***45.9%***	18	***48.6%***	30	***81.1%***	1	***2.7***
30-39	**81**	51	***63.0%***	22	***27.2%***	60	***74.1%***	6	***7.4***
40-49	**142**	88	***62.0%***	45	***31.7%***	98	***69.0%***	5	***3.5***
50-59	**294**	178	***60.5%***	75	***25.5%***	179	***60.9%***	33	***11.2***
60-69	**429**	232	***54.1%***	110	***25.6%***	198	***46.2%***	81	***18.9***
70-79	**241**	68	***28.2%***	58	***24.1%***	43	***17.8%***	110	***45.6***
80-89	**52**	4	***7.7%***	9	***17.3%***	2	***3.8%***	37	***71.2***
Total	**1313**	660	***50.3%***	349	***26.6%***	636	***48.4%***	273	***20.8***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy

In the high grade gliomas, the variation in treatment practices with age was similar to that seen amongst the lower grade tumours; surgery rates fell sharply in the older age groups (particularly the over 70s), and the proportion receiving radiotherapy reached a maximum of 89.5% in the 10-19 group before declining steadily with age.



4.1.3. Effects of Tumour Location on Surgery Rates

Tumour site information was relatively non-specific and was only available for approximately 60% of the gliomas. The number of cases within some of the site categories were small, making interpretation difficult. Furthermore, as the specific tumour site is known to be of importance in relation to treatment decisions and prognosis, this lack of detailed information also contributes to problems of interpretation and adequate adjustment for case mix in later sections of the report.

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Tumour Location and Influence on Treatment

Site Specified	N		DS		B		All S
Brain NOS	**39**	35	***89.7%***	3	***7.7%***	38	***97.4%***
Cerebral meninges	**384**	318	***82.8%***	22	***5.7%***	340	***88.5%***
Cranial nerves	**130**	121	***93.1%***	2	***1.5%***	123	***94.6%***
Spinal meninges	**45**	45	***100%***	0	***0.0%***	45	***100%***
Unknown	**53**	46	***86.8%***	4	***7.5%***	50	***94.3%***
Total	**651**	565	***86.8%***	31	***4.8%***	596	***91.6%***

DS = Definitive surgery
B = Biopsy
All S = Definitive Surgery or Biopsy

The tumours in this group were mainly located on the cerebral meninges or cranial nerves. Surgery rates were very high in all tumour sites listed, with the lowest rates (88.5%) being seen in the cerebral meninges group.

Glioma All Grades

▼ Tumour Location and Influence on Treatment: Glioma Grades I & II (GL)

Site Specified	N		DS		B		All S
Brain NOS	**105**	55	***52.4%***	35	***33.3%***	90	***85.7%***
Brain Stem	**3**	1	***33.3%***	2	***66.7%***	3	***100%***
Cerebellum	**7**	4	***57.1%***	2	***28.6%***	6	***85.7%***
Cerebrum	**6**	2	***33.3%***	3	***50.0%***	5	***83.3%***
Frontal lobe	**60**	39	***65.0%***	17	***28.3%***	56	***93.3%***
Occipital lobe	**9**	5	***55.6%***	4	***44.4%***	9	***100%***
Parietal lobe	**39**	16	***41.0%***	16	***41.0%***	32	***82.1%***
Spine	**4**	4	***100%***	0	***0.0%***	4	***100%***
Temporal lobe	**40**	26	***65.0%***	10	***25.0%***	36	***90.0%***
Ventricle	**8**	4	***50.0%***	4	***50.0%***	8	***100%***
Total	**281**	156	***55.5%***	93	***33.1%***	249	***88.6%***

DS = Definitive surgery
B = Biopsy
All S = Definitive Surgery or Biopsy

▼ Tumour Location and Influence on Treatment: Glioma Grades III & IV (GH)

Site Specified	N		DS		B		All S
Brain NOS	**551**	218	***39.6%***	160	***29.0%***	378	***68.6%***
Brain Stem	**14**	3	***21.4%***	8	***57.1%***	11	***78.6%***
Cerebellum	**11**	5	***45.5%***	5	***45.5%***	10	***90.9%***
Cerebrum	**14**	3	***21.4%***	6	***42.9%***	9	***64.3%***
Frontal lobe	**233**	129	***55.4%***	60	***25.8%***	189	***81.1%***
Occipital lobe	**60**	47	***78.3%***	9	***15.0%***	56	***93.3%***
Parietal lobe	**240**	132	***55.0%***	63	***26.3%***	195	***81.3%***
Spine	**2**	2	***100%***	0	***0.0%***	2	***100%***
Temporal lobe	**181**	118	***65.2%***	35	***19.3%***	153	***84.5%***
Ventricle	**7**	3	***42.9%***	3	***42.9%***	6	***85.7%***
Total	**1313**	660	***50.3%***	349	***26.6%***	1009	***76.8%***

DS = Definitive surgery
B = Biopsy
All S = Definitive Surgery or Biopsy

The lowest surgical rates were expected in the parietal lobe since surgery in this region is particularly difficult, with a greater risk of impairing the performance status of the patient. It was not, however, possible to demonstrate this clearly with the available data.

4.1.4. Treatment Practices by Time Period

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Combined Treatment Modalities

Treatment	Overall		1986-88		1989-91		1992-94	
DS	**555**	***85.3%***	203	***87.9%***	132	***77.2%***	220	***88.4%***
DS+RT	**10**	***1.5%***	4	***1.7%***	3	***1.8%***	3	***1.2%***
Any DS	**565**	***86.8%***	207	***89.6%***	135	***78.9%***	223	***89.6%***
B	**30**	***4.6%***	5	***2.2%***	11	***6.4%***	14	***5.6%***
B+RT	**1**	***0.2%***	1	***0.4%***	0	***0.0%***	0	***0.0%***
RT	**1**	***0.2%***	0	***0.0%***	0	***0.0%***	1	***0.4%***
None	**54**	***8.3%***	18	***7.8%***	25	***14.6%***	11	***4.4%***
Total	**651**	***100%***	231	***100%***	171	***100%***	249	***100%***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy

There was some variation in the overall proportion of patients undergoing definitive surgery, with a drop of 10% being seen during the middle three years 1989-91. By the end of the study period, the rate had returned to that of the earliest years, at approximately 90%.

Glioma Grades I & II (GL)

▼ Combined Treatment Modalities

Treatment	Overall		1986-88		1989-91		1992-94	
DS	**65**	***23.1%***	30	***27.3%***	21	***21.2%***	14	***19.4%***
DS+RT	**91**	***32.4%***	35	***31.8%***	32	***32.3%***	24	***33.3%***
Any DS	**156**	***55.5%***	65	***59.1%***	53	***53.5%***	38	***52.8%***
B	**25**	***8.9%***	10	***9.1%***	4	***4.0%***	11	***15.3%***
B+RT	**68**	***24.2%***	19	***17.3%***	31	***31.3%***	18	***25.0%***
RT	**5**	***1.8%***	2	***1.8%***	1	***1.0%***	2	***2.8%***
Any RT	**164**	***58.4%***	56	***50.9%***	64	***64.6%***	44	***61.1%***
None	**27**	***9.6%***	14	***12.7%***	10	***10.1%***	3	***4.2%***
Total	**281**	***100%***	110	***100%***	99	***100%***	72	***100%***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy

An overall 10% increase in the use of radiotherapy was seen over the study period (50.9% to 61.1%). There was a reduction in the proportion of patients receiving definitive surgery alone, with a corresponding increase in the use of biopsy, both with and without radiotherapy. The number of cases with no definitive treatment recorded decreased from 12.7% in 1986-88 to 4.2% in 1992-94.

Glioma Grades III & IV (GH)

▼ Combined Treatment Modalities

Treatment	Overall		1986-88		1989-91		1992-94	
DS	**221**	***16.8%***	63	***16.8%***	77	***18.3%***	81	***15.7%***
DS+RT	**439**	***33.4%***	103	***27.4%***	137	***32.5%***	199	***38.6%***
Any DS	**660**	***50.3%***	280	***54.3%***	166	***44.1%***	214	***50.8%***
B	**183**	***13.9%***	48	***12.8%***	44	***10.5%***	91	***17.6%***
B+RT	**166**	***12.6%***	44	***11.7%***	47	***11.2%***	75	***14.5%***
RT	**31**	***2.4%***	12	***3.2%***	10	***2.4%***	9	***1.7%***
Any RT	**636**	***48.4%***	283	***54.8%***	159	***42.3%***	194	***46.1%***
None	**273**	***20.8%***	106	***28.2%***	106	***25.2%***	61	***11.8%***
Total	**1313**	***100.0%***	376	***100.0%***	421	***100.0%***	516	***100.0%***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy

There was a steady increase in the use of radiotherapy in combination with definitive surgery, with a 11% rise being observed over the whole study period. All other treatment rates remained fairly constant, with the exception of an 8% increase in the number of cases having received a biopsy, as opposed to definitive surgery, either with or without radiotherapy.

Further discussion of changes in treatment practices over time continues within section 4.3.5., where trends are shown to vary by individual neurosurgical centre.

4.2. MANAGEMENT AT A NEUROSURGICAL CENTRE

4.2.1. Management at a Neurosurgical Centre

▼ Management at a Neurosurgical Centre

Study Group	Referred		Total Number	Proportion of Cases
Meningiomas & Nerve Sheath Tumours (M&N)	600	/	**651**	***92.2%***
Glioma Grades I & II (GL)	249	/	**281**	***88.6%***
Glioma Grades III & IV (GH)	1062	/	**1313**	***80.8%***
All	1911	/	**2245**	***85.1%***

85.1% of the patients included in the study were recorded as having been managed at one of the three neurosurgical centres. There were differences in the proportion of patients managed outside of a specialist neurosurgical centre across the three study groups, with the lowest rate being seen in the meningiomas and nerve sheath tumours and the highest in the high grade gliomas. This reflects the worsening prognosis of the study groups, where management by a general physician or geriatrician, instead of a neurosurgeon, is probably appropriate.

4.2.2. Influence of Age on Management at a Neurosurgical Centre

▼ Mean/Median Age of Cases Managed at a Specialist/Non-Specialist Centre

Centre	Mean / Median Age			
	Overall	M&N	GL	GH
Non-Specialist	**69 / 72**	75 / 76	58 / 56	69 / 72
Specialist	**54 / 58**	56 / 58	42 / 42	56 / 59
Total	**56 / 59**	57 / 60	43 / 44	58 / 61

Patients not actively managed at a specialist neurosurgical centre were generally older, with an average age of 69 years (median 72 years), whereas those managed at a specialist centre were younger, with an average age of 54 years (median 58 years).

▼ Proportion of Patients Managed at a Neurosurgical Centre by Age Group

Group	Age group	Proportion managed at a specialist centre	p
Meningiomas & Nerve Sheath Tumours (M&N)	<75 yr.	***95%***	p<0.001
	>=75 yr.	***61%***	
Glioma Grades I & II (GL)	<65 yr.	***92%***	p<0.001
	>=65 yr.	***62%***	
Glioma Grades III & IV (GH)	<65 yr.	***93%***	p<0.001
	65-75 yr.	***75%***	
	>=75 yr.	***30%***	

Appropriate cut-off points for the age below which all patients should ideally be managed at a neurosurgical centre, were agreed by the clinical representatives for the study. A cut-off of 75 years was chosen for the meningiomas/nerve sheath tumours, and of 65 years for the gliomas.

