

No 48, February 2010  
ISSN 0815-7219  
Registered by Australia Post  
PP 328866/00118

Canstat: A digest of facts and figures on cancer

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Published by the  
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## Cancers of the brain & central nervous system

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# Overview

Each year, nearly 800 Victorians are diagnosed with a brain tumour with over half of these being malignant.

Brain tumours are one of the leading cancers in children under 15 years with around 35 new cases diagnosed annually.

Central nervous system (CNS) cancers include tumours of the meninges, brain, spinal cord, cranial nerves and other structures of the central nervous system. They include malignant tumours, routinely reported in our annual incidence figures, as well as substantial numbers of benign tumours (mostly meningiomas) and tumours of uncertain behaviour. A summary of Victorian incidence in the years 2003–2007 by age group, sex and tumour type is shown in Table 1. We have used the Central Brain Tumour Registry of the United States (CBTRUS) classification<sup>1</sup>.

Between 2003 and 2007, 780 new cases of CNS cancer were diagnosed annually in Victoria, of which 52% were malignant. Malignant CNS cancer was the sixteenth most common cancer in Victoria with 407 new cases per year (226 in males and 181 in females; < 2% of all malignant tumours). In children under 15 years, these cancers rank second, after leukaemia, with 19 new cases annually.

Figure 1 shows the distribution of CNS tumours in children and adults. In children, the distribution is similar

in both sexes with the most common malignant tumours being astrocytoma (28% of cases), medulloblastoma - including primitive neuro-ectodermal tumours (PNET) (14%), ependymoma (10%) and nerve sheath tumours (mostly neurofibromatosis) (14%).

The distribution is very different in adults and also for men and women. In men the leading tumour is glioblastoma (38%) with smaller numbers of astrocytoma (15%) and meningioma (14%) whereas in women the most common tumour is meningioma (34%) with fewer glioblastoma (24%) and astrocytoma (8%). In both sexes, nerve sheath tumours account for 8% of new tumours - these are predominantly benign acoustic neuromas (83%) and neurofibromatosis (15%).

Figure 2 shows the age-specific incidence rates for the most common types of CNS tumour. This clearly shows the different patterns of glioblastoma and meningioma in men and women and the relatively flat curves of the common childhood CNS tumours, astrocytoma and other gliomas, as compared with the tumours more prevalent in adults.

**Table 1: The incidence of CNS malignancies by type, gender and age group, Victoria 2003–2007.**

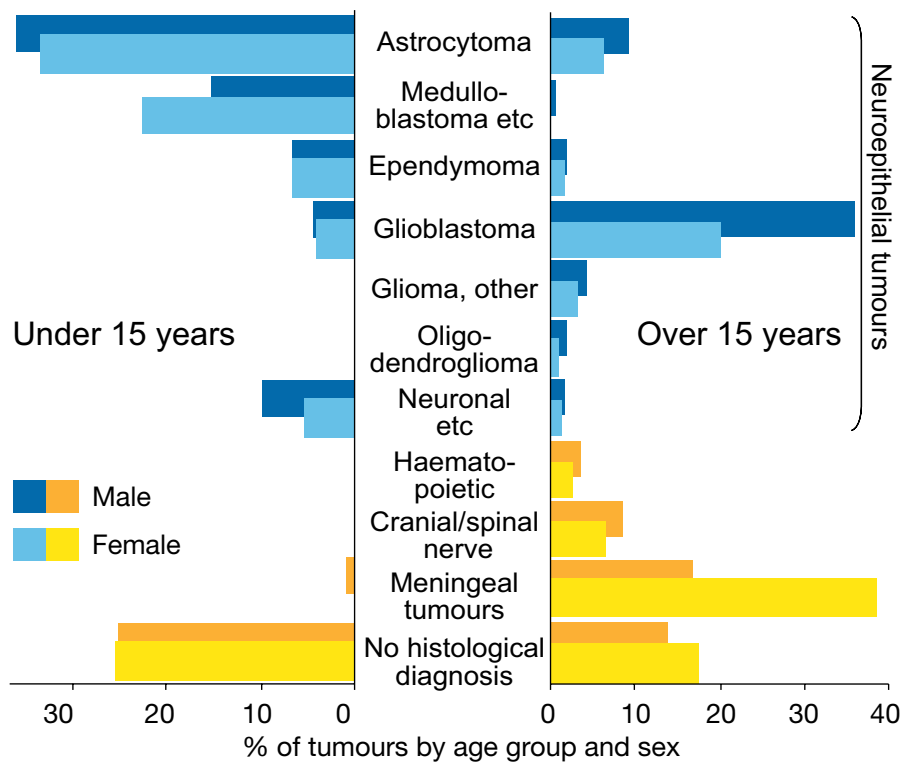
Rates are age-standardised (to World Standard Population) rates per 1,000,000 persons.

Tumour morphology	Age 0-14 years				Age 15+ years				All ages Rates	
	Male		Female		Male		Female		Male	Female
	Cases	%	Cases	%	Cases	%	Cases	%		
Neuroepithelial tumours	67	72.8%	54	72.0%	966	56.5%	695	34.2%	56.0	53.5
Astrocytoma, anaplastic	3	3.3%	0		86	5.0%	62	3.0%	4.6	3.9
Astrocytoma, NOS	4	4.3%	3	4.0%	33	1.9%	39	1.9%	2.7	2.2
Astrocytoma, pilocytic	23	25.0%	18	24.0%	14	0.8%	12	0.6%	3.7	2.9
Astrocytoma, all other variants	3	3.3%	4	5.4%	25	1.5%	15	0.7%	1.8	1.2
Embryonal/primitive/medulloblastoma	14	15.2%	17	22.7%	11	0.6%	4	0.2%	2.7	2.0
Ependymoma	6	6.5%	5	6.7%	33	1.9%	31	1.5%	2.8	2.1
Glioblastoma	4	4.3%	3	4.0%	614	35.9%	412	20.3%	28.0	26.3
Glioma, mixed	0		0		83	4.8%	68	3.4%	4.7	3.9
Neuronal, glial and mixed	9	9.8%	4	5.3%	30	1.8%	26	1.3%	2.9	2.3
Oligodendroglioma	0		0		34	2.0%	21	1.0%	1.8	1.2
Other tumours	1	1.1%	0		3	0.2%	5	0.2%	0.3	0.1
Lymphomas	0		0		64	3.7%	54	2.7%	3.1	2.6
Cranial/spinal nerve tumours	0		0		146	8.5%	135	6.6%	8.8	7.8
Meningeal tumours	0		0		289	16.9%	784	38.6%	30.5	28.8
No Histological confirmation	23	25.0%	19	25.3%	239	14.0%	358	17.6%	15.6	14.5
<b>Tumour behaviour</b>										
Malignant	51	55.4%	45	60.0%	1,077	63.0%	858	42.2%	68.4	50.3
Benign	8	8.7%	5	6.7%	495	29.0%	1,058	52.0%	29.2	57.5
Uncertain behaviour	33	35.9%	25	33.3%	137	8.0%	117	5.8%	13.5	10.1
<b>Total*</b>	<b>92</b>		<b>75</b>		<b>1,709</b>		<b>2,033</b>		<b>111.1</b>	<b>117.8</b>

