

REGULAR ARTICLE

# Classification, incidence and survival analyses of children with CNS tumours diagnosed in Sweden 1984–2005

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## Keywords

Childhood CNS tumours, Classification, Incidence, Population-based material, Survival

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## Abstract

**Aim:** Primary tumours in the central nervous system (CNS) are the second most common malignancy in childhood after leukaemia. Sweden has a high incidence and a high-survival rate in international comparative studies. This has raised the question about the type of tumours included in the Swedish Cancer registry. We therefore compared international data to the Swedish *Childhood Cancer* registry.

**Methods:** Central nervous system tumours registered in the Swedish *Childhood Cancer* Registry were reclassified according to ICC-3. Incidence and survival analyses were performed in the study population.

**Results:** There were 1479 children (<15 years) in Sweden diagnosed with CNS tumours 1984–2005. The distribution of diagnoses was similar to that reported in other studies. The annual incidence was 4.2/100 000 children. The survival rates have not improved significantly between the two time periods before/after 1995 (70% vs. 74%;  $p = 0.10$ ).

**Conclusions:** The mean annual incidence of children with CNS tumours was 4.2/100 000 and has not increased during the study period. Survival rate for brain tumours at 10 years follow-up was 72%.

## INTRODUCTION

Brain tumours are the second most common cancer diagnosis (after leukaemia) in children <15 years of age at diagnosis and represents 20–30% of all cases of childhood cancer (1,2).

There is a high incidence of childhood brain tumours in Sweden as well as in the other Nordic countries, and survival data shows high cure rates compared to international population-based studies (3–6). These figures are based on data from the Swedish Cancer Registry. However, reports from this registry show a high frequency of 'unspecified

cases' among childhood tumours (3). This has raised a question if the Swedish Cancer Registry includes patients with diagnoses not included in other National Cancer Registries.

With the aim to establish a complete registry with more detailed information – compared with the Swedish Cancer Registry – the Swedish *Childhood Cancer* Registry was initiated in the 1980s. Diagnostic criteria, treatment protocols and continuous follow-up data of the patients are recorded in a population-based setting from the six Pediatric Oncology Centers in Sweden. We report results from the Swedish *Childhood Cancer* Registry, where the tumours have been classified according to the latest guidelines from IARC published in 2005 (7).

## Abbreviations

APC, annual percentage change; ATRT, atypical teratoid/rhabdoid tumour; CNS, central nervous system; ICC-3, International Classification of Childhood Cancer; ICD, International Classification of Diseases for Oncology; OS, overall survival; RT, radiotherapy; SEER, Surveillance Epidemiology and End Results (NCI); SIOP, International Society of Paediatric Oncology; SNOMED, Systematized Nomenclature of Medicine; WHO, World Health Organization.

## PATIENTS AND METHODS

### Classification

The classification of cancer in children is based on morphological findings and not, as in adults, on the primary site of the affected organ. The first generally accepted classification of childhood cancer was published in 1987 (8) and was based on the International Classification of Diseases for

Oncology (ICD)-codes in the World Health Organization (WHO) classification, later revised several times (9). The diagnoses were divided into 12 main groups, in which central nervous system (CNS) tumours constituted group III and included six subgroups (a – ependymomas; b – astrocytomas; c – medulloblastomas; d – other gliomas; e – other specified; f – unspecified diagnoses). In the latest proposal for classification of childhood cancer published in 2005 – International Classification of Childhood Cancer-3 (ICCC-3) (7), the six CNS-groups were further divided into subgroups. This new classification forms the basis for the present study. We have used a combination of ICD/Systematized Nomenclature of Medicine (SNOMED) codes, pathology-report diagnoses and clinical information about the tumours.

### Patients

The material includes all children less than 15 years with CNS tumours diagnosed in Sweden between 1984 and 2005. Children with suspected CNS tumours were diagnosed and treated in one of the six Paediatric Oncology Centres. Children were not treated by neurosurgeons alone. At the centres, the diagnosis was confirmed by imaging and histology in the absolute majority of cases. However, in some patients a histological diagnosis of the tumour could not be obtained. To our knowledge, there were no diagnosis made primarily at autopsy during this period. Informed consent was obtained from patients or parents.

### Treatment

As the formation of the Swedish Childhood CNS Tumor Working Group in 1993, there has been consensus among the regional centres about treatment of brain tumours in Swedish children. Also, before this time point, treatment was very coherent due to close collaboration within the country. Because of the relatively low absolute numbers, most tumours have been treated according to international protocols. European International Society of Paediatric Oncology (SIOP) protocols (10,11) and later German Hirntumoren protocols (12) have been most widely used. A general outline of the treatment strategies for the main tumour groups is described below.