Analysis of the meningioma/nerve sheath tumour group indicated that 95% of patients under the cut-off age of 75 were managed at a neurosurgical centre. The corresponding figures for the low and high grade gliomas were 92% and 93% respectively. For all three study groups, it was also demonstrated that the proportion managed at a neurosurgical centre was significantly lower for those patients above the agreed cut-off age.

4.3. INDIVIDUAL NEUROSURGICAL CENTRES

There were three neurosurgical centres involved in the management of CNS tumours in Yorkshire during the study period, 1986-94: Leeds General Infirmary, Pinderfields Hospital and Hull Royal Infirmary. As the decision to refer a patient for radiotherapy is made at the neurosurgical centre, analyses of both surgery and radiotherapy by managing neurosurgical centre are included in this section.

4.3.1. Management at Individual Neurosurgical Centres

▼ Proportion of Cases in Each Study Group by Individual Neurosurgical Centre

Group	N	Centre 1		Centre 2		Centre 3	
Meningiomas & Nerve Sheath Tumours (M&N)	**651**	134	***23.1%***	280	***36.2%***	186	***33.4%***
Glioma Grades I & II (GL)	**281**	84	***13.1%***	102	***13.2%***	63	***11.3%***
Glioma Grades III & IV (GH)	**1313**	363	***62.5%***	392	***50.7%***	307	***55.3%***
Total	**2245**	581	***100%***	774	***100%***	556	***100%***

▼ Proportion of High to Low Grade Gliomas by Individual Neurosurgical Centre

Group	N	Centre 1		Centre 2		Centre 3	
Glioma Grades I & II (GL)	**281**	84	***18.8%***	102	***13.8%***	63	***17.0%***
Glioma Grades III & IV (GH)	**1313**	363	***81.2%***	392	***86.2%***	307	***83.0%***
All Gliomas	**1594**	447	***100%***	455	***100%***	370	***100%***

The distribution of the tumour groups across the three centres varied considerably, with a substantially lower proportion of meningiomas/nerve sheath tumours being managed at Centre 1. Allowing for this difference, the ratio of high to low grade gliomas was broadly similar; the proportion of high grade tumours being over 80% at all three centres. There was no evidence to suggest a difference in the classification of high grade gliomas and low grade gliomas between centres.

4.3.2. Age Distribution of Cases by Individual Centre

▼ Mean/Median Age of Cases Managed at Each Neurosurgical Centre

Centre	Mean / Median age							
	Overall		M&N		GL		GH	
1	**56 /**	**59**	59 /	61	43 /	43	57 /	60
2	**53 /**	**57**	54 /	56	41 /	40	55 /	59
3	**54 /**	**57**	56 /	61	42 /	42	55 /	58

Centre 1 patients were slightly older than those at the other two centres (mean age 56 years compared to 53 and 54 years at centres 2 and 3). These differences were significant for the meningiomas/nerve sheath tumours ($p<0.01$) and the high grade gliomas ($p=0.03$) but not for the smaller group of low grade gliomas ($p=0.77$). As mentioned in the section above, there was no evidence to support a difference in glioma grading between centres.

4.3.3. Management at Individual Centre by Time Period

▼ Proportion of Cases Managed at Each Neurosurgical Centre by Time Period : All Study Groups

Centre	Overall		1986-1988		1989-1991		1992-1994	
1	**581**	***25.9%***	206	***28.7%***	152	***22.0%***	223	***26.6%***
2	**774**	***34.5%***	239	***33.3%***	215	***31.1%***	320	***38.2%***
3	**556**	***24.8%***	168	***23.4%***	197	***28.5%***	191	***22.8%***

There was no significant change in the proportion of patients being managed at each of the neurosurgical centres over the study period.

4.3.4. Treatment Practices by Individual Centre

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Treatment Combinations by Neurosurgical Centre

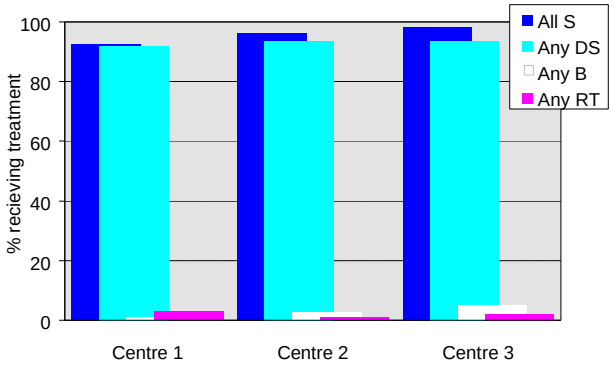
Treatment Modality	Centre 1		Centre 2		Centre 3	
DS+RT	3	***2.2%***	2	***0.7%***	5	***2.7%***
DS	120	***89.6%***	260	***92.9%***	169	***90.9%***
B	1	***0.7%***	7	***2.5%***	9	***4.8%***
B+RT	0	***0.0%***	0	***0.0%***	0	***0.0%***
RT	1	***0.7%***	0	***0.0%***	0	***0.0%***
None	9	***6.7%***	11	***3.9%***	3	***1.6%***
Total	134	***100%***	280	***100%***	186	***100%***

▼ Individual Treatments by Neurosurgical Centre

Centre	Any DS		Any B		All S		Any RT	
1	123	***91.8%***	1	***0.7%***	124	***92.5%***	4	***3.0%***
2	262	***93.6%***	7	***2.5%***	269	***96.1%***	2	***0.7%***
3	174	***93.5%***	9	***4.8%***	183	***98.3%***	5	***2.7%***

DS = Definitive surgery
B = Biopsy
RT = Radiotherapy
All S = Definitive Surgery or Biopsy

Little variation was demonstrated between the three neurosurgical centres for patients with meningiomas/nerve sheath tumours; definitive surgery alone was the primary treatment practice, with rates approximately 90% at all three centres. As explained at the beginning of Chapter 4, if definitive surgery was not recorded, supplementary biopsy information was obtained from the registry paper records. It is therefore possible that some patients who had definitive surgery may have had a biopsy also.



Glioma Grades I & II (GL)

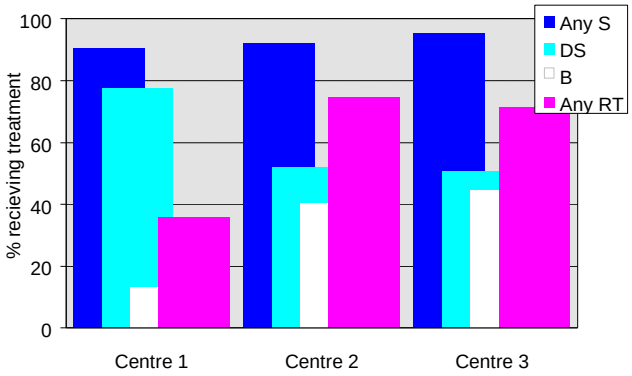
▼ Treatment Combinations by Neurosurgical Centre

Treatment Modality	Centre 1		Centre 2		Centre 3	
DS	39	***46.4%***	13	***12.7%***	11	***17.5%***
DS+RT	26	***31.0%***	40	***39.2%***	21	***33.3%***
B	7	***8.3%***	8	***7.8%***	4	***6.3%***
B+RT	4	***4.8%***	33	***32.4%***	24	***38.1%***
Any S+RT	30	***35.7%***	73	***71.6%***	45	***71.4%***
RT	0	***0.0%***	3	***2.9%***	0	***0.0%***
None	8	***9.5%***	5	***4.9%***	3	***4.8%***
Total	84	***100%***	102	***100%***	63	***100%***

▼ Individual Treatments by Neurosurgical Centre

Centre	Any DS		Any B		Any S		Any RT	
1	65	***77.4%***	11	***13.1%***	76	***90.5%***	30	***35.7%***
2	53	***52.0%***	41	***40.2%***	94	***92.2%***	76	***74.5%***
3	32	***50.8%***	28	***44.4%***	60	***95.2%***	45	***71.4%***

DS	=	Definitive surgery
B	=	Biopsy
RT	=	Radiotherapy
All S	=	Definitive Surgery or Biopsy



Over the period 1986-94, there was considerable variation between the three centres in the treatment policies employed for the low grade gliomas. At centre 1, there was a much higher rate of definitive surgery without the subsequent use of radiotherapy: 46.4% compared with 12.7% and 17.5% at the other two centres. Conversely, biopsy together with radiotherapy was used less frequently at Centre 1: only 4.8% compared with 32.4% and 38.1%. The rates of definitive surgery in combination with radiotherapy were fairly similar between each of the three centres, with approximately one third of patients receiving this combination.

The individual treatment modality table clearly demonstrates the lower rates of biopsy and of radiotherapy at Centre 1; a number of possible explanations have been suggested for this variation. There may have been a true difference in management practices during the period of the study. Evidence from randomised controlled trials demonstrating the benefits of radiotherapy for the low grade gliomas is currently lacking and there is no consensus regarding the optimal management of these patients. Further, the increased usage of definitive surgery, alongside the lower rate of biopsy, may perhaps reflect a more radical approach to surgery, resulting in a higher number of complete excisions and reducing the requirement for post-operative radiotherapy.

Alternatively, differences in the casemix of the patients managed at each of the centres have also been suggested as a possible explanation. The previous section mentioned that there was no evidence of a stage-shift, whereby differences in histopathological classification might have resulted in a greater number of gliomas being classified as low grade at different centres. Also, repeat age-adjusted analysis did not account for the variation in treatment practices. Within this study, it has not however, been possible to allow for other known prognostic factors (for example, performance status or specific tumour site), due to a lack of data. Further, it is recognised that studies such as these can never fully account for differences in the distribution of unknown casemix factors.

Finally, attention is again drawn to the fact that these data relate to the period 1986-94 and it is possible that management practices may have since changed.