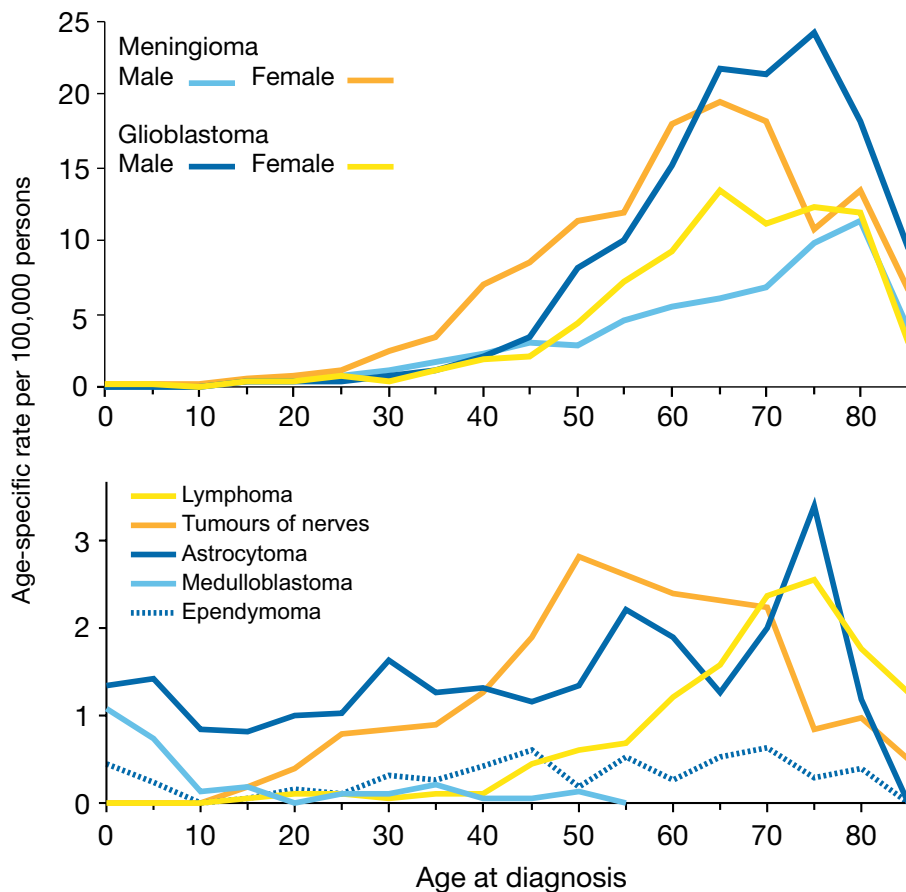
\* includes 14 other and unclassified tumours

**Figure 1: Distribution of all CNS tumours by age, sex and histological type, Victoria 2003–2007**

The two figures show the very different distributions of CNS tumours in children under 15 years and in adults by gender and histological type.



**Figure 2: Age-specific incidence rates for the major groups of CNS tumours (including benign) by sex, Victoria 1982–2007**



1. CBTRUS (2008). Statistical Report: Primary Brain Tumors in the United States, 2000–2004. Published by the Central Brain Tumor Registry of the United States. <http://www.cbtrus.org/reports//2007-2008/2007report.pdf> Table 1- page 28

# Epidemiology

In both men and women, Victorian incidence of CNS cancer has increased whilst mortality has decreased over the past two decades.

## Trends in Incidence and mortality

Age-standardised incidence rates for all malignant CNS cancer in Victoria have risen by an average of 0.5% per year in men and 1.1% per year in women from 1982-2007 (Figure 3). During the same period mortality rates declined by 0.4% per year in men and 0.1% per year in women.

National mortality data are available from 1950 (Figure 5) and CNS cancer mortality rates have shown increases of around 1% per year since this date.

The increasing rates of CNS cancer are considered to be largely due to increased diagnosis related to the advent of CT and MRI scanning. The more modest increases seen at younger ages add weight to the explanation of increased detection, and therefore incidence rates, in the elderly in who histological verification is less common (figure 4). Similar trends have been observed in other countries with similar level of economic development to Australia.

## Risk factors

### Personal characteristics

Items relating to personal characteristics or medical history including immunological status, family history, and genetic factors have been reported to be associated with CNS tumour risk. In most instances these associations are weak and inconsistent - a result of too many small studies trying to cover multiple factors. The strongest associations seen with respect to host factors are:

**Genetic factors.** Up to 5% of CNS tumours are related to rare genetic syndromes including neurofibromatosis, tuberous sclerosis, Bourneville's disease, ataxia telangiectasia, Li-Fraumeni, Gorlin, Turcot and Von Hippel-Lindau syndromes. Jewish people have a higher risk of meningiomas than other groups, which may also be due to genetic factors.

**Family history.** The risk of CNS tumours is increased in persons with a first degree relative having had a diagnosis.

**Congenital malformations.** Children with cerebral palsy or other birth defects of the central nervous system, such as spina bifida, hydrocephalus and encephalocele, are at increased risk of developing brain tumour.

**Immunodeficiency.** Primary cerebral lymphoma is more common in persons with immunodeficiency either as a result of immunosuppressive drugs following organ transplant or of HIV-AIDS.