#### *Ependymomas*

Primary surgery, repeated if necessary has been first-line treatment. In addition, radiotherapy (RT) has been given to most children. In cases of metastatic disease, a combination of chemotherapy and RT has been used.

#### *Astrocytomas*

For low-grade astrocytomas outside the supratentorial midline, radical surgery has been the accepted treatment. For low-grade astrocytomas in the supratentorial midline (optic nerve/chiasma), where surgery is rarely an option, chemotherapy has been given to younger children and RT to older children. The chemotherapy regimen has followed a low intensive protocol since the early 1990s similar to the SIOP Low-Grade Glioma protocols used today (13). Most

high-grade astrocytomas have in addition to surgery and RT been treated with combinations of alkylating chemotherapy.

#### *Medulloblastomas*

Patients over 3 years of age have received craniospinal RT in addition to surgery. Over the study period, doses of RT have been decreased in average risk patients and chemotherapy has been intensified (14).

#### *Other gliomas*

For these tumours the malignancy grade, i.e. WHO I–IV, has been used to stratify treatment. Oligodendrogliomas and mixed and unspecified gliomas have been treated according to low- (WHO I–II) or high-grade glioma protocols (WHO III–IV).

#### *Other specified tumours*

Craniopharyngeomas have been treated with the goal of radical surgery in all cases. Over time, this strategy has changed especially in larger tumours to a more conservative surgical approach combined with RT.

### Statistical methods

SPSS software was used in the statistical analyses (15). Age-standardized incidence adjusted to the world standard population according to the IARC-1998 (1) has been used for the whole material as well as diagnostic subgroups. Time trend in the incidence data was investigated by use of US NCI Joinpoint regression software, by which the annual percentage change (APC) was estimated (16). The probability of overall survival (OS) was estimated using the Kaplan–Meier method and the log-rank test was used for significance test between groups with a significance level of 0.05 (15). Events were all reported deaths. Incidence- and mortality rates are presented per 100 000 children. Mean follow-up time for living patients was 17.3 years for children diagnosed before 1995 and 6.8 years for children diagnosed during 1995 or later. Eight patients were lost at follow-up and the data base was frozen August 1, 2007.

### RESULTS

Between January 1, 1984 and December 31, 2005 there were 1513 children below 15 years of age diagnosed with a CNS tumour in Sweden. Of these, 34 were excluded (children with haemangioblastomas, hamartomas and adenomas) in accordance with the new ICC-3 classification, leaving 1479 children for further analyses. Intracranial germ cell tumours and nerve sheath tumours were not included in the study according to the ICC-3 classification but will be reported briefly in the text. The diagnostic subgroups of the 1479 patients are shown in Table 1. The ependymomas constituted 10.5%, astrocytomas 44.6%, medulloblastomas/primary neuroectodermal tumor (PNET) 18.8%, other gliomas 10.0% and other specified neoplasms 13.5% of the cases. In 37 patients (2.5%), the diagnosis was not specified.

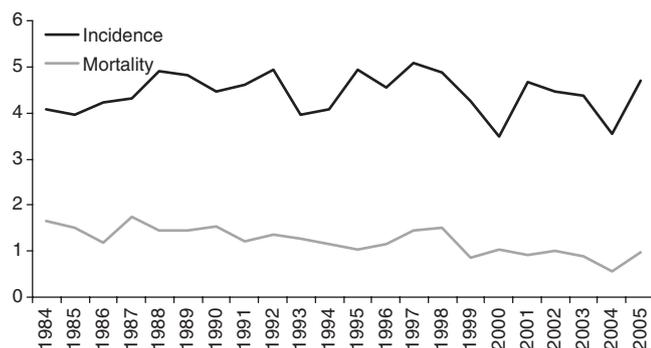
There were approximately 1.6 million children in Sweden less than 15 years of age. The overall annual incidence of

**Table 1** Classification of childhood CNS tumours in Sweden 1984–2005. Number, sex, age and age-standardized incidence rates