Glioma Grades III & IV (GH)

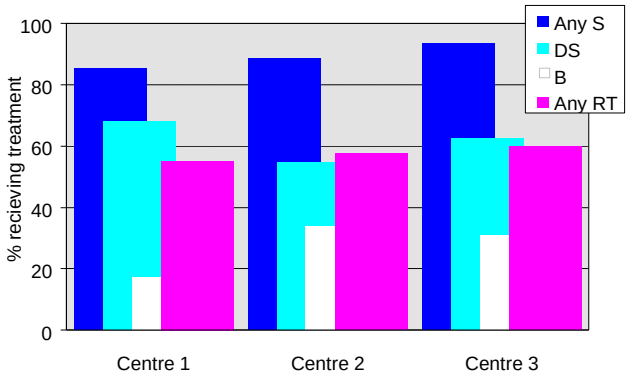
▼ Treatment Combinations by Neurosurgical Centre

Treatment Modality		Centre 1		Centre 2		Centre 3
DS	78	***21.5%***	71	***18.1%***	70	***22.8%***
DS+RT	169	***46.6%***	143	***36.5%***	122	***39.7%***
B	42	***11.6%***	58	***14.8%***	38	***12.4%***
B+RT	20	***5.5%***	75	***19.1%***	57	***18.6%***
Any S+RT	189	***52.1%***	218	***55.6%***	179	***58.3%***
RT	11	***3.0%***	8	***2.0%***	5	***1.6%***
None	43	***11.8%***	37	***9.4%***	15	***4.9%***
Total	363	***100%***	392	***100%***	307	***100%***

▼ Individual Treatments by Neurosurgical Centre

Centre		Any DS		Any B		Any S		Any RT
1	247	***68.0%***	62	***17.1%***	309	***85.1%***	200	***55.1%***
2	214	***54.6%***	133	***33.9%***	347	***88.5%***	226	***57.7%***
3	192	***62.5%***	95	***30.9%***	287	***93.4%***	184	***59.9%***

DS	=	Definitive surgery
B	=	Biopsy
RT	=	Radiotherapy
All S	=	Definitive Surgery or Biopsy



As with the lower grade gliomas, there was also some variation between the three centres in the management policies employed for the high grade gliomas, although the differences were not as great. At Centre 1, there was a slightly higher rate of radiotherapy following definitive surgery: 46.6% compared with 36.3% and 39.6% at Centres 2 and 3. In contrast, there was a greater use of biopsy in combination with radiotherapy at the other two centres: 5.5% compared with 19.1% and 18.6% at Centres 2 and 3. The rates of surgery alone (both definitive and biopsy) were similar across all three centres.

Examining the table showing the frequency of the use of each treatment modality, it can be seen that the overall rate of biopsy was lowest at Centre 1, and definitive surgery was lowest at Centre 2. The overall rate of radiotherapy did not differ greatly between centres.

The reader is referred to the above section on low grade gliomas for a discussion on the possible interpretation of these differences in management. It is of particular interest to note that there is only minimal variation in radiotherapy rates, reflecting the greater clinical consensus surrounding the use of this treatment in the higher grade gliomas.

4.3.5. Treatment Practices at Individual Centres by Time Period

For the meningioma/nerve sheath tumour patients, treatment patterns were constant throughout the study period, with a consistently high percentage receiving definitive surgery. Detailed results for this group are, therefore, not included in the section below, which concentrates upon management of glioma only.

Previous analyses in this report, which looked at changes in management practices over time were based upon three time periods: 1986-88, 1989-91, and 1992-94. When looking at time trends by individual neurosurgical centre over time, the numbers involved were relatively small. In chapters 5/6, survival analyses have been restricted to the 1986-1990 patients, as complete death data were only available for this time period. Consequently, the following centre-based analyses have been performed for the two time periods, 1986-1990 and 1991-1994. It should be noted that the numbers in each of the treatment categories for the low grade gliomas are still relatively small.

▼ Individual Treatments by Time Period

Group	Period	Modality	Centre 1		Centre 2		Centre 3	
Glioma (GL) Grades I & II	1986-90	Any DS	49	***80.3%***	27	***45.0%***	21	***58.3%***
		Any B	5	***8.2%***	29	***48.3%***	13	***36.1%***
		Any RT	18	***29.5%***	46	***76.7%***	27	***75.0%***
	1991-94	Any DS	16	***69.6%***	26	***61.9%***	11	***40.7%***
		Any B	6	***26.1%***	12	***28.6%***	15	***55.6%***
		Any RT	12	***52.2%***	30	***71.4%***	18	***66.7%***
Glioma (GH) Grades III & IV	1986-90	Any DS	122	***69.0%***	88	***47.8%***	90	***61.6%***
		Any B	16	***9.1%***	62	***33.7%***	44	***30.1%***
		Any RT	94	***53.4%***	87	***47.3%***	76	***52.1%***
	1991-94	Any DS	125	***66.8%***	126	***60.6%***	102	***63.4%***
		Any B	46	***24.6%***	71	***34.1%***	51	***31.7%***
		Any RT	106	***56.7%***	139	***66.8%***	108	***67.1%***

DS	=	Definitive surgery
B	=	Biopsy
RT	=	Radiotherapy

Glioma Grades I & II (GL)

Although the overall operative rate was similar across the three neurosurgical centres in the earlier years, large differences were demonstrated in the nature of the surgery undertaken; between 1986 and 1990 the biopsy rate was considerable lower at Centre 1 (8.2% compared to 43.3% and 36.1%). During the latter part of the study, the differences between Centres 1 and 2 disappeared, with a biopsy being performed in just over a quarter of patients. In contrast, the biopsy rate increased by nearly 20% to 55.6% at Centre 3.

Employment of radiotherapy for the low grade gliomas, was lowest at Centre 1 throughout the study period, although the proportion of patients receiving this treatment almost doubled from 29.5% to 52.2% in the later years.

Glioma Grades III & IV (GH)

During 1986-90, the number of patients undergoing surgery was greatest at Centre 3, with the difference being in the region of 10%. By the second half of the study period, the biopsy rate within Centre 1 and the definitive surgery rate at Centre 2 had both risen, leading to broadly similar surgical patterns across the three centres for this group.

The reverse was seen with respect to the employment of radiotherapy; little variation was evident in the earlier years (1986-90: 53.4%, 47.3%, 52.1%) but more frequent use of this therapy was demonstrated, particularly at Centres 2 and 3 during the latter period (1991-1994; 56.7%, 66.8%, 67.1%).

4.4. MANAGEMENT OUTSIDE NEUROSURGERY

4.4.1. Non-Neurosurgical Specialities Managing CNS Tumours

▼ Speciality of Primary Managing Consultants

Speciality	Centre 1		Centre 2		Centre 3		No Centre	
Geriatrician	8	***53.3%***	5	***13.2%***	3	***50.0%***	121	***36.2%***
G Medicine	4	***26.7%***	14	***36.8%***	2	***33.3%***	116	***34.7%***
Neurology	1	***6.7%***	0	***0.0%***	0	***0.0%***	33	***9.9%***
Paediatrics	2	***13.3%***	2	***5.3%***	0	***0.0%***	3	***0.9%***
ENT	0	***0.0%***	10	***26.3%***	0	***0.0%***	3	***0.9%***
Other	0	***0.0%***	7	***18.4%***	1	***16.7%***	58	***17.4%***
Total	15	***100%***	38	***100%***	6	***100%***	334	***100%***

Only a small proportion (393: 18%) of patients were recorded as having been managed outside neurosurgery. The majority of these were managed by geriatricians/general physicians at non-specialist centres. The 59 patients managed at a neurosurgical centre, but not recorded as being managed by a neurosurgeon, represent only 3% of all those managed at such a centre. This does not mean that these patients did not see a neurosurgeon at all. As mentioned at the beginning of Chapter 4, the neurosurgeon would not be recorded if opinion was given without the actual transfer of management of a patient.

4.4.2. Use of Radiotherapy

According to NYCRIS registration practice, the primary managing consultant for all surgically treated CNS tumours would be the neurosurgeon. The neurosurgeon would also be responsible, in those cases, for the decision to refer for radiotherapy. For patients not managed by a neurosurgeon, this decision would be made by a consultant of another specialty, often in consultation with a neurosurgeon. Radiotherapy rates for the non-surgically managed glioma patients are therefore presented below.

▼ Use of Radiotherapy in Patients Not Managed by a Neurosurgeon : Gliomas (GL & GH) only

Centre	n	RT		No RT	
1	15	0	***0.0%***	15	***100%***
2	37	4	***10.8%***	33	***89.2%***
3	6	1	***16.7%***	5	***83.3%***
No Centre	293	25	***8.5%***	268	***91.5%***
Total	351	30	***8.5%***	321	***91.5%***

RT = Radiotherapy

Of the 351 glioma patients managed outside the specialty of neurosurgery, only 30 (8.5%) received radiotherapy, and the majority of these were being cared for in a non-specialist centre. Low treatment rates are to be expected in this group, since prognosis is likely to be very poor with many patients being too old or unfit for surgery or radiotherapy.

4.5. RADIOTHERAPY CENTRES

Two centres are responsible for the provision of radiotherapy services in the Yorkshire region: Cookridge Hospital in Leeds and Princess Royal Hospital in Hull. As the number of patients receiving radiotherapy in the meningiomas/nerve sheath tumours was minimal, the analyses presented here focus upon the gliomas only.

▼ Numbers of Cases Referred to Each Radiotherapy Centre

RT Centre	Overall		GL		GH	
Centre A	**671**	***42.1%***	145	***51.6%***	526	***40.1%***
Centre B	**252**	***15.8%***	36	***12.8%***	216	***16.5%***
Extra regional RT	**18**	***1.1%***	4	***1.4%***	14	***1.1%***
Not referred at all	**653**	***41.0%***	96	***34.2%***	557	***42.4%***
Total	**1594**	***100.0%***	281	***100%***	1313	***100%***

▼ Treatment Rates by Radiotherapy Centre

	% Of those referred for RT who actually received therapy		
RT Centre	GL	GH	Overall RT Treatment Rate
Centre A	***91.0%***	***83.7%***	***83.3%***
Centre B	***77.7%***	***87.0%***	***85.6%***

Nearly three-fifths of those patients diagnosed as having glioma (both low and high grade) during the study period were referred to one of the two radiotherapy centres, with the majority going to Centre A and a small number being referred outside the region.

Of those referred, around 84% actually received radiotherapy**.** For the high grade gliomas, **t**here was little difference in the administration rates between the two centres. A lower rate was, however, seen at Centre B for the low grade gliomas, although it should be noted that the numbers referred to this centre were relatively small.

The notes were checked of all cases referred to a radiotherapy centre, where there was no record of treatment having been given. These patients were all found either to be too ill for treatment, to have refused treatment or to have died before treatment was administered.

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SURVIVAL (1986-90)

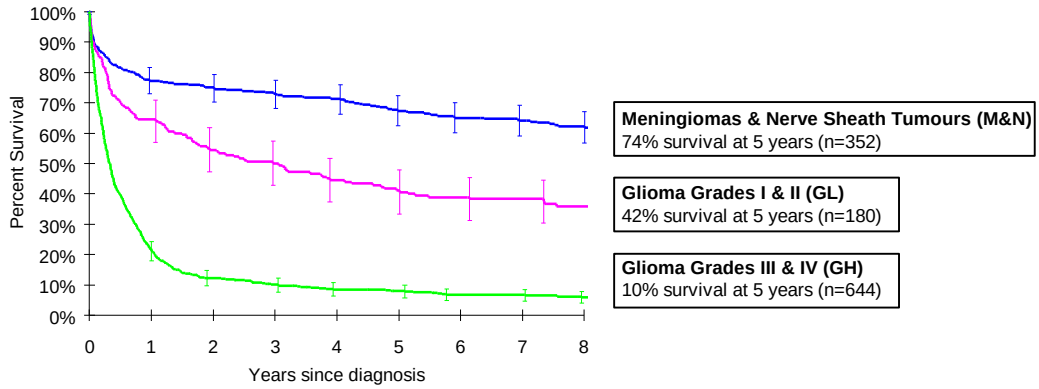
5

In planning the analysis of survival, consideration was given to identifying a cohort of patients with an adequate period of follow-up. Also, at the time of the CNS tumour review, information within the NYCRIS dataset relating to non-cancer deaths was complete only up to 1991, due to the introduction of a new National Cancer Registration Scheme computer system. As a result, the survival analyses presented within this chapter focus on patients diagnosed during the period 1986-90.