### Environmental factors

The literature contains many reports of associations between environmental agents and increased risk of CNS tumours. Given the number of studies, their low statistical power, and the number of multiple comparisons made, it is to be expected that many of these will have been chance associations

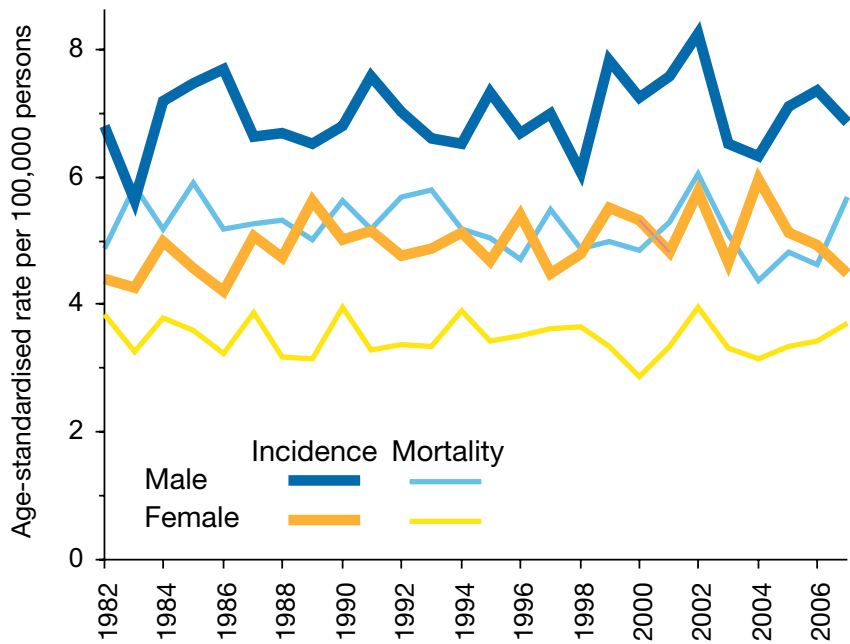
**Ionising radiation.** The strongest established risk factor for CNS tumours is ionising radiation, especially early in life. Evidence is growing that diagnostic and therapeutic exposures in utero, childhood and adult life might increase CNS tumour risk.

Atomic bomb survivor data are inconsistent and show either null or modest risks. However, Japanese have a low susceptibility to CNS tumours and may respond differently to radiation exposure.

**Viruses.** Evidence is accumulating that viruses may play a role in CNS carcinogenesis by gene rearrangement and amplification of normal proto-oncogenes.

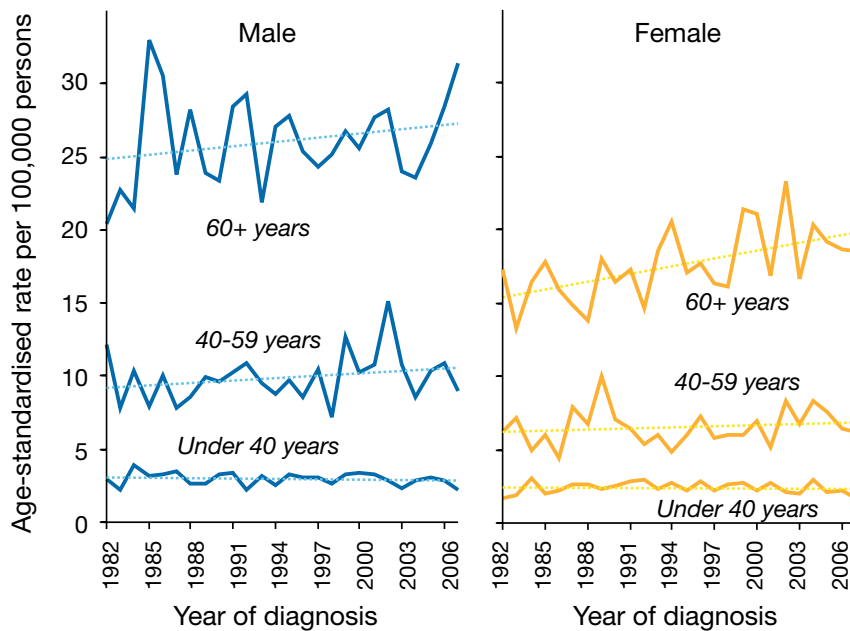
*Reference: Giles GG, Gonzales M. The epidemiology of brain tumours and factors in prognosis. In: A Kaye, E Laws 2nd edition. Brain Tumors: an encyclopedic approach. Edinburgh: Churchill Livingstone. 2000.*

**Figure 3: Trends in incidence and mortality of malignant CNS tumours, Victoria 1982–2007 by sex**

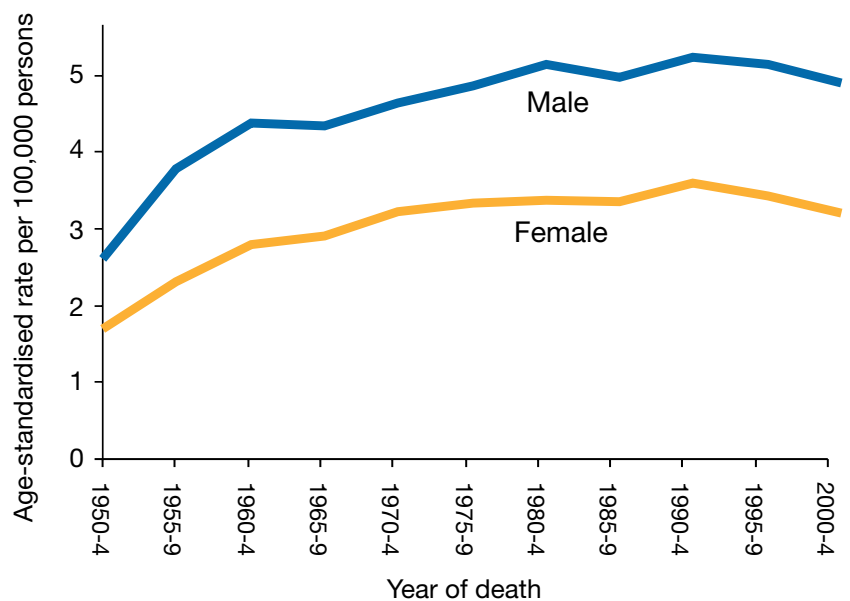


**Figure 4: Trends in incidence of malignant CNS tumours, Victoria 1982–2007 by sex and age group at diagnosis.**

Figures show annual age-standardised incidence rates in three age groups with fitted lines of best fit (dotted).



