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Increasing incidence rates of childhood malignant diseases in Sweden during the period 1960–1998

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Abstract

We analysed the trends in incidence rates of childhood cancer in Sweden. All cases of malignant diseases and benign brain tumours in children, 0–14 years old, reported to the Swedish Cancer Registry 1960 to 1998 were included, $n = 9298$. Cases were classified according to the International Classification of Childhood Cancer. Average annual change in incidence rate was calculated to +1.01%, (95% confidence interval CI = 0.80, 1.22). An increase in incidence rate per year was found for leukaemia, +0.85% (95% CI = 0.42, 1.28), lymphomas +1.87% (95% CI = 1.17, 2.58), CNS (central nervous system) tumours +1.45% (95% CI = 1.02, 1.88), sympathetic nervous system tumours +1.61% (95% CI = 0.79, 2.44), hepatic tumours +2.62% (95% CI = 2.02, 3.21), and germ cell and gonadal tumours +1.21% (95% CI = 0.23, 2.19). Of the CNS tumours, significant changes were seen for low-grade glioma/astrocytoma +2.10% (95% CI = 1.41, 2.80), benign brain tumours +3.77% (95% CI = 2.47, 5.10), and PNET/medulloblastoma +1.96% (95% CI = 0.48, 3.46). Changes in diagnostic criteria and better diagnostic tools may have contributed to these results.

Keywords: Incidence rate; Leukaemia; Lymphoma; Brain tumours; Germ cell and gonadal tumours; Neuroblastoma; Hepatic tumours

1. Introduction

Reports of increasing childhood cancer incidence rates are of concern because of the severe implications of the disease for the child and his/her family. In 1997, childhood cancer was the leading cause of death by disease among Swedish children aged 1–14 years [1]. In most studies, childhood cancer is defined up to and including 14 years of age.

A 0.8% increase in incidence rate per year of childhood cancer was observed from 1975 to 1999 in the USA [2]. From 1960 to 1991 a similar increase was seen for non-epithelial neoplasms (haematological, central nervous (CNS) and soft tissue tumours) in both Finland and Sweden [3]. An earlier Swedish study of childhood cancer incidence from 1958 to 1974 showed a significant increase, especially among boys [4]. During the period 1968–1995 in the North of England, incidence rates increased per decade by 12 cases per million [5]. An increase in incidence rate of 0.8% per year for non-CNS solid tumours and a 0.9% increase per year for brain tumours were observed in north-west England 1954–1998 [6]. However, encouraging reports of better survival from childhood cancer can be found [5,7,8].

Sweden has a Cancer Registry covering the entire population with good coverage of new cases; it was started in 1958 and is considered reliable since 1960. In a study on the completeness of the Registry comparing death certificates from 1978 with cancer registration, an overall 4.5% deficit was noted; for childhood cancer the deficit was 7.8% [9]. Reporting of new cases is compulsory and regulated by law [10]. Pathologists and clinicians report every newly diagnosed case. Treatment of childhood cancer is centralised to university hospitals. The Swedish population is mainly white and the childhood population (aged 0–14 years) has been numerically constant over the period studied, with approximately

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1.6–1.7 million children, except for a slight decline during the 1980s to 1.5 million.

The aim of this investigation was to study changes in the incidence rates of malignant diseases in children aged 0–14 years in Sweden from 1960 to 1998 and to present average annual incidence rates from 1990 to 1998.

2. Materials and methods

All cases of malignant diseases in children in the age group 0–14 years reported to the Swedish Cancer Registry between 1960 and 1998 were included in this study. Since the beginning of the Registry, all cases have been given an ICD-7 site code [11] and a morphology code (WHO/HS/CANC/24.1 Histology code; World Health Organisation. Expert committee on health statistics. Sub-committee on the registration of cases of cancer as well as their statistical presentation. August 15, 1956. Reference obtained from the Swedish Cancer Registry). ICD-O/2 coding has been in use from 1993 at the Cancer Registry but new cases are also given the older codes. In this study ICD-7 codes 140–209 were included. Some benign conditions are reported; of these only benign brain tumours were considered here.