Throughout previous sections of this report, the impact of variation in casemix upon interpretation has been discussed. The results presented in this chapter are not adjusted for casemix. The reader is referred to chapter 6 for a more in-depth casemix adjusted, multivariate analysis. Statistical methodologies used for the survival analyses in this report are outlined in the appendix (Chapter 9).

5.1. SURVIVAL BY STUDY GROUP

▼ Survival by Study Group



The three study groups were defined on the basis of likely common management/prognosis and distinct and significant differences in survival were displayed. Meningiomas/nerve sheath tumours had the best prognosis, with 74% being alive at five years. In contrast, survival of the high grade gliomas was very poor, only 10% still being alive at five years.

5.2. SURVIVAL BY TREATMENT

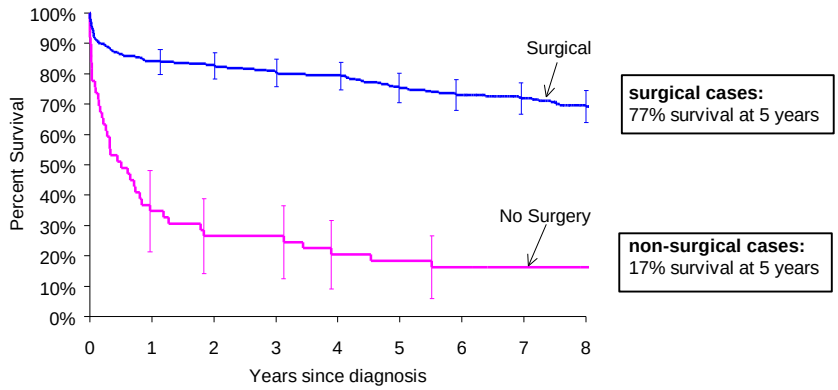
In practice (as opposed to the controlled environment of a randomised clinical trial), management decisions are based upon clinical judgement and prognosis of the individual patient, leading to systematic differences in casemix across the treatment groups. It is understood that retrospective reviews of outcome following treatment, such as this, do not provide evidence regarding the relative effectiveness of treatment modalities. Instead, analyses of survival by treatment are presented in order to explore the extent to which the results of research transfer to the population as a whole. Further it is hoped that, where evidence regarding optimal management is lacking, the information provided will help to promote discussion and inform future research strategies.

Attention is again drawn to the fact that only definitive treatment is routinely recorded within the NYCRIS dataset and where no definitive surgery was recorded, supplementary details of any biopsies performed were obtained from the registration paper records. Those figures which give an overview of all treatment modalities (as opposed to those making specific comparisons) reflect the analyses that would have been undertaken were the core NYCRIS dataset alone available. Because biopsy data were only obtained for those patients for whom no definitive

surgery was recorded, biopsy patients were grouped either with those who, according to NYCRIS computer records, received no treatment or with those who received radiotherapy alone, as appropriate.

Meningiomas & Nerve Sheath Tumours (M&N)

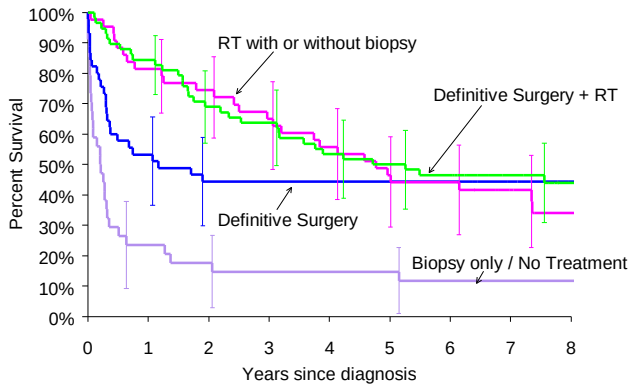
▼ Overview of All Treatment Modalities



Survival of patients who received definitive surgery was significantly better than those who did not ($p<0.001$). This does not, of course, imply that surgery was indicated in all cases; the majority of the non-surgical group were managed outside of a specialist centre and the review of registration records (described in section 4.1.1.) indicated that two-thirds of those not operated upon were considered either too old or too unfit for surgery.

Glioma Grades I & II (GL)

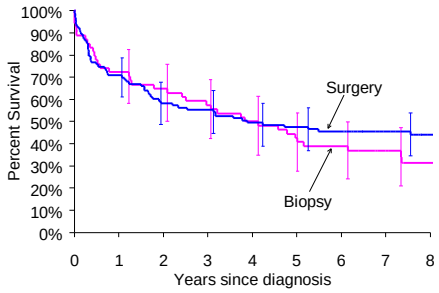
▼ Overview of All Treatment Modalities



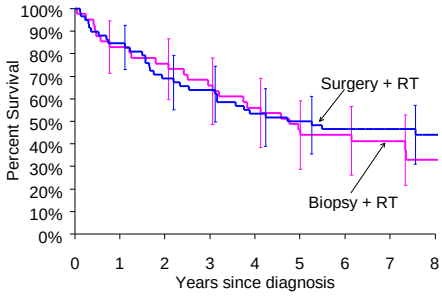
Examination of the overview graph indicates that survival was considerably lower amongst those patients who received either no treatment or a biopsy alone. Although differences were seen across the other treatment modalities, higher survival rates within the first three years seen for those patients who received radiotherapy, by five years these had disappeared and the survival rates were similar.

▼ Two-way Comparisons of Specific Treatment Modalities

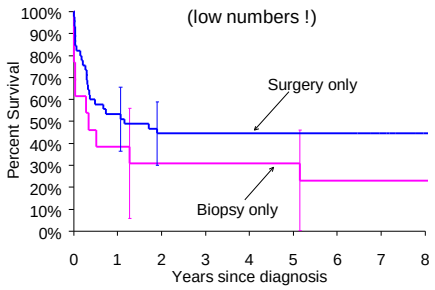
Definitive Surgery v Biopsy
(Whether RT was given or not)



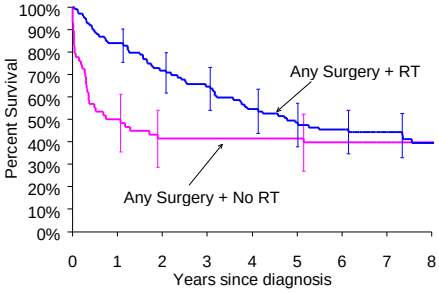
Definitive Surgery + RT v Biopsy + RT



Definitive Surgery Alone v Biopsy Alone



Surgery with RT v Surgery Alone
(Including both definitive surgery and biopsies)



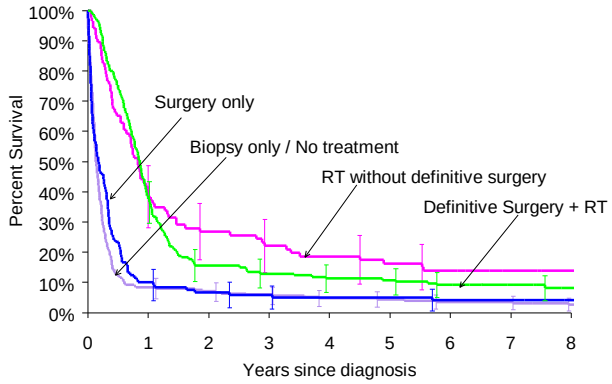
A two-way comparison of definitive surgery against biopsy, revealed only slight differences in survival, and this remained the case when the analysis was restricted to those who went onto receive radiotherapy. In the absence of further treatment, however, survival was better (although not significantly so) amongst those receiving definitive surgery, but the small numbers should be noted. A possible explanation may be the existence of two subgroups within the biopsy patients: the very poor prognosis cases who were too unwell for more aggressive treatment, and those generally fitter patients for whom surgical intervention was not possible due to the location of the tumour but who might benefit from radiotherapy.

Focusing next on patients who underwent surgery (regardless of its nature), large differences in short-term survival were seen according to whether or not radiotherapy was administered (survival rate at three years with RT : 65%, without RT : 40%). By five years these differences had disappeared. As stated in earlier chapters, current evidence from randomised clinical trials does not provide a clear indication as to the value of radiotherapy in the low grade gliomas and there is no consensus regarding optimal management of these tumours. Initial consideration of this result suggested that, whilst the retrospective design of the study did not allow conclusions on efficacy to be drawn, the magnitude of the observed difference in survival did add weight to the need for a clinical trial.

A number of deaths within the first few days of treatment was observed in patients receiving surgery alone. It is important to note that the available data relate to actual, rather than intended treatment. As a result, all post-operative deaths would fall within the surgery alone group. In order to investigate the extent to which post operative mortality influenced the results, the analysis was repeated after excluding patients who died within 30 days of surgery. The short term difference in survival between surgically treated patients who did and did not receive radiotherapy was still evident. The effect of excluding patients who died within 30 days of surgery is investigated further in the multivariate analysis in Chapter 6.

Glioma Grades III & IV (GH)

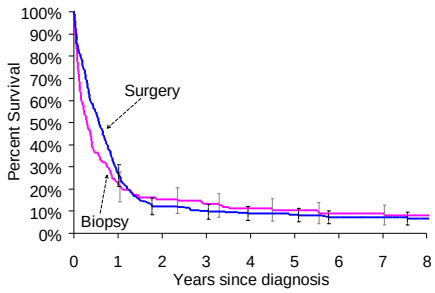
▼ Overview of All Treatment Modalities



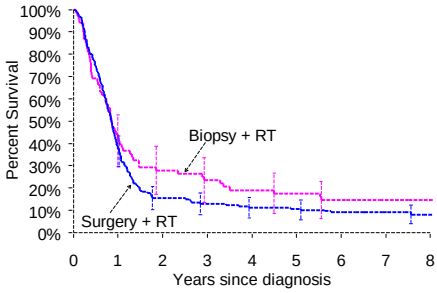
As with the low grade gliomas, survival was generally similar for patients given surgery and biopsy However, differences in survival by the nature of surgery were seen in patients who went on to receive radiotherapy, with the biopsy group demonstrating slightly better prognosis (but not significantly so).