**Figure 5: Trends in mortality from malignant CNS tumours, Australia 1950–2004**



# Survival

Five-year survival from malignant CNS tumours is 23%.

Increasing age at diagnosis was associated with poorer survival reflecting the age distribution of tumour types.

The overall five-year relative survival of Victorians with malignant central nervous system cancers in 2004 was 23%. Survival curves by period of diagnosis, sex, age and tumour type are shown in Figures 3–6.

**Sex** - Relative survival was similar for both men and women.

**Age at diagnosis** - Older age at diagnosis was strongly associated with poorer relative survival with estimates of 54% in persons under 45 years falling to only 4% in cases over 75 years at diagnosis. This, in part, reflects the mix of tumour types occurring in each group

In children, in whom CNS tumours are more prevalent, survival was more favourable than in adults with five-year relative survival of 54% in those aged under 15 years at diagnosis.

**Tumour morphology** - Survival was higher for astrocytomas (40%), other gliomas (61%) and malignant meningiomas (46%) than in tumours without histological confirmation (27%). Glioblastomas had the poorest survival (4%) .

The types of tumour common in childhood - ependymoma, astrocytoma and medulloblastoma - have more favourable prognosis than the high-grade gliomas common in adults.

**Period of diagnosis** - There was no significant improvement in survival during this period. This reflects the lack of substantive new treatment options.

An analysis of childhood cancer survival from 1975 to 2007 showed a significant improvement from 38% to 54%.

**Table 2: Relative survival from malignant brain and CNS cancers<sup>1</sup>**

*Relative survival (%) by year, gender, age group and morphology for persons with malignant CNS tumours in 2004 and for selected years in Victoria .*

**Relative survival** is a measure of net survival usually interpreted as the proportion of patients who would have survived to a certain time (usually five years) if the cancer they had were the only cause of death in the population. This is defined as the ratio of observed survivors in the cohort of cancer patients to expected survivors in a comparable group of cancer-free individuals (calculated from Victorian life tables stratified by age, sex and calendar year).

*Source: English D, Farrugia H, Thursfield V, Chang P, Giles G. Cancer Survival Victoria 2007. Estimates of survival in 2004 (and comparison with earlier periods). The Cancer Council Victoria, Melbourne. 2007*

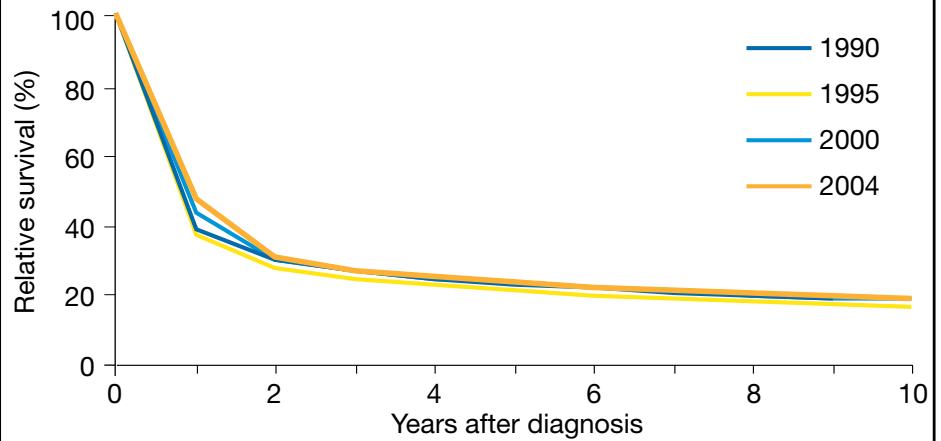
Years after diagnosis	Survival (%)	95% confidence interval	
1	47	(43-50)	
2	30	(27-33)	
3	26	(23-30)	
4	25	(21-28)	
5	23	(20-26)	

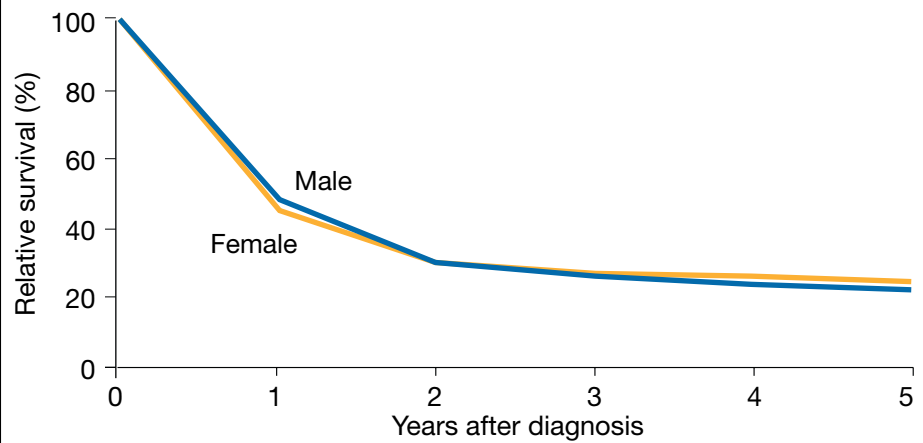
By subgroup	Number of deaths	5-year survival (%)	95% confidence interval	p-value
<b>All cases</b>	<b>1,412</b>	<b>23</b>	<b>(20-26)</b>	
<b>Sex (Figure 7)</b>				<b>0.43</b>
Male	814	22	(18-26)	
Female	598	25	(20-30)	
<b>Age at diagnosis (Figure 8)</b>				<b>&lt;0.01</b>
0-44	198	54	(46-62)	
45-54	211	27	(18-36)	
55-64	290	11	(6-16)	
65-74	353	6	(2-10)	
75+	360	4	(1-7)	
<b>Tumour morphology group (Figure 9)</b>				<b>&lt;0.01</b>
Glioblastoma	930	4	(2-5)	
Astrocytoma	168	40	(31-50)	
Other glioma	92	61	(51-71)	
No histological confirmation	206	27	(17-36)	
<b>Specific years (Figure 6)</b>				<b>0.22</b>
1990		23	(20-27)	
1995		21	(18-25)	
2000		24	(20-27)	
2004		23	(20-26)	