Diagnostic subgroup	No. patients	Relative %	Gender		<1 year	1 to <5 years	5 to <10 years	≥10 years	Incidence age-standard
			M/F	Ratio					
IIIa. Ependymomas	156	10.5	76/80	1.0	22	58	41	35	0.47
a1. Ependymomas	126	8.5	62/64	1.0	9	48	35	34	0.38
a2. Plexus choroideus tumours	30	2	14/16	1.0	13	10	6	1	0.09
IIIb. Astrocytomas	660	44.6	333/327	1.0	30	202	212	216	1.87
b1. Astrocytomas – low grade	461	31.2	233/228	1.0	13	121	153	174	1.28
b2. Astrocytomas – high grade	84	5.7	40/44	1.0	7	14	32	31	0.21
b3. Optic nerve/chiasma gliomas	115	7.8	60/55	1.1	10	67	27	11	0.38
IIIc. Medulloblastomas/PNET	278	18.8	156/122	1.3	16	99	109	54	0.82
c1. Medulloblastomas	219	14.8	125/94	1.4	12	73	92	42	0.64
c2. Supratentorial PNETs	50	3.4	27/23	1.0	4	22	15	9	0.16
c3. Medulloepitheliomas	4	0.3	2/2		0	1	0	3	<0,01
c4. Atypical teratoid/rhabdoid tumours	5	0.3	2/3		0	3	2	0	<0,01
IIId. Other gliomas	148	10	74/74	1.0	10	34	64	40	0.43
d1. Oligodendrogliomas	37	2.5	24/13	0.6	3	5	15	14	0.09
d2. Mixed and unspecified gliomas	73	4.9	37/36	1.0	5	20	28	20	0.24
d3. Neuroepithelial glial tumours of uncertain origin	38	2.6	13/25	0.6	2	9	21	6	0.1
IIIe. Other specified neoplasms	200	13.5	112/88	1.4	3	38	68	91	0.53
e1. Pituitary adenomas and carcinomas	10	0.7	5/5	1.0	0	0	1	9	0.02
e2. tumours of the sellar region (craniopharyngiomas)	83	5.6	41/42	1.0	1	15	37	30	0.22
e3. Pineal parenchymal tumours	15	1	10/5	2.0	0	5	5	5	0.04
e4. Neuronal and mixed neuronal-glial tumours	74	5	44/30	1.5	2	17	16	39	0.2
e5. Meningeomas	18	1.2	12/6	2.0	0	1	9	8	0.04
III f. Unspecified. intracranial/intraspinal neoplasms	37	2.5	19/18	1.0	2	8	12	15	0.09
All CNS tumours	1479	100	770/709	1.11	83	439	506	451	4.23

PNET, primary neuroectodermal tumour.

brain tumours in this age group was 4.2/100 000 children (Fig. 1). The Joinpoint regression analyses indicated that the interval could be broken down into two segments, the Joinpoint occurring at 2001, giving segments 1984–2001 and 2001–2005. The first interval had a non-significant APC of 1.1 (95% CI: –0.1 to 2.2) which was nearly flat whereas the second interval had a slope of –10.50 (95% CI: –12.1 to –8.9). Thus, the incidence was stable 1984–2001 but during the last 5 years there was a negative trend. The incidence rates were 4.3 for males and 4.2 for females. The M/F ratio was 1.1 for the whole material, close to 1.0 in ependymomas, astrocytomas and other gliomas but 1.3 for the medulloblastomas and 1.4 for other specified neoplasms.



**Figure 1** Age-standardized annual incidence- and mortality rates over time in Swedish children with CNS tumours diagnosed 1984–2005.

The mean age at diagnosis was 6.8 for the whole patient group. The diagnostic groups in different age intervals are shown in Table 1. The 5-, 10- and 20-year survival estimates for the whole group were  $76 \pm 1\%$ ,  $72 \pm 1\%$  and  $69 \pm 2\%$  respectively (Table 2). The survival rates have not improved significantly over time (Table 2), although the mortality rates have been reduced from 1.4 to 0.9/100 000 during the study period (Fig. 1; trend test: not significant). There was no difference in survival at 10 years between males and females (males:  $71 \pm 2\%$ , females:  $73 \pm 2\%$ ;  $p = 0.4$ ). Infants (<1 year of age) had an inferior prognosis ( $58 \pm 6\%$ ) compared with older children and especially children over 10 years at diagnosis ( $77 \pm 2\%$ ;  $p < 0.01$ ) (Table 2).

Of the 1479 patients, 548 had died within 60 months from diagnosis while 931 were still alive at 5 years. The survival rate for these 931 patients was  $95 \pm 1\%$  after another 5 years, i.e. 10 years from diagnosis and they had a 90% estimate of long-term survival after 15 years, except for the medulloblastoma group where the corresponding estimate was 80%. As shown in Table 2, all deceased infants died within 5 years from diagnosis while older children had higher initial survival rates but continued to die even after 10–20 years from diagnosis.