▼ Two-way Comparisons of Specific Treatment Modalities

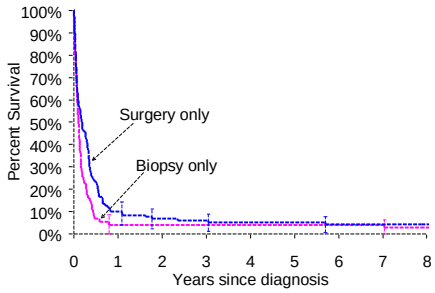
Definitive Surgery v Biopsy
(Whether RT was given or not)



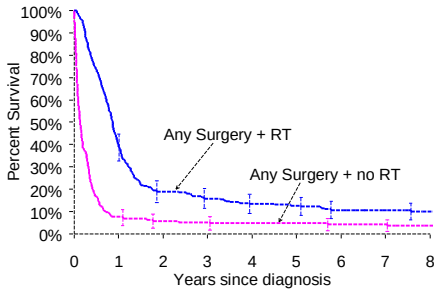
Definitive Surgery + RT v Biopsy + RT



Definitive Surgery Alone v Biopsy Alone



Surgery with RT v Surgery Alone
(Including both definitive surgery and biopsies)



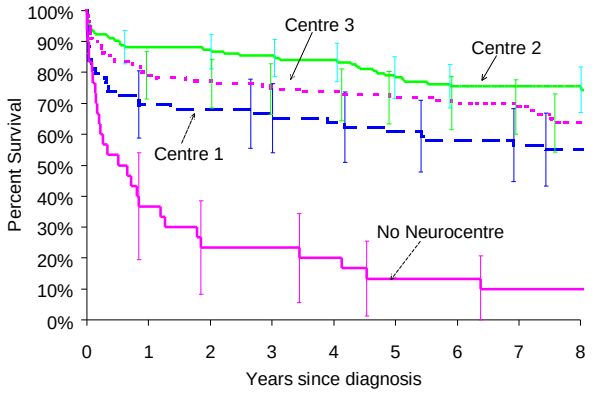
Throughout the eight year follow-up period, survival rates were generally higher when surgery (both definitive and biopsy) was given in combination with radiotherapy, as opposed to alone. In this case, the shape of the two survival curves was broadly similar and the possibility of a large number of deaths within the group of patients who only received surgery was less obvious (see previous section on low grade gliomas). A repeat analysis, excluding all deaths which occurred within 30 days of surgery, was nevertheless performed (and is also part of the multivariate analysis in Chapter 6). The differences in survival were still apparent, suggesting that the benefits of using radiotherapy within the high grade gliomas (as demonstrated by research evidence) appear to translate when administered in a population setting.

5.3. SURVIVAL BY NEUROSURGICAL CENTRE

Randomised clinical trials are the only established methodology for evaluating the relative effectiveness of different treatment modalities. However, the current restructuring of cancer services, in line with the Calman-Hine recommendations, and the greater emphasis on quality within the NHS has led to a particular interest in comparative, benchmarking information. Problems associated with the lack of relevant casemix data are well understood however, and in various parts of the UK, prospective management reviews are currently underway for a number of cancers. The methodology for such comparative studies continues to be developed, and some further refinement is still required. Nevertheless, in Yorkshire, the extent of the NYCRIS dataset was felt to provide an ideal basis for beginning to explore actual variation in management and outcome, and for promoting discussion about appropriate comparative methodologies.

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Survival by Neurosurgical Centre



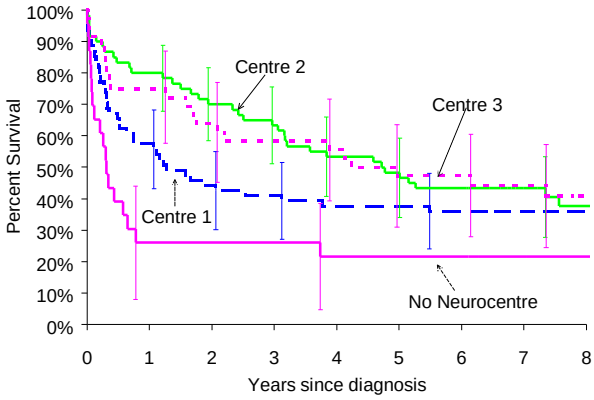
5 Year Survival:	No centre	= 12%
	Centre 1	= 60%
	Centre 2	= 79%
	Centre 3	= 72%

As described in section 4.3, management practices for this group were broadly similar across the three neurosurgical centres; the majority of patients were treated by definitive surgery alone, with limited use of radiotherapy. Despite this lack of variation in the treatment modalities employed, differences in survival were seen, with patients being managed at Centre 1 having significantly poorer survival than at the other two centres ($p<0.003$).

The characteristics of patients attending a particular neurosurgical centre is more likely to be determined by the hospital catchment area rather than by case selection, and the large numbers within any one catchment population are likely to minimise differences in casemix to a considerable extent. Given the similarity in treatment practices, however, casemix variation is one possible explanation for the differences in survival. It is possible, for example, that a higher proportion of patients within the catchment area for Centre 1 underwent surgery (including those more complex cases where the tumour is relatively inaccessible), whereas similar patients in the rest of the region may have been managed outside of the neurosurgical centres. The apparent higher numbers of post-operative deaths at Centre 1, as suggested by a greater drop in survival within a few days of surgery, may support such an explanation. Further investigation of this hypothesis is unfortunately not possible due to a lack of detailed tumour site information, as reported earlier in this report. However, adjustment for age have been made in the multivariate analysis of survival in Chapter 6.

Glioma Grades I & II (GL)

▼ Survival by Neurosurgical Centre

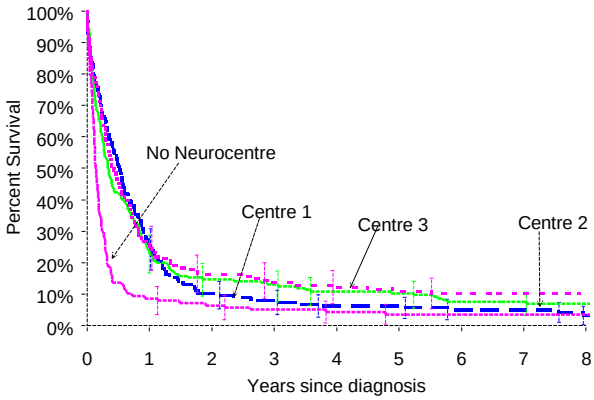


5 Year Survival:	No centre	= 22%
	Centre 1	= 38%
	Centre 2	= 48%
	Centre 3	= 48%

Survival for patients managed at Centres 2 & 3 was fairly similar, but that for Centre 1 was somewhat different, with generally lower rates being demonstrated up to approximately five years (although not significantly so). In section 4.3, a corresponding pattern in relation to treatment practices was described, where Centre 1 was shown to have lower rates of both biopsy and of radiotherapy. Possible explanations included a true difference in management practices, possibly reflecting the current lack of consensus regarding optimal treatment, or variations in casemix. Data were also presented in section 5.2 demonstrating improved survival (up to three years from diagnosis) amongst those patients receiving radiotherapy, although again the retrospective design of this study did not make it possible to determine whether this was due to actual benefits of treatment or to a better underlying prognosis in the radiotherapy group. Nevertheless, the existence of variation in both treatment practices and in survival across neurosurgical centres would seem to support the value of further work to explain these differences.

Glioma Grades III & IV (GH)

▼ Survival by Neurosurgical Centre



5 Year Survival:	No centre	= 3%
	Centre 1	= 7%
	Centre 2	= 11%
	Centre 3	= 11%

Referring back to the review of treatment for the high grade gliomas in section 4.3, the rates of surgery (definitive surgery and biopsies combined) and radiotherapy were similar across all three neurosurgical centres, although a higher proportion of biopsies was performed at both Centres 2 & 3. Consistency was also seen in relation to survival, where only slight differences were observed, the five-year rates being relatively poor at all the centres.

5.3.1. Post Operative Mortality (1986 to 1990)

▼ % of definitive surgical cases where death occurred within 30 days from operation

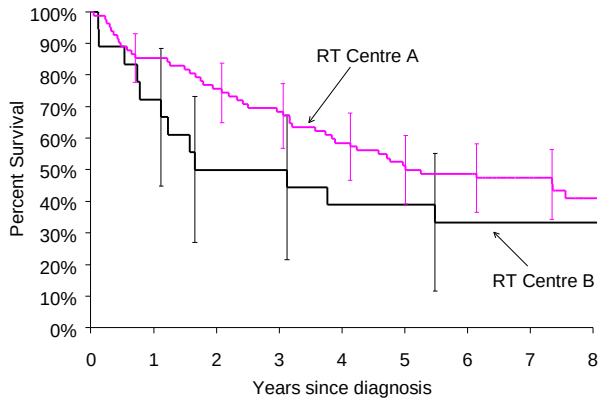
	Post Operative Mortality (deaths within 30 days / no. of definitive surgical cases)					
Centre	M&N		GL		GH	
1	10/60	*16.7%*	5/38	*13.2%*	14/95	*14.7%*
2	4/102	*3.9%*	2/24	*8.3%*	13/67	*19.4%*
3	5/62	*8.1%*	1/16	*6.3%*	13/72	*18.1%*
All	19/229	*8.3%*	8/80	*10.0%*	41/237	*17.3%*

Within the time period 1986 to 1990, the interval used for the survival analyses, post operative mortality was slightly higher at Centre 1 for the patients with meningiomas and nerve sheath tumours and low grade gliomas. For the patients with high grade glioma, post operative mortality was higher at Centres 2 and 3.

5.4. SURVIVAL BY RADIOTHERAPY CENTRE

Glioma Grades I & II (GL)

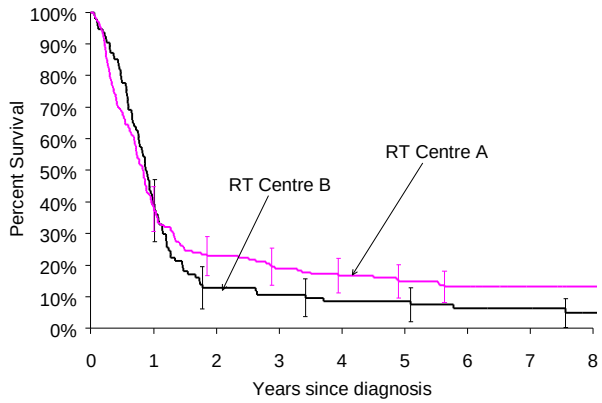
▼ Survival by RT Hospital



Although some difference in survival between the two Yorkshire radiotherapy centres was suggested, numbers were small (particularly in the low grade glioma group) and no statistically significant differences were observed. Data relating to radiotherapy intent were not available and it was not possible to distinguish between radical and palliative courses of treatment, adding to the problems of interpretation.

Glioma Grade III & IV (GH)

▼ Survival by RT Hospital



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6 MULTIVARIATE SURVIVAL

6.1. RELATIVE RISK

The survival analyses shown in Chapter 5 did not account for any differences in patient case mix. Limited casemix information was available within the NYCRIS dataset and it was not, therefore, possible to allow for certain known prognostic factors, such as performance status and tumour site within the multivariate analysis of survival presented in this chapter. It is recognised that studies such as this can never fully account for differences in the distribution of unknown casemix factors. Despite this, the results show interesting survival trends which are worthy of discussion. A brief outline of the statistical methodologies employed in this section and how the relative risk tables are interpreted, is given in the appendix (Chapter 9).