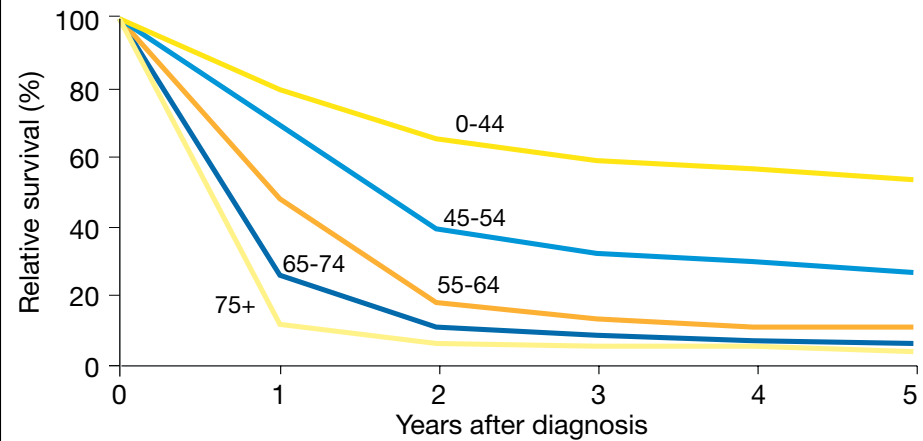
**Figure 6: Relative survival by years from diagnosis, Victoria - survival by diagnosis year**



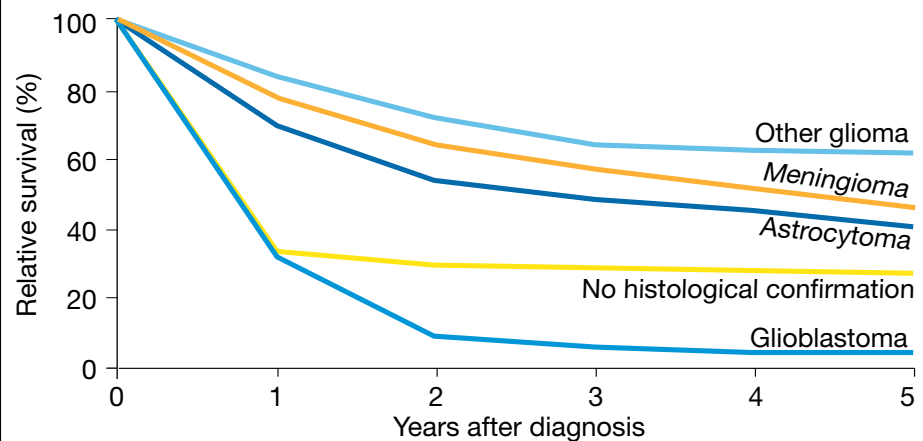
**Figure 7: Relative survival by years from diagnosis, Victoria 2004 - survival by gender**



**Figure 8: Relative survival by years from diagnosis, Victoria 2004 - survival by age group at diagnosis**



**Figure 9: Relative survival by years from diagnosis, Victoria 2004 - survival by tumour morphology**



# Comparisons

Source: Giles GG, Gonzales M. *The epidemiology of brain tumours and factors in prognosis*. In: A Kaye, E Laws. 2nd edition. *Brain Tumors: an encyclopedic approach*. Edinburgh: Churchill Livingstone. 2000

## Regional variation

CNS tumours vary in incidence from population to population as shown for selected countries in Figure 10. Some of the variation may be due to varying levels of detection linked with the availability of, and access to, medical technology. Interestingly, Japan which has comparable technological development to Western industrialised countries, has rates of CNS cancer that are a third or less of those observed in the USA. Incidence in other Asian countries is also low. The exclusion of cases older than 65 years does not remove all of the variation between populations.

Historically, geographic variation in childhood CNS tumours has been greater than for other childhood malignancies suggesting that there may exist real differences between populations due to genetic or environmental factors. However, more recent rates do not provide much evidence of variation in total CNS tumour rates but some support for differences in subtypes.

## Migrants to Australia

Malignant CNS tumour incidence in Victoria between 1997 and 2006 was compared between migrant groups and the Australian-born population (Figure 11). Incidence was found to

be significantly lower in female migrants from Southern Europe and North-East Asia, and in males from the British isles, Europe (other than Southern Europe or the British Isles), the Middle East and Asia. These differences are consistent with differences in incidence rates between Australia and the migrants' countries of origin.

## Ethnic variation

Incidence rates in ethnic sub-populations reported to Cancer Incidence in Five Continents are shown in Figure 12.

Jews living in Israel have elevated rates compared to non-Jews. Historically, Jewish migrants to Israel from Europe, America, Africa and Asia had higher incidence rates than in Jews born in Israel, but much of this excess occurred in the elderly and may have been a consequence of increased screening.

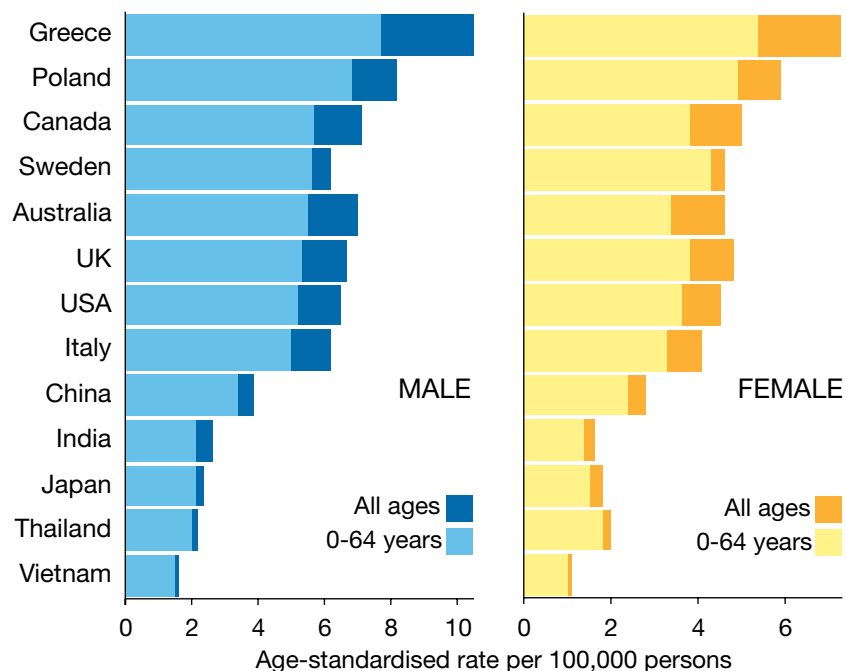
Asians tend to have low rates with these rates remaining similar in migrants to the USA to those in the countries of origin.