The diseases were classified here into main diagnostic groups according to the International Classification of Childhood Cancer (ICCC) [12]. For the classification, the ICD-7 and the histology code mentioned above were used. However, some subgroups, mainly lymphomas and CNS tumours, could not be classified in detail according to ICCC by using the coding of the Cancer Registry, these tumour types were assigned to their

Table 1
Childhood malignancies in Sweden 1960–1998 and estimated changes in incidence rates

Diagnosis	Change in incidence rate/year (%)	95% CI	*P*	No. of cases	% of all diagnoses
All diagnoses	+1.01	0.80, 1.22	0.0001	9298	100.0
All diagnoses, benign brain tumours excluded	+0.90	0.67, 1.12	0.0001	8819	94.8
Leukaemia, all types	+0.85	0.42, 1.28	0.0003	2766	29.7
ALL	+5.80	4.66, 6.95	0.0001	1668	17.9
AML	−0.04	−1.11, 1.05	0.94	324	3.5
Others + unspecified	−6.38	−8.24, −4.48	0.0001	774	8.3
Lymphomas	+1.87	1.17, 2.58	0.0001	947	10.2
Hodgkin's disease	+1.81	0.59, 3.05	0.0047	268	2.9
Non-Hodgkin's lymphomas	+0.92	−0.05, 1.90	0.062	513	5.5
Other lymphomas[a]	+5.50	3.68, 7.34	0.0001	166	1.8
CNS tumours, all types	+1.45	1.02, 1.88	0.0001	2569	27.6
CNS tumours, benign excluded	+1.04	0.52, 1.55	0.0002	2090	22.5
Ependymoma[b]	+0.07	−0.50, 0.64	0.81	242	2.6
Astrocytomas/gliomas	+1.42	0.85, 1.99	0.0001	1220	13.1
Low-grade gliomas	+2.10	1.41, 2.80	0.0001	917	9.9
High-grade gliomas	−0.22	−1.31, 0.88	0.68	303	3.3
PNET/medulloblastoma	+1.96	0.48, 3.46	0.01	422	4.5
Benign brain tumours	+3.77	2.47, 5.10	0.0001	479	5.2
Unspecified neoplasms	−0.71	−2.19, 0.80	0.35	206	2.2
Sympathetic nervous system	+1.61	0.79, 2.44	0.0003	459	4.9
Retinoblastoma	+0.25	−1.21, 1.73	0.73	254	2.7
Renal tumours	+0.29	−0.51, 1.10	0.46	547	5.9
Hepatic tumours[c]	+2.62	2.02, 3.21	0.0001	100	1.1
Malignant bone tumours	+0.21	−0.81, 1.25	0.68	360	3.9
Osteosarcoma[d]	−0.10	−0.58, 0.37	0.66	182	2.0
Chondrosarcoma[e]				16	0.2
Ewing's sarcoma[f]	+0.66	−0.01, 1.33	0.052	147	1.6
Other bone tumours[e]				15	0.2
Soft tissue sarcoma	+0.13	−0.76, 1.04	0.76	510	5.5
Germ cell and gonadal tumours	+1.21	0.23, 2.19	0.02	249	2.7
Carcinomas	−0.02	−1.14, 1.11	0.97	276	3.0
Other and unspecified[g]	+0.43	0.01, 0.85	0.04	261	2.8

[a] No cases 1960, 1971 and 1977; change in annual incidence rate estimated using average 5-year incidence rates.
[b] No cases 1980; change in annual incidence rate estimated using average 5-year incidences rates.
[c] No cases 1963, 1966, 1977 and 1981; change in annual incidence rate estimated using average 5-year incidence rates.
[d] No cases 1990; change in annual incidence rate estimated using average 5-year incidence rates.
[e] No estimate due to because of small number of cases.
[f] No cases 1967; change in annual incidence rate estimated using average 5-year incidence rates.
[g] No cases 1973; change in annual incidence rate estimated using average 5-year incidence rates.

respective diagnostic groups (cf. Table 1). Regarding CNS tumours, the Swedish Cancer Registry codes the glioma into two groups: one includes low-grade glioma (e.g. astrocytoma grade I and II, and oligodendroglioma) and one high-grade glioma (e.g. astrocytoma grade III and IV and oligodendroblastoma). Benign brain tumours are reported to the Registry and constitute one subgroup in the analysis. A total of 9482 cases were reported, of which we excluded 184. Of these 184 children, 152 had a benign morphology code with site other than the CNS. The remaining 32 cases had a premalignant/in situ code or were misclassified. A total of 9298 children remained for further investigation. The analysis was made on all malignant diseases taken together as well as for each diagnosis separately.