### Diagnostic groups

#### Ependymomas ( $n = 156$ )

This WHO group included patients with ependymomas (62 males, 64 females) and 30 patients with tumours localized

**Table 2** Classification of childhood CNS tumours in Sweden 1984–2005. Survival by diagnostic group

	Number	Survival (%)		
		5 years	10 years	20 years
IIla. Ependymomas	156	72 ± 4	66 ± 4	65 ± 5
a1. Ependymomas	126	68 ± 4	60 ± 5	58 ± 5
a2. Plexus choroideus tumours	30	90 ± 6	90 ± 6	90 ± 6
IIlb. Astrocytomas	660	84 ± 1	82 ± 2	79 ± 2
b1. Astrocytomas – low grade	461	93 ± 1	91 ± 1	89 ± 2
b2. Astrocytomas – high grade	84	28 ± 5	26 ± 5	23 ± 5
b3. Optic nerve/chiasma gliomas	115	91 ± 3	89 ± 3	85 ± 3
IIlc. Medulloblastomas/PNET	278	61 ± 3	53 ± 4	49 ± 3
c1. Medulloblastomas	219	63 ± 4	55 ± 4	51 ± 4
c2. Supratentorial PNETs	50	47 ± 7	41 ± 7	35 ± 8
c3. Medulloepitheliomas	4	–	–	–
c4. Atypical teratoid/ rhabdoid tumours	5	–	–	–
IIId. Other gliomas	148	44 ± 4	44 ± 4	40 ± 4
d1. Oligodendrogliomas	37	78 ± 7	77 ± 8	70 ± 9
d2. Mixed and unspecified gliomas	73	42 ± 6	40 ± 6	40 ± 6
d3. Neuroepithelial glial tumours of uncertain origin	38	12 ± 6	12 ± 6	–
IIIf. Other specified neoplasms	200	94 ± 2	90 ± 2	82 ± 4
e1. Pituitary adenomas and carcinomas	10	100	100	100
e2. Tumours of the sellar region (craniopharyngiomas)	83	97 ± 2	92 ± 3	85 ± 5
e3. Pineal parenchymal tumours	15	73 ± 12	64 ± 13	–
e4. Neuronal and mixed neuronal-glial tumours	74	93 ± 3	91 ± 3	91 ± 3
e5. Meningeomas	18	94 ± 5	94 ± 5	76 ± 17
IIIf. CNS-unspecified intracranial/ intraspinial neoplasms	37	64 ± 8	64 ± 8	64 ± 8
Diagnosed (p = 0.1)				
1984–1994	715	74 ± 2	70 ± 2	67 ± 2
1995–2005	764	77 ± 2	74 ± 2	–
Gender (p = 0.4)				
Males	770	74 ± 2	71 ± 2	67 ± 2
Females	709	77 ± 2	73 ± 2	70 ± 2
Age at diagnosis (p overall < 0.01)				
<1 year		58 ± 6	58 ± 6	58 ± 6
1 to <5 years		74 ± 2	71 ± 2	68 ± 3
5 to <10 years		75 ± 2	70 ± 2	68 ± 2
10 to <15 years		80 ± 2	77 ± 2	70 ± 3
All CNS tumours	1479	76 ± 1	72 ± 1	69 ± 2

to the plexus choroideus (27 papillomas, 3 carcinomas). Survival rate at 10 years was 60% for the ependymomas and 90% for the plexus choroideus tumours (24/27 papillomas and the three children with plexus carcinoma were alive at follow-up) (Table 2, Figs 2 and 3a).

#### Astrocytomas (n = 660)

The astrocytomas constituted the largest group and made up 44.6% of all CNS tumours. The patients were divided into three groups; low-grade astrocytomas (n = 461), high-grade astrocytomas (n = 84) and optic nerve/chiasma

gliomas (n = 115) (Table 1). The M/F ratio was close to 1.0 for all three subgroups. The children with optic nerve/chiasma gliomas were younger (mean age 4.1) than both the low- and high-grade astrocytoma patients (mean age 7.6 and 7.4, respectively). The OS at 10 years for the whole group was 82%; 91% for the low-grade tumour group, 26% for children with high-grade astrocytomas (p < 0.01) and 89% for patients with optic nerve/chiasma gliomas (Table 2, Figs 2 and 3b).