Meningiomas & Nerve Sheath Tumours (M&N)

▼ Relative Risk

Factors		Relative Risk					
		Factors Alone		Allowing Age		All Factors Together	
Casemix							
Age (yr)	<50	1.00		1.00		1.00	
	50-64	1.81	(0.98 - 3.32)	1.81	(0.98 - 3.32)	1.72	(0.93 - 3.19)
	65-74	5.44	(3.07 - 9.61)	5.44	(3.07 - 9.61)	4.43	(2.45 - 8.02)
	75+	6.70	(3.58 - 12.53)	6.70	(3.58 - 12.53)	2.97	(1.43 - 6.18)
Period	1986	1.00		1.00		1.00	
	1987	1.13	(0.68 - 1.87)	1.48	(0.89 - 2.47)	1.45	(0.86 - 2.44)
	1988	1.13	(0.66 - 1.93)	1.30	(0.76 - 2.23)	1.24	(0.70 - 2.17)
	1989	1.18	(0.66 - 2.11)	1.40	(0.78 - 2.52)	1.41	(0.77 - 2.59)
	1990	1.53	(0.91 - 2.58)	1.80	(1.06 - 3.06)	1.74	(1.00 - 3.05)
Other Patient Factors							
Treatment	None	1.00		1.00		1.00	
	DS alone	0.19	(0.13 - 0.29)	0.30	(0.18 - 0.50)	0.42	(0.23 - 0.76)
	DS+RT	0.70	(0.27 - 1.81)	0.76	(0.28 - 2.04)	1.00	(0.34 - 2.94)
	B alone	1.15	(0.55 - 2.42)	1.14	(0.53 - 2.46)	1.28	(0.56 - 2.93)
	B+RT	2.06	(0.28 - 15.18)	4.28	(0.55 - 33.33)	3.22	(0.38 - 27.15)
Hospital Factors							
Neuro-surgical centre	Centre 1	1.00		1.00		1.00	
	Centre 2	0.48	(0.30 - 0.76)	0.57	(0.35 - 0.91)	0.54	(0.33 - 0.89)
	Centre 3	0.68	(0.43 - 1.09)	0.68	(0.42 - 1.09)	0.64	(0.38 - 1.08)
	No Centre	3.27	(1.94 - 5.50)	2.19	(1.26 - 3.78)	1.38	(0.75 - 2.55)

Patient age was found to have the largest impact on survival. After allowing for both casemix and hospital factors, the expected improvement in survival was seen amongst those who received definitive surgery (relative risk : 0.42 (0.23-0.76)). The previously described differences across neurosurgical centres were still evident following a casemix adjusted analysis, with Centre 1 having significantly poorer survival (relative risk : 1.0) compared to Centre 2 (relative risk : 0.54 (0.33-0.89)). The reader is referred to section 5.3. for further discussion of this. In contrast, the lower survival of patients managed at a non-specialist centre was no longer significant when controlling for age and treatment factors, reflecting the fact that this group were generally older, with more advanced disease.

Glioma Grades I & II (GL)

▼ Relative Risk

Factors		Relative Risk					
		Factors Alone		Allowing Age		All Factors Together	
Casemix							
Age (yr)	<50	1.00		1.00		1.00	
	50-64	3.37	(2.20 - 5.16)	3.37	(2.20 - 5.16)	3.56	(2.24 - 5.64)
	65-74	7.54	(3.93 - 14.49)	7.54	(3.93 - 14.49)	5.00	(2.24 - 11.15)
	75+	13.09	(6.25 - 27.45)	13.09	(6.25 - 27.45)	7.34	(2.80 - 19.25)
Period	1986	1.00		1.00		1.00	
	1987	0.61	(0.35 - 1.07)	0.93	(0.52 - 1.66)	1.03	(0.56 - 1.88)
	1988	0.89	(0.52 - 1.52)	0.91	(0.53 - 1.55)	1.03	(0.60 - 1.79)
	1989	0.67	(0.38 - 1.19)	0.93	(0.52 - 1.68)	1.05	(0.57 - 1.94)
	1990	0.56	(0.31 - 1.00)	0.88	(0.48 - 1.61)	0.96	(0.51 - 1.82)
Other Patient Factors							
Treatment	None	1.00		1.00		1.00	
	DS alone	0.22	(0.12 - 0.41)	0.51	(0.24 - 1.08)	0.55	(0.25 - 1.22)
	DS+RT	0.17	(0.09 - 0.30)	0.39	(0.18 - 0.83)	0.43	(0.20 - 0.92)
	B alone	0.45	(0.21 - 0.95)	0.92	(0.41 - 2.08)	1.00	(0.44 - 2.26)
	B+RT	0.20	(0.11 - 0.36)	0.58	(0.26 - 1.27)	0.64	(0.29 - 1.44)
	RT alone	0.16	(0.02 - 1.17)	0.30	(0.04 - 2.31)	0.27	(0.03 - 2.13)
	Any DS	0.19	(0.11 - 0.32)	0.46	(0.23 - 0.94)	0.48	(0.23 - 0.98)
	Any Non-DS	0.24	(0.14 - 0.42)	0.67	(0.33 - 1.37)	0.72	(0.35 - 1.49)
	Any B	0.24	(0.14 - 0.42)	0.70	(0.34 - 1.46)	0.78	(0.37 - 1.62)
	Any Non-B	0.19	(0.11 - 0.32)	0.47	(0.23 - 0.95)	0.48	(0.24 - 0.99)
	Any RT	0.18	(0.11 - 0.31)	0.47	(0.23 - 0.97)	0.50	(0.24 - 1.03)
	Any Non-RT	0.26	(0.15 - 0.46)	0.61	(0.30 - 1.23)	0.68	(0.33 - 1.40)
Hospital Factors							
Neuro-surgical centre	Centre 1	1.00		1.00		1.00	
	Centre 2	0.78	(0.50 - 1.22)	1.02	(0.64 - 1.62)	0.96	(0.55 - 1.66)
	Centre 3	0.74	(0.43 - 1.25)	0.80	(0.46 - 1.38)	0.79	(0.44 - 1.42)
	No Centre	1.78	(1.02 - 3.12)	1.35	(0.76 - 2.39)	1.34	(0.71 - 2.51)

As with the meningiomas/nerve sheath tumours, the largest differences in survival were attributable to age and there was little variation by year of diagnosis. In relation to treatment, the univariate analyses presented in Chapter 5 demonstrated better survival for patients receiving either definitive surgery alone or surgery (regardless of its nature) in conjunction with radiotherapy. When adjusted for age and treatment and hospital factors, only the most radical combination of definitive surgery, together with radiotherapy, continued to show significantly decreased relative risk (relative risk: 0.43 (0.20-0.92)). In a repeat analysis, excluding patients who died within 30 days post-operatively, however, there was found to be no survival difference between patients given definitive surgery alone (relative risk : 0.12 (0.06-0.24)) and definitive surgery with radiotherapy (0.13 (0.07-0.23)). The results do not show a clear-cut difference in the survival of low grade glioma patients given definitive surgery with radiotherapy and those treated with definitive surgery alone. Univariate analysis in chapter 5 suggested an improvement in early survival (up to three years from diagnosis) for those patients who received radiotherapy, but these multivariate analyses address overall survival.

Examination of each individual treatment modality, indicated better survival for both definitive surgery and radiotherapy, although differences only remained significant in the case of definitive surgery when controlling for casemix and hospital factors. In the context of the current lack of clinical trial evidence on the value of radiotherapy, the results demonstrated here perhaps highlight further, the need for a randomised controlled trial to determine the optimal management of these patients.

There were no significant differences in survival between neurosurgical centres across the whole time period, although the univariate analysis in the previous chapter suggested a difference in survival during the earlier years.

Glioma Grades III & IV (GH)

▼ Relative Risk

Factors		Relative Risk					
		Factors Alone		Allowing Age		All Factors Together	
Casemix							
Age (yr)	<50	1.00		1.00		1.00	
	50-64	2.30	(1.83 - 2.89)	2.30	(1.83 - 2.89)	2.25	(1.78 - 2.84)
	65-74	3.48	(2.72 - 4.46)	3.48	(2.72 - 4.46)	2.63	(2.02 - 3.43)
	75+	4.58	(3.36 - 6.25)	4.58	(3.36 - 6.25)	2.83	(1.97 - 4.06)
Period	1986	1.00		1.00		1.00	
	1987	0.96	(0.74 - 1.26)	1.02	(0.78 - 1.33)	1.05	(0.80 - 1.39)
	1988	0.96	(0.73 - 1.25)	1.01	(0.77 - 1.33)	1.05	(0.80 - 1.38)
	1989	0.91	(0.69 - 1.20)	0.93	(0.70 - 1.22)	0.89	(0.67 - 1.17)
	1990	1.00	(0.76 - 1.32)	1.16	(0.87 - 1.53)	1.24	(0.93 - 1.65)
Other Patient Factors							
Treatment	None	1.00		1.00		1.00	
	DS alone	0.92	(0.72 - 1.16)	1.15	(0.89 - 1.48)	1.31	(0.98 - 1.75)
	DS+RT	0.38	(0.30 - 0.47)	0.52	(0.41 - 0.66)	0.56	(0.42 - 0.74)
	B alone	1.46	(1.11 - 1.92)	1.86	(1.40 - 2.48)	1.98	(1.47 - 2.68)
	B+RT	0.33	(0.24 - 0.45)	0.51	(0.37 - 0.70)	0.53	(0.38 - 0.75)
	RT alone	0.44	(0.26 - 0.73)	0.56	(0.33 - 0.93)	0.58	(0.34 - 0.99)
	Any DS	0.51	(0.42 - 0.62)	0.76	(0.61 - 0.95)	0.84	(0.65 - 1.09)
	Any Non-DS	0.58	(0.47 - 0.73)	0.92	(0.71 - 1.17)	0.97	(0.74 - 1.26)
	Any B	0.60	(0.48 - 0.75)	0.98	(0.76 - 1.26)	1.03	(0.78 - 1.36)
	Any Non-B	0.51	(0.42 - 0.62)	0.75	(0.60 - 0.94)	0.83	(0.64 - 1.07)
	Any RT	0.37	(0.30 - 0.45)	0.53	(0.42 - 0.67)	0.58	(0.45 - 0.75)
	Any Non-RT	1.07	(0.87 - 1.32)	1.36	(1.09 - 1.70)	1.56	(1.21 - 2.02)
Hospital Factors							
Neuro-surgical centre	Centre 1	1.00		1.00		1.00	
	Centre 2	1.02	(0.82 - 1.26)	1.13	(0.91 - 1.40)	1.01	(0.81 - 1.26)
	Centre 3	0.92	(0.73 - 1.16)	1.08	(0.86 - 1.37)	0.95	(0.75 - 1.21)
	No Centre	1.90	(1.51 - 2.39)	1.48	(1.15 - 1.91)	1.27	(0.95 - 1.69)

Patient age was again found to have the greatest effect on survival, although this was to a lesser degree than for either of the other two study groups. All treatment modalities involving radiotherapy (either alone or following surgery) demonstrated better survival, both in the univariate analysis in chapter 5, and when controlling for casemix and hospital factors here. This was also illustrated by the much improved survival of patients receiving radiotherapy, compared with both the groups receiving other forms of treatment and those receiving no active intervention. This was still found to be true when the analysis was repeated after excluding patients who died within 30 days post operatively. These results again suggests that the benefits of radiotherapy within the high grade gliomas, as recommended in the light of RCT evidence, appear to translate when administered in a population setting (see section 5.3.).