3. Statistical methods

The age standardised incidence rates were calculated for each year from 1960 to 1998, expressed per 100,000 person-years (py). The background population was obtained from *Statistical Yearbooks 1960–1967* and from *Statistics Sweden* (SCB) *1968–1998*. The incidence rates were standardised to the 1970 world population [13]. By using age standardisation to the 1970 world population, the US 1970 population and the Swedish 1970 population, the results were similar and thus results using the world population are presented for international comparison. Linear regression analysis with calculation of the 95% confidence interval (CI) of the incidence rates was used in Fig. 1. Trends were analysed using the exponential regression model to obtain the annual percent change of the incidence rate, the corresponding P value and a 95% CI (see Table 1) [14]. However, for rare tumours, in some years there were no cases reported (see footnote in Table 1). For these tumours, average annual incidence rates for the following year intervals where calculated: 1960–1965, 1966–1970, 1971–1975, 1976–1980, 1981–1985, 1986–1990, 1991–1995 and 1996–1998. The incidence rate for each year was replaced with the average incidence rate in the respective time period and exponential regression was performed. For each estimated annual change in incidence rate a P value was obtained, and a 95% CI was calculated [15]. For the three most common childhood malignancies, leukaemia, CNS tumours and malignant lymphomas, we also examined trends in incidence for both sexes separately and for three different age groups: 0–4, 5–9 and 10–14 years. Childhood tumours are rare diseases and there is a variation in incidence from one year to another; to present the current incidence rates of the diseases we calculated an average annual incidence rate per 100,000 py during 1990–1998 (see Table 2).

4. Results

During the study period from 1960 to 1998, the average change in incidence rate for childhood malignant diseases was +1.01% per year (95% CI = 0.80, 1.22), $P = 0.0001$. Excluding benign brain tumours the

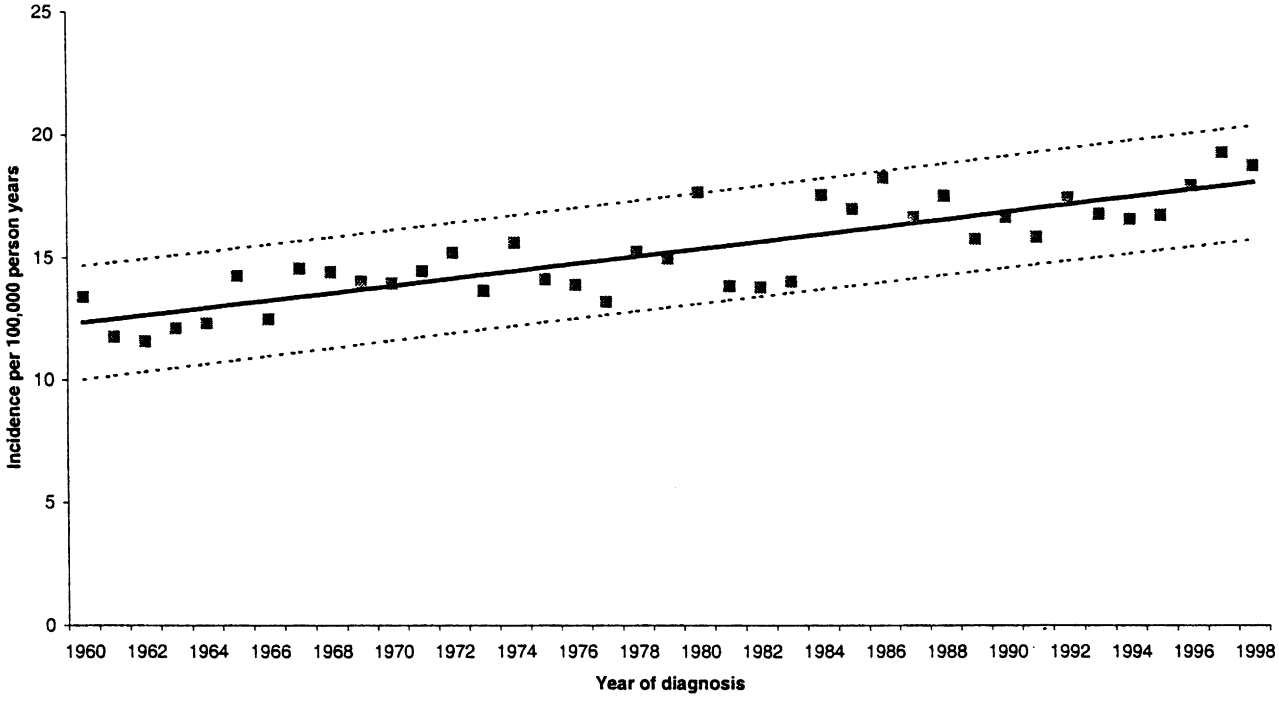

Fig. 1. Incidence rates of childhood malignancies in Sweden 1960–1998. Age adjusted to the world standard population. Linear regression line with 95% confidence interval for the incidence rates.