#### Medulloblastomas/PNET (n = 278)

The patients within this group were further subdivided into four groups; medulloblastomas, supratentorial PNETs, medulloepitheliomas and atypical teratoid/rhabdoid tumours (ATRT). There was predominance of male patients in these groups (M/F ratio 1.3; Table 1). Patients with ATRT in cerebellum were previously classified as medulloblastomas and have only been identified as a separate entity for the last 5 years.

The 10-year OS was 53%. Girls (58%) had a better survival compared to boys (42%; p = 0.04). Infants had a significantly inferior survival (38%) compared to older children (54%; p < 0.01). The 219 children with tumours classified as medulloblastomas did significantly better than the 50 patients with supratentorial PNET (55% vs. 41%; p = 0.01) (Table 2, Figs 2 and 3c).

#### Other gliomas (n = 148)

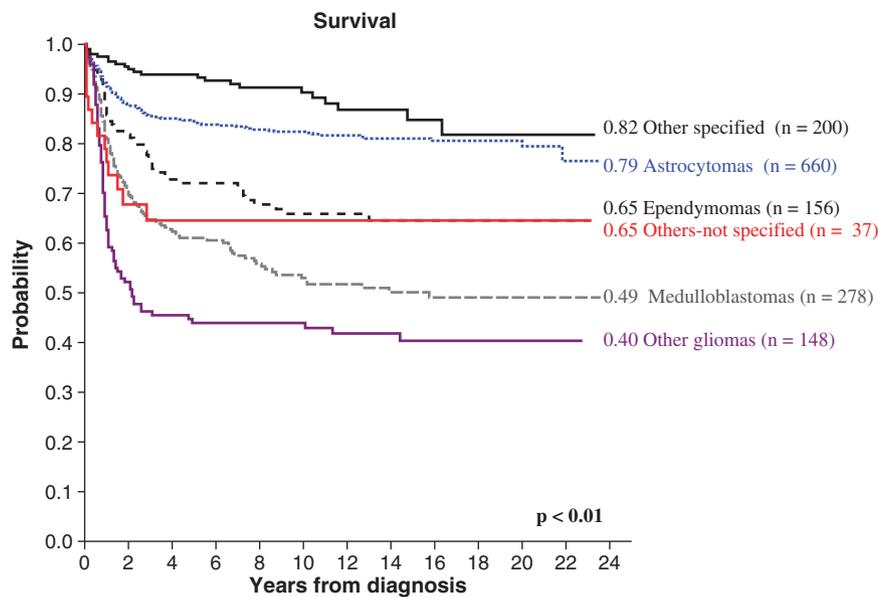
This group included three tumour types with different prognosis, oligodendrogliomas (n = 37), mixed and unspecified gliomas (n = 73) and neuroepithelial glial tumours of uncertain origin (n = 38). The 10-year survival rates varied from 77% for the oligodendroglioma group, to 40% for patients with mixed gliomas and 12% for children with neuroepithelial glial tumours, who have the worst prognosis of all groups in this material (Table 2, Figs 2 and 3d). Of the 73 children with mixed and unspecified tumours, 36 were located in the brainstem, (28 dead, 8 alive) and among the 38 children with neuroepithelial glial tumours, 35 were located in the brainstem (32, dead, 3 alive). Thus, 71 tumours were localized in the brain-stem region and the 10 year survival rate for these children was 17% (11/71 alive at follow-up).

#### Other specified neoplasms (n = 200)

This group of patients included five different diagnoses with a fairly good prognosis. Most patients were more than 5 years of age at diagnosis (Table 1). Patients with craniopharyngeomas, DNETs (dysembryonic neuroepithelial tumours) and gangliogliomas constituted 80% of this group. The 10-year survival rate exceeds 80% for the group (Table 2, Figs 2 and 3e).

#### Unspecified neoplasms (n = 37)

There were 37 patients (2.5%) from which a specific tumour diagnosis was missing. Twenty-seven out of 37 were more than 5 years of age at diagnosis and five out



**Figure 2** Actuarial survival curves by diagnostic main groups in Swedish children with CNS tumours diagnosed 1984–2005.

of 37 had a spinal tumour. The OS was 64% at 10 years (Table 2).

### Special topics

#### *Intraspinal tumours (n = 70)*

Of the 1479 children included in this study, 70 (4.7%) had an isolated intraspinal localization of the tumour without metastasis (44 boys, 26 girls). There were 21 patients with ependymomas, 33 with astrocytomas, six with medulloblastomas, three with other gliomas, two with other diagnosis and five with unspecified tumours. One infant had an intraspinal neoplasm, 24 children were 1 to <5 years, 18 were 5 to <10 years and 27 were  $\geq 10$  years of age at diagnosis. The 10-year survival rate was 76%. The patients with medulloblastomas had the worst prognosis (5/6 dead).