Rates in whites are consistently significantly higher than those in blacks and migrants from Asia and the same patterns are observed in both men and women.

**Figure 10: International incidence of malignant CNS cancer, 2002.**

CNS cancer incidence for selected countries for all ages and for persons less than 65 years. Though detection in the elderly differs considerably between countries, the exclusion of cases older than 65 years does not remove all of the variation between populations.

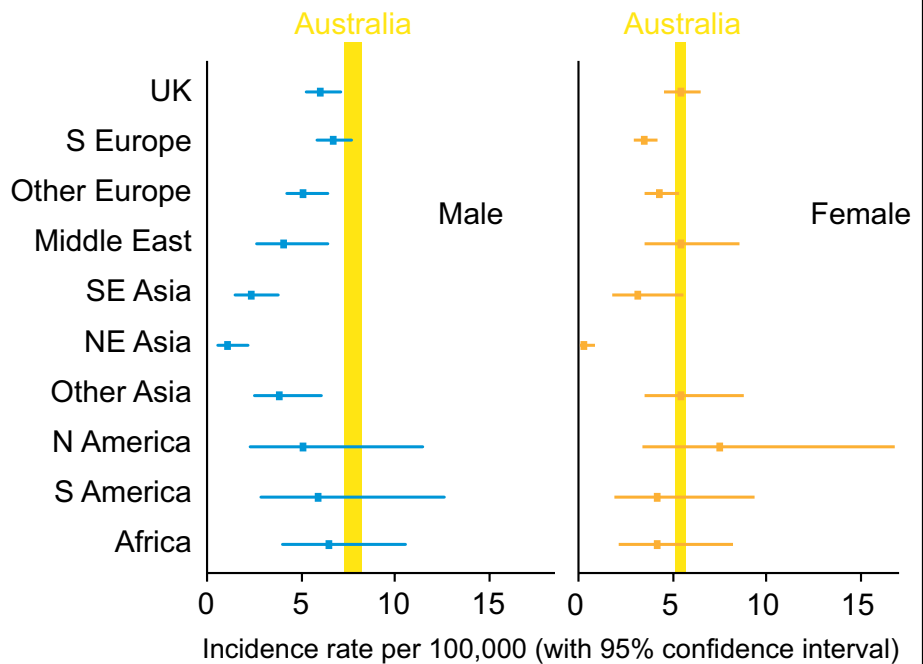
J. Ferlay, F. Bray, P. Pisani and D.M. Parkin. *GLOBOCAN 2002. Cancer Incidence, Mortality and Prevalence Worldwide IARC CancerBase No. 5, version 2.0 IARC Press, Lyon, 2004.*





**Figure 11: Malignant CNS cancer incidence in Victoria by birthplace, 1997–2006**

The graph of migrant rates displays age-standardised rates and their 95% confidence intervals as horizontal lines. The graph also contains a vertical band representing the 95% confidence interval of the rate in the Australian-born. Each migrant rate can be directly compared to the vertical band. If the migrant 95% confidence interval overlaps the Australian-born band, the rates do not differ significantly.

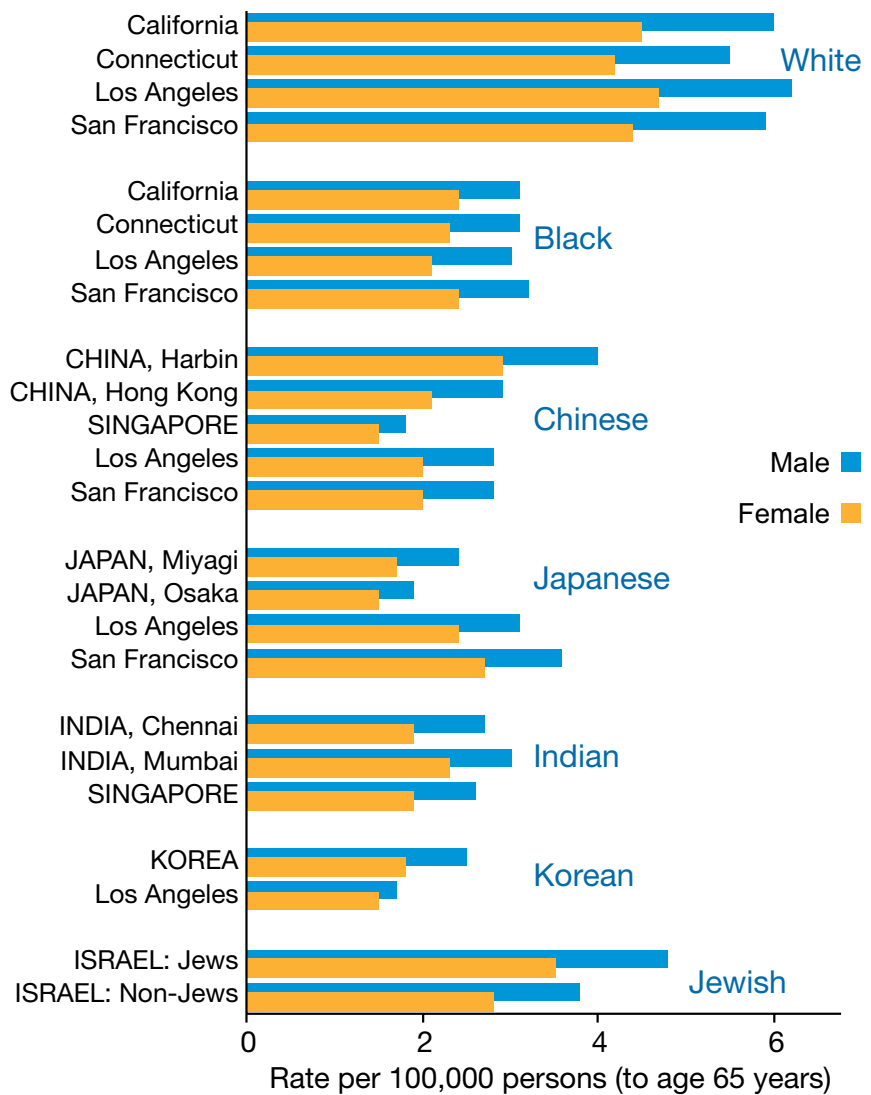


**Figure 12: Ethnic variation in CNS tumour incidence (1992-2002)**

Male and female age-standardised incidence rates for malignant CNS tumours in Whites, Blacks, Chinese, Japanese, Indians, Koreans and Jews from selected cancer registries from Cancer Incidence in Five Continents Volume IX.