Table 2
Average annual incidence rates of childhood malignancies in Sweden 1990–1998; rates per 100,000 person years, age-adjusted to the world standard population

Diagnosis	Children 0–14 years	Boys	Girls	0–4 years	5–9 years	10–14 years
All diagnoses	17.34	18.43	16.20	23.68	12.98	13.73
All diagnoses, benign brain tumours excluded	16.19	17.28	15.03	22.52	11.83	12.59
Leukaemia, all types	5.10	5.56	4.61	8.04	3.53	2.92
ALL	4.01	4.52	3.49	6.36	2.94	2.08
AML	0.49	0.47	0.50	0.72	0.22	0.46
Others + unspecified	0.60	0.57	0.62	0.95	0.37	0.38
Lymphomas	1.86	2.42	1.27	1.56	1.76	2.39
Hodgkin's disease	0.51	0.63	0.38	0.12	0.32	1.24
Non-Hodgkin's lymphomas	0.88	1.26	0.48	0.64	1.12	0.95
Other lymphomas	0.47	0.53	0.40	0.80	0.32	0.20
CNS tumours, all types	4.89	5.26	4.50	5.22	4.87	4.48
CNS tumours, benign excluded	3.73	4.12	3.32	4.05	3.71	3.33
Ependymoma	0.41	0.44	0.38	0.64	0.32	0.20
Astrocytomas/gliomas	2.24	2.41	2.05	2.08	2.27	2.41
Low-grade gliomas	1.76	1.94	1.58	1.67	1.81	1.83
High-grade gliomas	0.48	0.47	0.48	0.41	0.47	0.57
PNET/medulloblastoma	0.78	0.88	0.67	0.88	0.93	0.49
Benign brain tumours	1.16	1.14	1.17	1.17	1.16	1.15
Unspecified neoplasms	0.30	0.39	0.21	0.45	0.18	0.24
Sympathetic nervous system	1.08	1.12	1.04	2.47	0.32	0.07
Retinoblastoma	0.54	0.39	0.71	1.32	0.10	0.00
Renal tumours	0.97	0.94	1.00	2.08	0.45	0.07
Hepatic tumours	0.27	0.36	0.17	0.60	0.10	0.00
Malignant bone tumours	0.51	0.49	0.53	0.16	0.63	0.84
Osteosarcoma	0.26	0.22	0.31	0.06	0.37	0.42
Chondrosarcoma	0.02	0.01	0.03	0.00	0.02	0.04
Ewing's sarcoma	0.20	0.24	0.16	0.08	0.24	0.33
Other bone tumours	0.02	0.01	0.03	0.02	0.00	0.04
Soft tissue sarcoma	0.79	0.91	0.67	0.99	0.57	0.77
Germ cell and gonadal tumours	0.51	0.47	0.55	0.68	0.24	0.57
Carcinomas	0.37	0.24	0.51	0.08	0.16	0.99
Other and unspecified	0.45	0.26	0.66	0.49	0.24	0.64

increase was still significant, +0.90% (95% CI = 0.67, 1.12). Estimated annual changes in incidence rate for the different diagnoses are presented in Table 1. The linear regression line with 95% CI of the incidence rates for all malignancies is shown in Fig. 1. For leukaemia, malignant lymphoma, CNS tumours, sympathetic nervous system tumours (neuroblastoma), germ cell/gonadal tumours, and hepatic tumours we found a significant annual increase in incidence rate during the study period (Table 1; Fig. 2). For all diagnoses together, the annual increase in incidence rate was significant for both sexes and for three 5-year age groups studied (0–4, 5–9 and 10–14 years). The annual incidence rate increased more among girls than among boys, +1.12% (95% CI = 0.80, 1.43) and +0.93% (95% CI = 0.65, 1.21), respectively. The annual change of incidence rate was similar in the three age groups.

The average annual incidence rate for all childhood cancer (including benign brain tumours) from 1990 to 1998 was 17.34/100,000 py, for boys 18.43/100,000 py and for girls 16.20/100,000 py. The incidence rate was highest in the youngest age group (0–4 years), 23.68/100,000 py (Table 2).

Leukaemia ($n = 2766$) was the most common childhood malignant disease. It was classified into three subgroups, acute lymphoid leukaemia (ALL), acute myeloid leukaemia (AML), and other or unspecified. Only 60 cases had chronic myeloid leukaemia, and therefore we classified them in the 'other' group. The remaining cases in the unspecified group were coded as unspecified myeloid leukaemia or unspecified leukaemia.