#### *Germ cell tumours (n = 38)*

There were 38 children (23 boys, 15 girls), who had a germ cell tumour diagnosed with an intracranial localization. These tumours are not included as they belong to group Xa according to this WHO classification. Of the 38 patients, 25 were alive at follow-up.

#### *Nerve sheath tumours (n = 20)*

Twenty children had an intracranial or intraspinal nerve sheath tumour which was classified as group IXb and not included in the study. All children were alive at follow-up.

## DISCUSSION

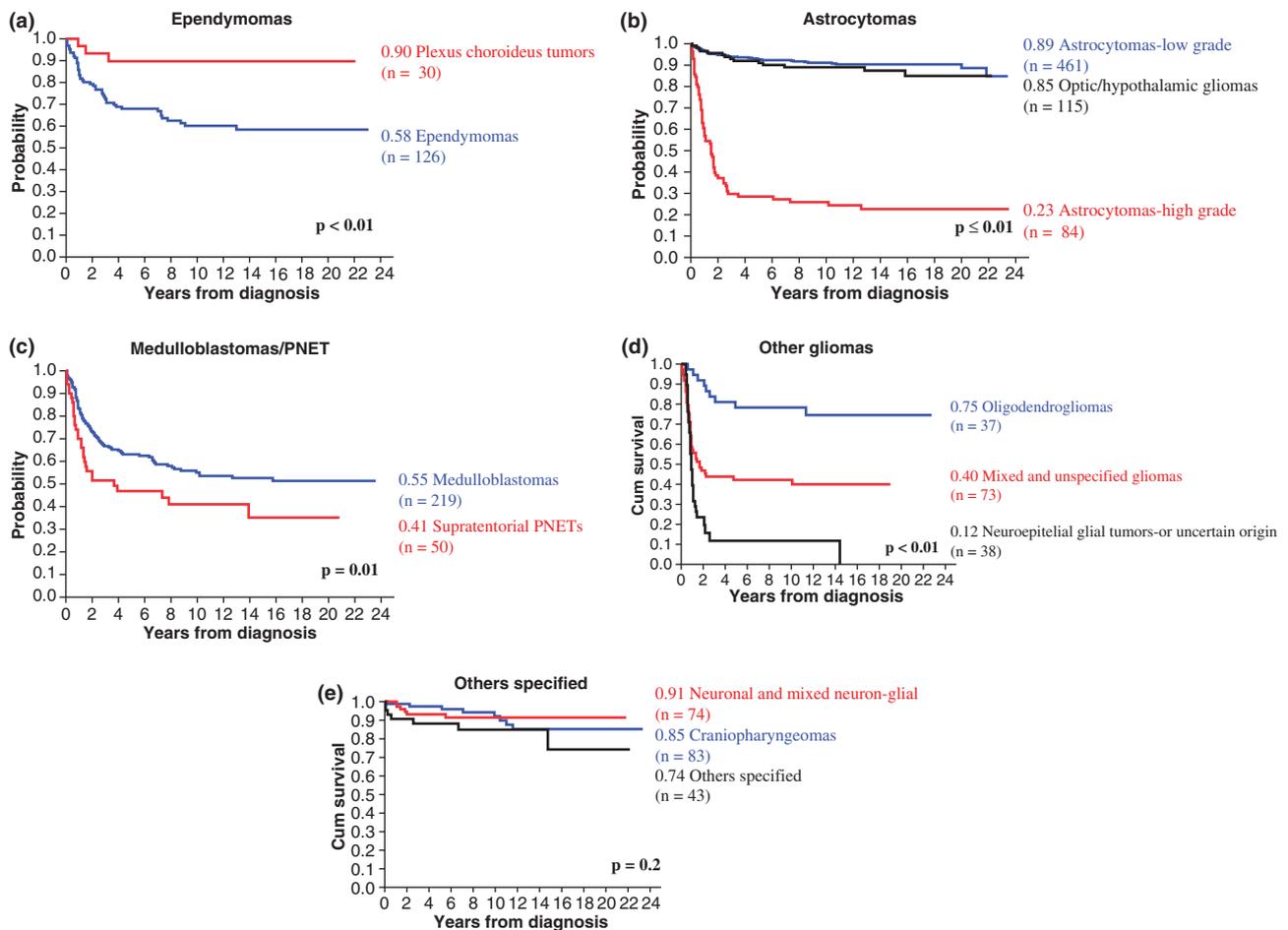
During recent years, there have been several publications in which information from pooled European Cancer Registries has been used to present incidence- and survival data in childhood CNS tumours (2,4–6). The conclusions from most of these studies have been that the Nordic countries