Note: Registries are from the USA unless otherwise specified. Rates from Chinese registries include also benign tumours.

Source: Curado. M. P., Edwards, B., Shin. H.R., Storm. H., Ferlay. J., Heanue. M. and Boyle. P., eds (2007). Cancer Incidence in Five Continents, Vol. IX. IARC Scientific Publications No. 160, Lyon, IARC.



# Treatment & Outcomes

A population-based survey was conducted to describe the treatment and outcomes for all Victorians diagnosed with malignant glioma in 1998-2000. Questionnaires were completed (from medical histories of neurosurgeons, radiation and medical oncologists and other clinicians involved in treatment) for 828 (93%) of eligible cases making the results representative of the whole population and the largest reported glioma management survey in the world to date.

The study showed that the general approach to management in Victoria conformed to recent standards of care. That is, histological diagnosis was obtained, a macroscopic resection was performed (if feasible), patients were referred for radiotherapy and then received chemotherapy, either as adjuvant therapy or at disease recurrence. However, some observations were of concern:

- 13% of patients did not have a histological diagnosis and 23% had only a biopsy.
- only 74% and 54% of patients were referred to a radiation oncologist or neuro-oncologist respectively.
- 12% of patients had no active anti-cancer therapy - surgery, radiotherapy or chemotherapy.
- it appeared that few patients were referred for rehabilitation, allied health support or psychiatric assessment.
- only 5% of patients were enrolled into a clinical trial.

## Patients with no histological diagnosis

For 13% of eligible patients, diagnosis of glioma was based only on clinical and radiological features. Reported reasons for lack of histological diagnosis included advanced age, anatomical location of the lesion, comorbidities and patient refusal. Ninety-five percent of these patients received neither radiotherapy nor chemotherapy, which represents 12% of all cases in our study.

**Treatment** – About a quarter of patients underwent only a biopsy, with the major reasons including location of the lesion, extensive or multifocal disease and patient age. Of the 456 (55%) patients who underwent craniotomy, 209 (46%) achieved a gross macroscopic resection. with reported reasons for failure to achieve this including location or extent of the lesion and involvement of cerebral vessels.

**Survival** - Overall survival times for all patients and by tumour grade are shown in Figure 12. Five-year survival was 19% for the entire cohort and 3% for patients with GBM.

Figures 13 & 14 show survival by radiotherapy and chemotherapy for patients with grade 3 and 4 glioma.

The management of gliomas has become more complex since the completion of this study with a number of significant changes in treatment practice - in particular, the increasing roles of palliative chemotherapy (temozolomide) for recurrent high-grade gliomas and radiotherapy and temozolomide therapy in the treatment of newly diagnosed GBM. A follow-up survey of GBM will be conducted in 2010.

## Characteristics of 828 patients in the management survey

Characteristic	N (%)
<b>Sex</b>	
Male	470 (57%)
Female	358 (43%)
<b>Age</b>	
<40	141 (17%)
40-60	253 (31%)
>60	434 (52%)
<b>Tumour site</b>	
Frontal lobe	241 (29%)
Temporal lobe	170 (20%)
Parietal	133 (16%)
Cerebrum	48 (6%)
Occipital	38 (5%)
Other or not specified	198 (24%)
<b>Side of tumour</b>	
Left	374 (45%)
Right	351 (42%)
Bilateral	54 (7%)
Central	23 (3%)
Not specified	26 (3%)
<b>Resection</b>	
Complete	209 (25%)
Less than complete	247 (30%)
Biopsy only	190 (23%)
No biopsy	105 (13%)
Not specified	77 (9%)
<b>Tumour Grade (if applicable)</b>	
Grade I	9 (1%)
Grade II	33 (4%)
Grade III	147 (18%)
Grade IV (GBM)	472 (57%)
Grade unknown	62 (7%)
<b>Radiotherapy given</b>	506 (61%)
<b>Chemotherapy</b>	
Neoadjuvant/adjuvant	123 (15%)
At recurrence	175 (21%)

## References:

- Dally M, Rosenthal M, Drummond K, Murphy M, Cher L, Ashley D, Thursfield V, Giles G. Radiotherapy management of patients diagnosed with glioma in Victoria (1998-2000): a retrospective cohort study. *J Med Imaging Radiat Oncol.* 2009 Jun;53(3):318-24. PubMed PMID: 19624300.
- Cher L, Rosenthal MA, Drummond KJ, Dally M, Murphy M, Ashley D, Thursfield V, Giles GG. The use of chemotherapy in patients with gliomas: patterns of care in Victoria from 1998-2000. *J Clin Neurosci.* 2008 Apr;15(4):398-401. Epub 2008 Jan 31. PMID: 18249119
- Rosenthal MA, Ashley DM, Drummond KJ, Dally M, Murphy M, Cher L, Thursfield V, Giles GG. Brain stem gliomas: patterns of care in Victoria from 1998-2000. *J Clin Neurosci.* 2008 Mar;15(3):237-40. Epub 2008 Jan 15. PMID: 18226529
- Rosenthal MA, Drummond KJ, Dally M, Murphy M, Cher L, Ashley D, Thursfield V, Giles GG. Management of glioma in Victoria (1998-2000): retrospective cohort study. *Med J Aust.* 2006 Mar 20;184(6):270-3. PMID: 16548830

Figure 13: Survival for all gliomas and by tumour grade.

Figure shows Kaplan-Meier curves for all-cause survival for all patients in the survey, and by tumour grade. A test of the equality of the survival distributions between tumour grades was significant with  $p < 0.001$  (log-rank test).