For all leukaemia in the age group 0–14 years, the average change in incidence rate per year during the study period was +0.85%, (95% CI = 0.42, 1.28); for boys +0.85% (95% CI = 0.33, 1.37) and for girls +0.82% (95% CI = 0.21, 1.43). The increase was largest for the age group 0–4 years, +1.13% (95% CI = 0.52, 1.74) and especially among the girls, +1.41% (95% CI = 0.56, 2.27), compared to boys +0.90% (95% CI = 0.22, 1.57). In the age group 5–9 years we found no significant change in leukaemia incidence over the period for neither boys nor girls. In the age group 10–14 years, the estimated annual incidence rate increased with +0.83% (95% CI = 0.19, 1.49), but for boys and girls separately we found no significant trend. The ALL incidence rate increased by 5.80% per year (95% CI = 4.66, 6.95), but

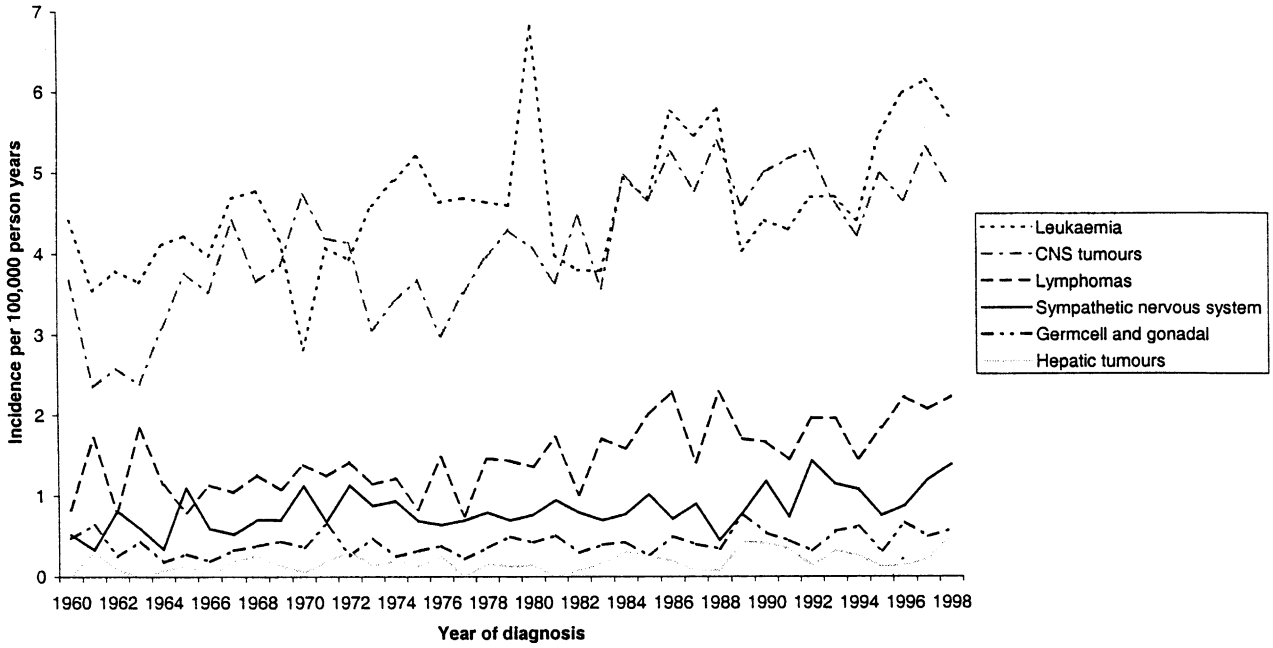

Fig. 2. Incidence rates of childhood malignancies 1960–1998. Age adjusted to the world standard population. Diagnoses with significant increase in incidence rates.

the incidence rate of AML showed no specific pattern. The incidence rate of the unspecified leukaemia declined markedly during the late 1970s. Parallel to this decline, the ALL incidence increased, as shown in Fig. 3. During the last 20 years (1978–1998) there was no significant change in incidence rate of ALL, +0.73% (95% CI = −0.49, 1.97).

The average annual incidence rate 1990–1998 for all leukaemias was 5.10/100,000 py, for boys 5.56/100,000 py and for girls 4.61/100,000 py. For ALL the corresponding rates were 4.01/100,000 py, for boys 4.52/100,000 py and for girls 3.49/100,000 py. A marked difference in incidence rate was seen between the age groups.