No differences in survival were seen across the specialist neurosurgical centres, both in the univariate and the casemix adjusted analyses.

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REFERRAL TIMES 7

7.1. AVAILABILITY OF REFERRAL DATA

Recording of referral data within hospital notes is generally poor, particularly in relation to the date of referral by the GP where, in the case of the CNS tumours, information was available in less than a third of patients. Further, experience suggests that the more aggressive management of good prognosis patients is often associated with a greater level of detail within the casenotes. The planning of radical treatment commonly requires longer than the organisation of palliative therapy and, as a result, the bias towards good prognosis patients within the group for which referral data is available may have inflated the management intervals presented within this chapter. Care should, therefore, be taken in the interpretation of the results.

▼ Availability of Referral Data

Date Type	Number Available	Percent Available
Date of GP referral	674	***30.0%***
Date of first hospital visit*	2214	***98.6%***
Date of first definitive treatment or date of decision not to treat	1977	***88.1%***

* Date of first hospital visit relates to initial attendance at the hospital of primary management rather than that of presentation.

7.2. GP REFERRAL TO START OF TREATMENT

Analysis of the interval between GP referral and the start of treatment was based upon 594 patients, approximately 26.5% of all cases. Particular attention is drawn to completeness across the various factors, which confirms previous experience that referral information is generally more limited for the poorer prognosis groups, such as the high grade gliomas and patients aged 60 and over.

7.2.1. Length of Management Interval

▼ GP Referral to Start of Treatment

	Factor	Complete	Management Interval									
			Within 2 wks		2 wks-1 mth		1-6 mths		6 mths-1 yr		Over 1 yr	
Study Group	M&N	***31.8%***	30	***14.5%***	41	***19.8%***	118	***57.0%***	12	***5.8%***	6	***2.9%***
	GL	***29.9%***	20	***23.8%***	17	***20.2%***	36	***42.9%***	8	***9.5%***	3	***3.6%***
	GH	***23.1%***	114	***37.6%***	70	***23.1%***	107	***35.3%***	9	***3.0%***	3	***1.0%***
Age Group	0-29	***30.7%***	16	***29.6%***	18	***33.3%***	18	***33.3%***	1	***1.9%***	1	***1.9%***
	30-59	***35.9%***	64	***25.4%***	41	***16.3%***	121	***48.0%***	17	***6.7%***	9	***3.6%***
	60	***25.8%***	84	***29.2%***	69	***24.0%***	122	***42.4%***	11	***3.8%***	2	***0.7%***
Time Period	1986-88	***35.9%***	84	***32.6%***	59	***22.9%***	103	***39.9%***	8	***3.1%***	4	***1.6%***
	1989-91	***24.0%***	56	***33.7%***	34	***20.5%***	66	***39.8%***	7	***4.2%***	3	***1.8%***
	1992-94	***20.3%***	24	***14.1%***	35	***20.6%***	92	***54.1%***	14	***8.2%***	5	***2.9%***
Overall		***26.4%***	164	***27.6%***	128	***21.5%***	261	***43.9%***	29	***4.9%***	12	***2.0%***

For all study groups combined, nearly half (49.1%) of patients were treated within one month of referral. This proportion was greatest for the high grade gliomas (60.7%), reflecting the more severe and rapidly progressive nature of the symptoms associated with these tumours. In contrast, the interval between referral and treatment exceeded a month in nearly 65.7% of the meningiomas/nerve sheath tumours and 56% the low grade gliomas, consistent with both less urgent referral and a 'wait-and-see' management policy.

Treatment was started more rapidly amongst children and younger adults (under the age of 30), with 62.9% being treated within a month of referral. This fell to 41.7% in the 30-59 agegroup and 53.2% in the over 60's. This result should, however, be viewed with caution due to the small numbers in the younger age band.

In the latter third of the study period, the length of time between GP referral and the start of treatment generally increased, the proportion being treated within a month falling from 55.5% (1986-88) to 34.7% (1992-94).

7.2.2. Impact on Survival

Within the low grade gliomas, there were no significant differences in survival (p>0.2) according to the interval between referral by the GP and start of treatment, in line with the clinical approach of adopting a 'wait-and-see' policy where treatment is employed once symptoms necessitate intervention. Differences were, however, seen in both the meningiomas/nerve sheath tumours (p=0.02) and the high grade gliomas (p=0.001); survival rates were poorest amongst those being treated within a month of referral, confirming the suggestion in 7.1. above that management intervals are likely to be shorter for patients with a more serious condition, who were more likely to need a more urgent and quicker referral.

7.3. First Hospital Visit to Start of Treatment

Information regarding the interval between the first hospital visit and the start of treatment were much more complete, both dates being available for 87% of all patients. Although these increased levels of completeness allow for greater confidence in the results presented within this section, the proportion of cases with referral data available again fell with worsening prognosis (from 91.1% in the low grade gliomas to 84.2% in the high grade gliomas) and increasing age (from 97.9% in the under 30's to 80.5% in the over 60's), again demonstrating the need for caution in interpretation.

7.3.1. Length of Management Interval

▼ First Hospital Visit to Start of Treatment

	Factor	Complete	Management Interval							
			Within 2 wks		2 wks-1 mth		1-6 mths		Over 6 mths	
Study Group	M&N	***90.5%***	332	***56.4%***	82	***13.9%***	155	***26.3%***	20	***3.4%***
	GL	***91.1%***	135	***52.7%***	32	***12.5%***	72	***28.1%***	17	***6.6%***
	GH	***84.2%***	748	***67.7%***	142	***12.9%***	199	***18.0%***	16	***1.4%***
Age Group	0-29	***97.0%***	106	***62.4%***	26	***15.3%***	33	***19.4%***	5	***2.9%***
	30-59	***92.5%***	553	***62.7%***	102	***11.6%***	196	***22.2%***	31	***3.5%***
	60	***80.5%***	556	***61.9%***	128	***14.3%***	197	***21.9%***	17	***1.9%***
Time Period	1986-88	***91.8%***	434	***66.0%***	84	***12.8%***	124	***18.8%***	16	***2.4%***
	1989-91	***87.3%***	395	***65.5%***	69	***11.4%***	125	***20.7%***	14	***2.3%***
	1992-94	***82.3%***	386	***56.0%***	103	***14.9%***	177	***25.7%***	23	***3.3%***
Neurosurgical Centre	Centre 1	***90.0%***	317	***60.6%***	86	***16.4%***	109	***20.8%***	11	***2.1%***
	Centre 2	***91.5%***	442	***62.4%***	76	***10.7%***	164	***23.2%***	26	***3.7%***
	Centre 3	***93.5%***	352	***67.7%***	61	***11.7%***	95	***18.3%***	12	***2.3%***
Overall		***86.8%***	1215	***62.3%***	256	***13.1%***	426	***21.8%***	53	***2.7%***

Over three-fifths (62.3%) of all patients were treated within two weeks of their first hospital visit (as defined in section 7.1.). The proportion of patients waiting in excess of one month was highest in the low grade gliomas (34.7%) again, consistent with the possibility of a 'wait-and-see' management policy for this group. In contrast to the findings of the previous section, results for the meningiomas/nerve sheath tumours and the high grade gliomas were broadly similar (M&N=29.7%, GH=19.4%). This may suggest that the increased intervals between GP referral and start of treatment within the former group (M&N) were attributable to differences in the urgency of referral (in the presence of more general and less severe symptoms) rather than the time taken to arrange treatment.

No differences were seen across the age groups, and increases over the study period were much reduced, again suggesting that the variations outlined in section 7.2.1. may be explained by longer waiting times for an initial visit. It should, however, be remembered that the datasets on which these two analyses were based are somewhat different, with a much smaller proportion of patients being included in the study of the time between GP referral and start of treatment.

Centre 2, the hospital managing the greatest number of CNS tumours during the period 1986-94, had a slightly higher proportion of patients being treated more than a month after their first hospital visit (Centre 1 : 22.9%, Centre 2 : 26.9%, Centre 3 : 20.6%).

7.4. DEFINITIVE SURGERY TO RADIOTHERAPY

As the number of patients receiving radiotherapy in the meningiomas/nerve sheath tumours was minimal, the analysis of the interval between definitive surgery and radiotherapy described within this section was limited to the gliomas. This aspect of management has been the subject of consideration within published guidelines (Grant et al. 1994), where it was recommended that 'the delay from surgical diagnosis to starting radiotherapy should be kept to a minimum, and ideally should not exceed four weeks'. Of the 531 glioma patients who received definitive surgery, in combination with radiotherapy, complete referral data was available in one third of cases.

7.4.1. Length of Management Interval

▼ Definitive Surgery to Radiotherapy (Gliomas Only)

	Factor	Complete (n=531)	Management Interval					
			Within 1 month		1-2 mths		Over 2 mths	
Study Group	GL	31.7%	41	***46.1%***	32	***36.0%***	16	***18%***
	GH	33.7%	283	***64.0%***	137	***31.0%***	22	***5.0%***
Age Group	0-29	33.3%	21	***44.7%***	19	***40.4%***	7	***14.9%***
	30-59	43.9%	175	***59.5%***	95	***32.3%***	24	***8.2%***
	60	24.2%	128	***67.4%***	55	***28.9%***	7	***3.7%***
Time Period	1986-88	27.8%	103	***76.3%***	25	***18.5%***	7	***5.2%***
	1989-91	32.5%	97	***57.4%***	56	***33.1%***	16	***9.5%***
	1992-94	38.6%	124	***54.6%***	88	***38.8%***	15	***6.6%***
Neurosurgical Centre	Centre 1	43.4%	152	***78.4%***	26	***13.4%***	16	***8.2%***
	Centre 2	38.1%	103	***54.8%***	76	***40.4%***	9	***4.8%***
	Centre 3	37.8%	64	***45.7%***	65	***46.4%***	11	***7.9%***
Radiotherapy Centre	Centre A	50.8%	168	***49.3%***	148	***43.4%***	25	***7.3%***
	Centre B	72.2%	154	***84.6%***	16	***8.8%***	12	***6.6%***
Overall		33.3%	324	***61.0%***	169	***31.8%***	38	***7.2%***

Overall, 61% of patients received radiotherapy within the recommended period of four weeks. Differences by tumour grade were once again demonstrated, with a delay of less than four weeks in nearly half (46.1%) of the low grade gliomas, compared to nearly two-thirds of patients with high grade tumours. The increased amount of time required for planning radical, as opposed to palliative, treatment has previously been discussed and is thought to be a likely contributing factor to the longer intervals seen amongst the better prognosis, low grade gliomas. This constraint may, perhaps, also explain the variation seen across the age groups, where the proportion of patients receiving radiotherapy within four weeks of surgery was over 20% lower in those under the age of 30, compared with those over the age of 60.