have a high incidence of CNS tumours compared with other European countries. The Nordic countries also have high-survival rates for children with CNS tumours. The accrual of patients to the Swedish Cancer Registry has been very high over the years due to the fact that the reports come from two sources, both from the pathologists and from the clinicians, although each patient is just counted once. The problem with data from the Swedish Cancer Registry has been the classification of the CNS tumours as a significant part were classified as unspecified type of tumour raising the question if these were really brain tumours.

In the present study, we have classified the patients with CNS tumours in the Swedish *Childhood Cancer Registry* according to the latest suggestion published in Cancer 2005 (7) with the only addition that patients with astrocytomas (group IIIb) have been further subdivided into three subgroups (low- or high-grade astrocytomas and optic nerve/chiasma gliomas).

### Incidence

The total incidence of CNS childhood tumours in the Swedish *Childhood Cancer Registry* was 4.2/100 000 children which is close to the results in the Swedish Cancer Registry and the other Nordic Cancer registries (1). The incidence has not increased throughout the study period from 1984 to 2005. Two earlier publications based on the Swedish Cancer Registry have shown an increase in the incidence rate. One study on brain tumours in children diagnosed between 1973 and 1992 describes an increase in astrocytomas in girls (17). The other study which includes children from 1960 to 1998 found a general annual increase in incidence of 1% (18). Both these studies cover long time periods starting in the 1960s and 1970s with low incidence figures during these decades. The present survey covers the interval from 1984 to 2005 during which period, no significant increase in the



**Figure 3** Actuarial survival curves by diagnostic subgroups in Swedish children with CNS tumours diagnosed 1984–2005. (a) ependymomas, (b) astrocytomas, (c) medulloblastomas/PNETs, (d) other gliomas, (e) others specified.

incidence rate occurred. Earlier reports of increased incidence in childhood CNS tumours in Sweden may partly be explained by a low incidence in the 1960s and 1970s, and furthermore, explained by the ‘jumping phenomenon’, suggested by Smith et al. (19) as an effect of the introduction of computed tomography and magnetic resonance imaging. The incidence presented in this study is high compared with some earlier publications covering the 1980s and 1990s. Results from the IARC study (1) showed incidence rates ranging from 2.5 to 4.1/100 000 children; Spain had an incidence of 2.6, France 2.8, Italy and Israel 3.0, Finland and Denmark 3.9 and Sweden 4.1/100 000 children <15 years of age.

After publication of the new classification of childhood CNS tumours in 2005 (7), some recent studies have presented new data. The first and most complete publication based on the new classification includes all children in Britain diagnosed with cancer 1991–2000 (20). The overall incidence rate for CNS tumours was 3.35 (ependymomas 0.35, astrocytomas 1.43, embryonal tumours 0.66, other gliomas 0.35, other specified 0.41 and unspecified 0.16), rates that compare well with data in the present study. The main

difference was seen in astrocytomas (1.87 vs. 1.43; especially low-grade astrocytomas) with higher incidence in the present study. In the ependymoma group, the plexus choroideus tumours were almost all (27/30) of the papilloma type, whereas in the British material these constituted only half of the plexus choroideus tumours (32/62).

In a recent publication from the USA (21) including children aged 0–19 years and diagnosed 1992–2004 based on Surveillance Epidemiology and End Results (SEER) data including only malign CNS tumours, the incidence was 2.8 but stable throughout the diagnostic period according to the Joinpoint regression method (16).

In the SEER publication from the U.S. in April, 2008 (22), CNS tumour incidence data was presented with inclusion of benign CNS tumours, a group of children not included in earlier SEER studies. The overall incidence for children diagnosed with CNS tumours in the USA in 2004 and 2005 was 3.97, which corresponds well with our data. No trend in incidence rate has been shown since the 1980s in SEER material from the USA (22).

In a recent report from the German childhood cancer registry including children with CNS tumours diagnosed

1991–2004, the reported incidence rates were 2.9 and 2.7/100 000 children for West and East Germany respectively. However, the incidence had increased during the study period and the rates for 2004 were 3.0 in West and as high as 4.3 in East Germany. They conclude that the increase in incidence is explained by improved registration but the true incidence of CNS tumours in Germany is still unknown (23).