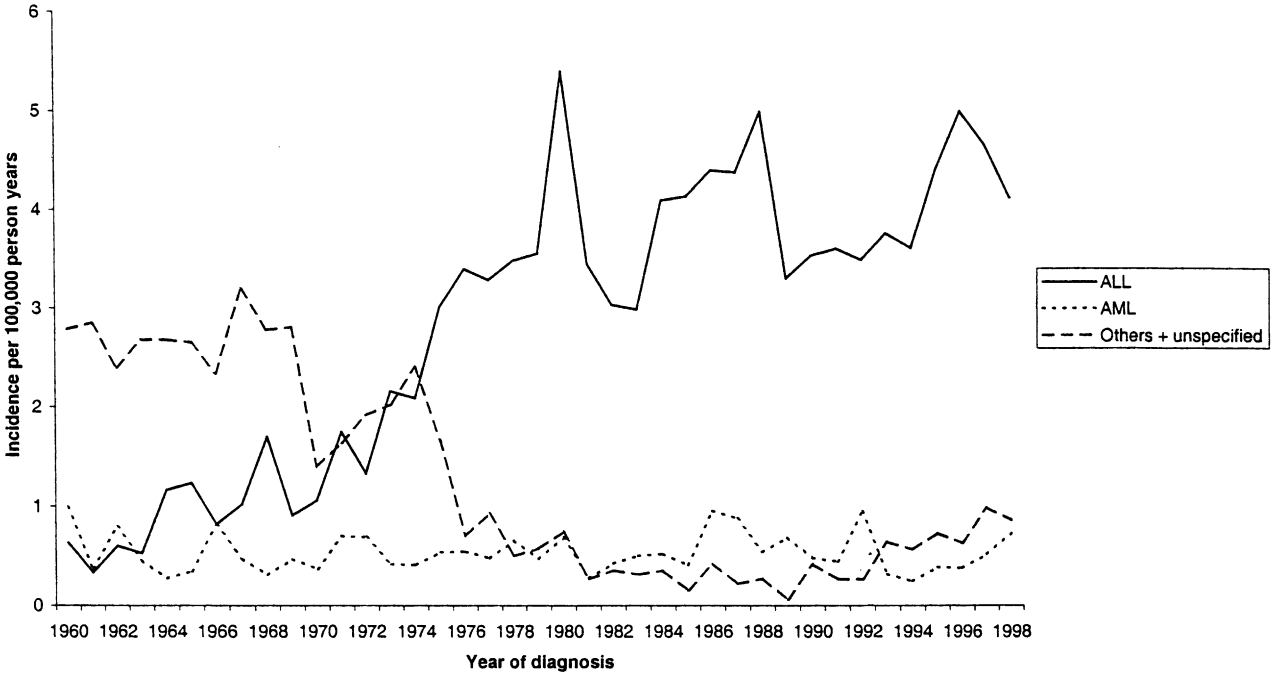

Fig. 3. Incidence rates of childhood leukaemias 1960–1998. Age adjusted to the world standard population.

The lymphomas ($n = 947$) were classified into Hodgkin's disease (ICD-7 code 201; $n = 268$), non-Hodgkin's lymphomas (NHL) (ICD-7 code 200; $n = 513$), and other lymphomas (ICD-7 code 202; $n = 166$). For the lymphoma group there was a significant increase of the incidence rate per year with +1.87% (95% CI = 1.17, 2.58). We saw a significant increase for Hodgkin's disease +1.81% (95% CI = 0.59, 3.05), for other lymphomas +5.50% (95% CI = 3.68, 7.34) but not for NHL. Looking at the entire lymphoma group, the annual increase was significant for both boys and girls in the three different age groups, 0–4, 5–9 and 10–14 years.

From 1990 to 1998, the average annual incidence rate of Hodgkin's disease was 0.51/100,000 py, being highest in the age group 10–14 years. For NHL, the average annual incidence rate was 0.88/100,000 py, 1.26/100,000 py for boys and 0.48/100,000 py for girls.

For all CNS tumours including benign brain tumours the average change in incidence rate per year from 1960 to 1998 was +1.45% (95% CI = 1.02, 1.88). The increase in incidence rate was similar for boys and girls. Excluding benign brain tumours the increase was still significant +1.04% (95% CI = 0.52, 1.55). The increase in incidence rate was significant for both sexes in the three different age groups, being highest for children 5–9 years old, +2.08% (95% CI = 1.29, 2.88); for boys +2.17% (95% CI = 1.15, 3.19) and for girls +2.42% (95% CI = 0.91, 3.95).