Between 1986-88 and 1989-91, there was a sharp rise in the numbers of patients for whom the delay in starting radiotherapy was longer than the recommended interval of four weeks, with the rate almost doubling from 23.7% to 45.4%.

Variation was seen across hospitals; a high proportion of cases began radiotherapy within four weeks at both Neurosurgical Centre 1 (78.4%) and at Radiotherapy Centre B (84.6%). The proportion of patients receiving radiotherapy within four weeks at the other hospitals were somewhat lower, but as three-quarters of all radiotherapy was administered at Centre A, it is possible that availability of machines could have had an impact on this management interval.

7.4.2. Impact of Management Interval on Survival

No significant survival differences were demonstrated, for either the low or the high grade gliomas, in relation to the interval between definitive surgery and radiotherapy. Although it may have been expected that shorter intervals would be associated with better survival, it should again be remembered that the casemix of patients grouped according to delay in radiotherapy is unlikely to be comparable with those being treated quickly, generally having a poorer prognosis.

8 ADDITIONAL DATA ANALYSIS

The casenotes of a stratified, random sample of 299 patients (10% of all CNS tumour registrations during the period 1986-94) were reviewed and the core NYCRIS dataset re-extracted by trained and experienced registration staff. Details of treatment administered within six months of the first episode (as opposed to nine weeks which was standard until 1994) were also collected. This was primarily undertaken with a view to assessing the quality of the analysis dataset and, with the exception of the brief discussion below on the impact of the 'nine-week rule', the results of this evaluation will be the subject of a separate report (see 9.1.3 for an outline of the data quality methodologies employed) .

A further objective was to repeat certain key analyses on this small subset of patients, looking at differences in casemix, and a limited amount of additional prognostic factor and treatment information was, therefore, extracted. In the event, many casenotes were found to have been destroyed or to be unavailable, and the resulting dataset was consequently biased towards the later years and towards radiotherapy cases. For completeness, a descriptive analysis of this data is included, but the selective nature of the sample precluded a more in-depth study.

8.1. IMPACT OF THE NINE-WEEK RULE

▼ Comparison of Casenote Review with NYCRIS Dataset

		Casenote review		
		Surgery	Biopsy	Neither
NYCRIS dataset*	Surgery	191	0	6
	No Surgery	0	44	58

		Casenote review	
		RT	No RT
NYCRIS dataset	RT	130	6
	No RT	0	161
	Not known	0	2

* Biopsy details not routinely recorded within the NYCRIS dataset

The amount of information available within the NYCRIS dataset was greater than that obtained from the casenote review; for both surgery and radiotherapy, details were not found of treatment known to have been given to six patients (2%). In many instances, the problems with casenote availability made it necessary for the review to rely upon one data source, in contrast to the multi-source nature of the original registration. Of the 58 cases where the review confirmed that surgery had not been performed, 34 (58.6%) were found to have been assessed (without formal transfer of management) by a neurosurgeon.

8.2. SUMMARY OF ADDITIONAL DATA

▼ Summary of Additional Data

Factor	N	Description	n	Affected
Symptoms at Presentation	299	Headaches	122	***40.8%***
		Personality Changes	25	***8.4%***
		Fits	54	***18.1%***
		Focal Signs	140	***46.8%***
		Other	194	***64.9%***
		Unknown	6	***2.0%***
WHO Performance Status at Diagnosis	130	0	34	***26.2%***
		1	50	***38.5%***
		2	19	***14.6%***
		3	13	***10.0%***
		4	13	***10.0%***
		Insufficient information	1	***0.8%***
Level of Consciousness at Presentation	299	Fully Conscious	271	***90.6%***
		Semi Conscious	12	***4.0%***
		Unconscious	7	***2.3%***
		Not Known	9	***3.0%***
Level of Consciousness after Treatment	299	Fully Conscious	258	***86.3%***
		Semi Conscious	4	***1.3%***
		Unconscious	0	***0%***
		Died before completion	20	***6.7%***
		Not Known	17	***5.7%***
Change in Level of Consciousness on completion of treatment	299	Improvement	10	***3.3%***
		No Change	247	***82.6%***
		Deterioration/Died	21	***7.0%***
		Not Known	21	***7.0%***
Elective or Acute Admission[ii]	299	Elective	116	***38.8***
		Acute	55	***18.4***
		Not Known	128	***42.8***
Radiotherapy Intent[iii]	130	Radical	55	***42.3%***
		Intermediate	47	***36.2%***
		Palliative	28	***21.5%***

▼ Notes to above table

i **WHO Performance Status**

Category definitions described below - Status determined by one of the clinical representatives from information contained within the casenotes; details available for radiotherapy patients only

Grade	Summary	Description of performance status
0	Normal	Able to carry out all normal activity without restriction
1	With Effort	Restricted in physically strenuous activity; ambulatory, can do light work
2	Restricted	Ambulatory and capable of all self-care but unable to carry out any work; up and about more than 50% of waking hours
3	Dependent	Capable of only limited self-care; confined to bed or chair for more than 50% of waking hours
4	Immobile	Completely disabled; cannot carry out any self-care; totally confined to bed or chair

ii **Elective/Acute Admission**

Information obtained from hospital notes only; the majority of cases for whom the admission route was not known are, therefore, likely to be GP referrals

iii **Radiotherapy Intent**

Details of dosage given were obtained from the radiotherapy notes, and used to define the following (not exhaustive) treatment intent categories

Treatment Intent	Radiotherapy Dosage
Radical :	From 30 fractions over 6 weeks to 25 over 5 weeks. Initial performance status 0, 1, 2.
Intermediate :	20-22 fractions over 4 weeks. Performance status 2 or 3.
Palliative :	5 fractions in a week to 15 over 3 weeks. Performance status 4.

APPENDIX 9

9.1. DATA AND METHODS

9.1.1. Overview of Study Dataset

Data held by the Northern and Yorkshire Cancer Registry and Information Service (NYCRIS) relate to the population of the former Yorkshire Regional Health Authority, a socially diverse yet relatively stable population of 3.6 million. In total, approximately 17,500 new malignant cancer patients are registered annually within this region, the details being extracted from hospital clinical notes by trained cancer registration staff.

▼ Availability of Relevant Data Items

Data Type	Available	Not Available
Patient	Age	Performance status
	Sex	
	District of residence	
	Year of diagnosis	
Tumour	Site of Tumour	
	Histology of tumour	
	Grade of tumour	
Management	Managing consultant & speciality	Consultants providing specialist opinion only
	Managing hospital	Investigations
	Radiotherapy hospital	
	Date of first hospital visit	
Treatment	Definitive surgical procedures	
	Biopsies	
	Radiotherapy (both radical & palliative)	Radiotherapy intent
	Chemotherapy (both radical & palliative)	Drugs used & dosage
	Dates of treatment	Other palliative care (e.g. dexamethasone)

Extra-regional Management : Information was collected on all patients managed within the Yorkshire region, regardless of the place of treatment. For cases managed outside of the region, however, details of treatment were not generally available and consequently such patients were excluded, having a particular effect on the results presented for districts close to the border of the region (for example, Northallerton).

Managing Hospital/Consultant : The hospital of primary management (whether this be a neurosurgical centre or a district general hospital) was available for all patients, as was information about attendance at a radiotherapy centre. Details were not, however, recorded of referral for a specialist assessment at a neurosurgical centre, where management of the patient was not formally transferred.

Nature of Surgery : For the period covered by this study (1986-94), only definitive treatment given within nine weeks of the first treatment episode was routinely recorded. Supplementary details of biopsies were obtained retrospectively from the registration paper records.

Definitive surgery was defined as either surgery with curative intent, or the maximum safe macroscopic resection possible. Strict registration practice would have ensured consistency in the classification of definitive surgical procedures for registration details obtained from all hospitals throughout the region. Therefore it can be certain that any variation in definitive surgical rates observed between hospitals or districts are in fact true differences and not an artefact of variation in registration practice .

Use of Chemotherapy : As there was only minimal usage of chemotherapy during the study period, data relating to this modality have not been analysed. The few patients who received chemotherapy as the only form of treatment have, therefore, been included in the "no treatment" category.

9.1.2. Statistical Methods

Definitions

For the purposes of this report, the region studied was that covered by the former Yorkshire Regional Health Authority, and District refers to the district of residence, and corresponds to the District Health Authority of the period. Statistics are provided for patients who were resident within the Yorkshire Health region at the time of diagnosis and treated within the region.

All populations referred to in the methodology are the ONS mid-year population estimates based on the 1981 or 1991 censuses.

Registrations and Deaths

A registration is any new case of primary invasive cancer, identified by the Northern and Yorkshire Cancer Registry, arising in the population under study. The incidence rate gives the annual number of new patients registered with an invasive tumour per 100,000 population.

Age-Standardised Rate

Age-standardised registration rates (ASRs) have been computed where the comparison of incidence between groups was of interest. This rate enables such comparisons to be made allowing for differences in their population structures, and is equivalent to the rate that would be seen if the standard population were subject to the same rates as that of the group. ASRs have been standardised against the European standard population.

To obtain the observed annual rate by five-year age groups for each area, the total number of registrations in the time period was divided by the area population for that period.

The ASR was then calculated by multiplying the Standard population for the five-year period by the observed rate, within each age group.

The result was summed to give a rate per 100,000 population. This is known as the direct method of age standardisation.

The charts show the ASR as a dot, with the 95% Confidence Interval for the ASR as an error line around it. The Yorkshire rate is shown as a double line, the middle representing the rate and the line thickness depicting the confidence interval.

Survival

Survival times were calculated from date of diagnosis (taken as date of first hospital visit) to date of death or censoring. Death certificate only registrations were excluded, as their survival times were unknown, so they could not contribute to any survival analysis. Patients were deemed to be alive if no death certificate had been received by the time the analysis was undertaken. They were censored at the 1st January 1997.

Survival distributions were estimated for each variable separately using the Kaplan-Meier method. These have been presented as curves.

Multivariate survival comparisons were made by Cox Proportional Hazards regression. For each tumour type separately, age, period of diagnosis, treatment and hospital centre were entered into the model. The results are presented as relative risk estimates, compared to a base category (value 1.00). Estimates are presented for each factor separately, for each factor allowing for casemix (age) and for all factors entered into the model together. Interactions between factors were examined, but were insignificant and omitted from the results tables.

9.1.3. Data Quality

A substantial part of this project was concerned with the measurement and improvement of NYCRIS data quality. This work consisted of two main strands - systematic data cleaning and a quality assurance exercise.

Data cleaning involved systematically checking all the CNS data against predefined rules, to identify records that fail. Cases that failed these pre-defined checks were reviewed and resolved appropriately by experienced registration personnel. The checks were wide ranging and tested for example, for any inappropriate values and non-sensible combinations of hospital, consultant, tumour, treatment and referral data.

The quality assurance exercise involved a comparison of the current NYCRIS data of a representative sample of 299 patients, with information available in the hospital casenotes. A full report of the data quality methodologies employed within this project, and the results and conclusions will shortly be available.

Report Produced by

NY CRIS *Northern and Yorkshire*
Cancer Registry and Information Service
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CANCER OUTCOMES MONITORING

in collaboration with the

Research School of Medicine

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