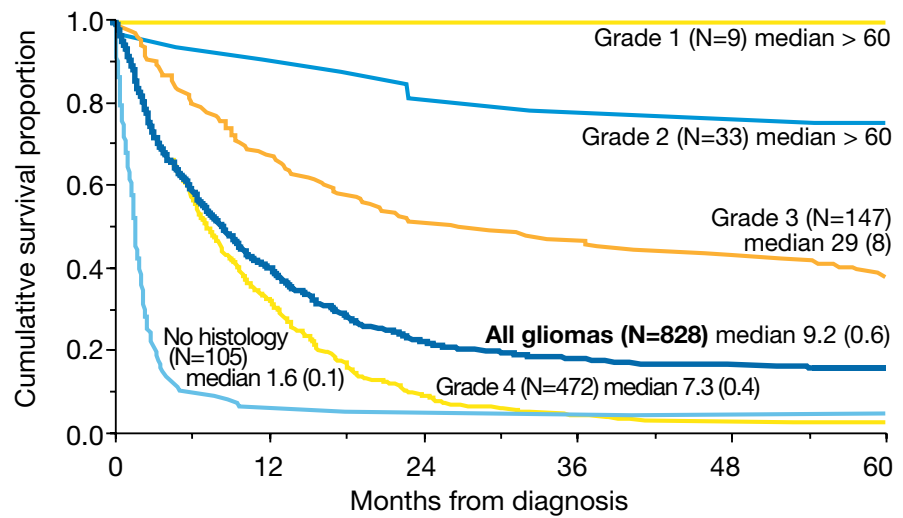


Figure 14: Survival for patients with grade 3 and 4 glioma by radiotherapy dose.

Figure shows survival for patients with grade 3 and 4 glioma by administered radiotherapy dose. Survival was significantly better ( $p < 0.001$ ) in those who received radiotherapy than for those who received none but there was no significant difference in survival between the two doses.

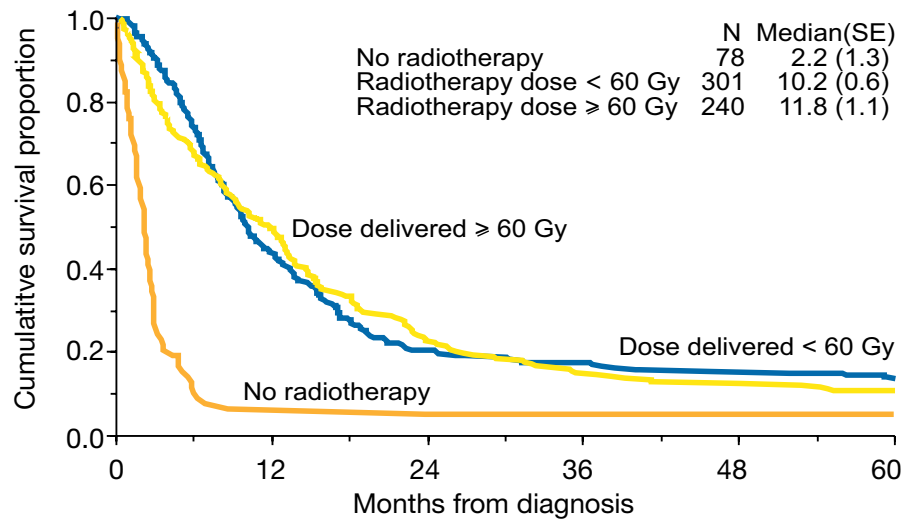
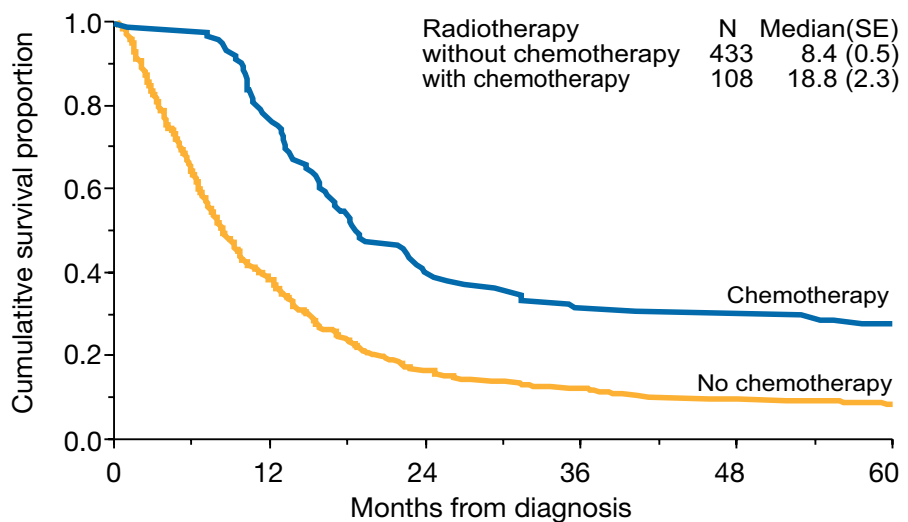


Figure 15: Survival for patients with grade 3 and 4 glioma treated with radiotherapy with or without chemotherapy.

Figure shows survival for patients with grade 3 and 4 glioma who received radiotherapy with or without chemotherapy. Survival was significantly better ( $p < 0.001$ ) in those who received chemotherapy.



# Victorian Cancer Registry publications

## Canstats

Annual Victorian Cancer Registry statistical reports were produced for the years 1982–1990. From 1991- 2006 these annual data are published in the Canstat series.

Other Canstat titles include:

- Cancer in Adolescents and Young Adults
- Prostate Cancer
- Testicular Cancer
- Trends in Cancer Mortality, Australia 1910–1999
- Lung Cancer
- A Guide to the Victorian Cancer Registry
- Breast Cancer
- Skin Cancer
- Ovarian Cancer

## Reports

English D, Farrugia H, Thursfield V, Chang P, Giles G. April 2007. Cancer Survival Victoria 2007. Estimates of survival in 2004 (and comparison with earlier periods).

Karahalios E, English D, Thursfield V, Simpson J, Farrugia H, Giles G. Aug 2009. Second primary Cancers in Victoria.

All publications are available for download, in pdf format, from our website at :  
<http://www.cancervic.org.au/about-our-research/cancer-statistics>

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