The average annual incidence rate for CNS tumours during 1990–1998 was 4.89/100,000 py, higher for boys (5.26/100,000 py) than for girls (4.50/100,000 py). The highest incidence rates were seen for low-grade glioma, benign brain tumours and PNET/medulloblastoma. The incidence rates 1960–1998 for low- and high-grade glioma and benign brain tumours are shown in Fig. 4.

Ependymoma constituted 9% of the brain tumours. Its incidence rates were low and did not show any specific trend.

Of the CNS tumours 47% were referred to the astrocytoma/glioma group and 75% of these were low grade. For all astrocytoma/glioma the estimated annual increase was significant, +1.42% (95% CI = 0.85, 1.99). The subgroup analysis showed that the incidence of the high-grade glioma had not changed significantly over time, whereas the incidence rate of the low-grade glioma increased yearly by +2.10% (95% CI = 1.41, 2.80). The average incidence rate 1990–1998 of high-grade glioma was low, 0.48/100,000 py, compared to 1.76/100,000 py for low-grade glioma.

The PNET/medulloblastoma group constituted 16% of all brain tumours. The incidence rate of PNET/medulloblastoma increased annually by 1.96% (95% CI = 0.48, 3.46).

Almost 19% of the brain tumours had a benign histology. The estimated annual change in incidence rate of benign brain tumours was +3.77% (95% CI = 2.47, 5.10) over the study period. Average annual incidence rate was 0.44/100,000 py during the 1960s, 0.56/100,000 py during the 1970s, 0.92/100,000 py during the 1980s and 1.16/100,000 py during 1990–1998.

Of all childhood cancers, 4.9% were classified as tumours from the sympathetic nervous system; neuroblastoma and ganglioneuroblastoma. The estimated annual change in their incidence rate showed an increase

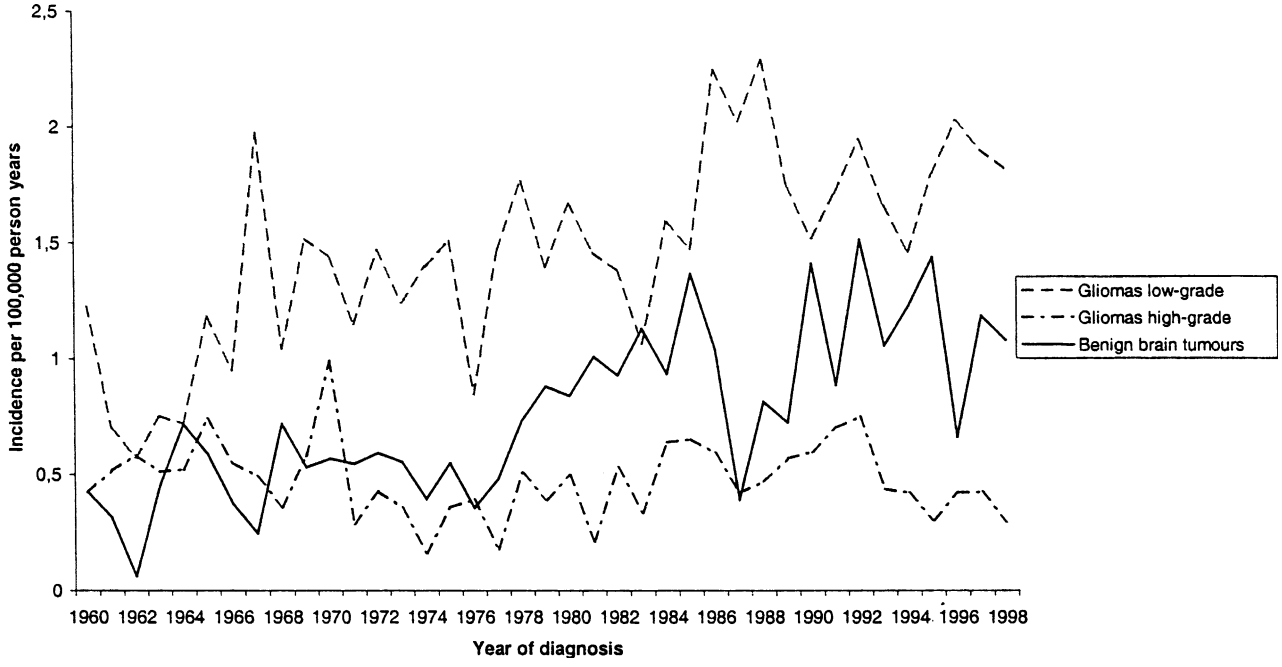

Fig. 4. Incidence rates of childhood gliomas and benign brain tumours 1960–1998. Age adjusted to the world standard population.

of +1.61% (95% CI = 0.79, 2.44) during the study period. The average annual incidence rate during 1990–1998 was highest in the age group 0–4 years.