Results from a population-based study from Denmark (24) of children with CNS tumours diagnosed 1980–1996 showed that the incidence had increased with 2.9%, annually. However, there was an obvious increase of incidence after 1988 which continued in a *post hoc* analysis 1997–2001 with rates exceeding 4.0/100 000 children. If this is due to a real increase of incidence or due to other explanations is still unclear. Other studies have suggested that similar increases in incidence should be explained with the 'Jumping phenomena' during the 1980s (20). A study from the Netherlands showed no increase in incidence in children with gliomas diagnosed 1989–2003 (25). Most but not all of the recent reports conclude that the incidence rate of CNS tumours in children has been stable during the last decades.

### Survival

In two studies based on National Cancer Registries from 20 European countries, it was concluded that the Nordic countries had the best OS results in children with CNS tumours (2,3).

The results of this 20 years registration of Swedish children with CNS tumours confirm that this is a large but very heterogeneous group of patients. Although the OS exceeds 70% at 10 years, this number includes many low-grade tumours that are cured by surgery alone. The prognosis for malignant brain tumours is still poor. This means that a large group of children who die from their cancer are children with brain tumours.

The overall mortality has decreased from 1.4 to 0.9/100 000 children age <15 years at diagnosis during the study period (Fig. 1). In clinical studies, the 5-year survival rate is usually the end-point. For CNS tumours in children this may not be appropriate considering that the survival curve continues to decline after 5 years in most subgroups. Such late decline was most pronounced in the medulloblastoma group. No infant in this study died later than 5 years from diagnosis in contrast to older children and teenagers where the survival estimates decreased even after 10–20 years from diagnosis (Table 2).

The 10-year survival rates differ considerably between the diagnostic CNS-groups. The worst prognosis in the present study was observed for patients with brain-stem tumours. Patients with medulloblastomas had a survival of 53%. The best prognosis (exceeding 80% survival) were found in children with plexus choroideus tumours, low-grade astrocytomas, optic nerve/chiasma gliomas and among the group IIIe-patients including hypophyseal adenomas, craniopharyngeomas, DNETs and gangliogliomas (Table 2).

There was no significant difference in survival between children diagnosed before or after 1995 ( $p = 0.1$ ) or between girls and boys ( $p = 0.4$ ) but age was a significant factor in this material with the worst prognosis among infants compared with older children ( $p < 0.01$ ; Table 2).

Actual and detailed survival data for children with CNS tumours in Britain classified according to the ICC-3 system have recently been published (20). The OS at 10 years for children diagnosed 1991–2000 was 66%, which is slightly below survival in the present material (72%) but with almost similar survival figures for most of the diagnoses. The main differences concerned the group supratentorial PNETs where the survival estimates were 23% in the UK study compared with 41% in the present study and for the plexus choroideus tumours (60% vs. 90%) completely explained with the higher frequency of plexus carcinomas in Britain compared with the present material. Both studies found a worse prognosis for infants, who had a clear tendency of early deaths within the first years from diagnosis.

The data from the U.S. based on SEER Cancer Statistics 2008 for children 0–19 years of age diagnosed with CNS tumour (benign tumour included) in 1996–2000 (22) showed an overall 5-year survival of 72% with almost similar results for the subgroups ependymomas, astrocytomas and medulloblastomas but a higher survival estimate for other gliomas compared with the present study (53% vs. 44%).

The major differences in both incidence and survival data in the present material compared with other earlier studies were found among astrocytomas where both incidence and survival data were higher compared with other studies (2,3). If we assume that almost all cases are diagnosed and reported in Sweden, this difference may be explained by under-reporting of particularly low-grade astrocytomas in other countries. This assumption is also supported by the fact that the prognosis for high-risk astrocytomas as well as for medulloblastomas is poor in Sweden and similar to results from other studies (20,21).

The health systems in European countries were compared in a recent publication (26). The authors concluded that countries with a publicly funded health sector, in which diagnostic and treatment strategies are equal for all children throughout the country, give all children the same and increased chance of cure. This may be one contributing factor to the good survival data in the present study.

The present study confirms results from recent other publications that the incidence of childhood CNS tumours is close to 4.0/100 000 children. This estimation is not biased by a high number of unspecified cases (2.5%) and the distribution of subgroups of tumours is similar to other studies. The OS rate is around 70% at 10 years.

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