The retinoblastomas constituted 2.7% of all tumours. The estimated annual change in retinoblastoma incidence rate did not show any specific trend. The average annual incidence rate during 1990–1998 was highest in the youngest age group. The renal tumours, mainly Wilms' tumour, constituted 5.9% of all childhood cancer and were seen mostly in the youngest age group. The incidence rate did not change significantly during the study period. Hepatic tumours were extremely rare, only 1.1% of all tumours. They occurred mainly in the youngest age group. In some years there where no cases reported, and therefore we estimated the annual change in incidence rate by using average incidence rates in 5-year periods and found an increase of +2.62% (95% CI = 2.02, 3.21).

The malignant bone tumours constituted 3.9% of all tumours and included osteosarcoma (51% of bone tumours), chondrosarcoma (4%), Ewing's sarcoma (41%), and other bone tumours (4%). During 39 years, only 16 cases of chondrosarcoma and 15 of 'other' type were registered. The incidence rates did not change significantly during the studied decades. The average annual incidence rate during 1990–1998 for osteosarcoma was 0.26/100,000 py and for Ewing's sarcoma 0.20/100,000 py, the incidences being highest in the age group 10–14 years.

Soft tissue sarcomas include several histological types that are not presented separately. They constituted 5.5% of all childhood tumours. The incidence rates did not change significantly over time. The germ cell and gonadal tumours were 2.7% of all tumours. The estimated annual change in incidence rate increased over time by +1.21% (95% CI = 0.23, 2.19). Even so, the annual average incidence during 1990–1998 was low and similar for boys and girls.

Carcinomas were rare in children, 3.0% of all tumours, and did not show any significant change of incidence rate during the study period. Thyroid cancer and malignant melanoma were the most common diagnoses in this group. The incidence rate of the group 'other and unspecified' (2.8% of tumours) increased over time by +0.43% (95% CI = 0.01, 0.85).

5. Discussion

The Swedish Cancer Registry covers the entire population and registration started in 1958. The reporting of new cases is compulsory. The incidence rate for malignant diseases in childhood rose during the period of 39 years that we studied from an average of 13.12/100,000 py during the 1960s to 17.34/100,000 py during 1990–1998. Excluding benign brain tumours, the average annual childhood cancer incidence rate during 1990–1998 was 16.19/100,000 py. This incidence is among the highest reported worldwide [16]. Good case ascertainment might explain this high incidence. Sweden is a small country with unique personal identification numbers and public health care; reporting to the Cancer Registry is compulsory. The estimated average annual change in incidence rate per year from 1960 to 1998 was +1.01% (95% CI = 0.80, 1.22). This is similar to what has been observed in other countries [5,6,17,18]. The increase was, in our study, significant for both sexes and the three different age groups (0–4, 5–9 and 10–14 years).

As observed in other Western populations, the neoplasms that most commonly affect Swedish children are leukaemia (30%), brain tumours (28%) and lymphoma (10%). The observed incidence rates corresponded to an average of 209 childhood cancer cases per year during the 1960s and 275 cases per year in 1990–1998.

The diagnoses for which we found a significant increase in annual incidence rate were leukaemia, lymphomas, CNS tumours, sympathetic nervous system tumours, hepatic tumours and germ cell/gonadal tumours.

For leukaemia the estimated annual change in incidence rate was significant for all leukaemia combined, +0.85%. The increase in ALL was highly significant and the largest increase occurred during 1970–1980. Parallel to this rise the incidence rates of other and unspecified leukaemia declined, suggesting a change in the diagnosis and classification of the leukaemia. In 1976 the FAB classification (French–American–British Cooperative Working Group) of acute leukaemia, based on morphology, was introduced [19] and thereafter unspecified leukaemias where probably diagnosed as ALL to greater extent. A similar shift in classification was reported from the USA and attributed to new knowledge in immunology enabling the classification of different types of lymphocytes [20]. The incidence rates of AML showed no specific trend; the total increase in all leukaemias is attributed to the increase in ALL. Because of differences in diagnostic practices, a trend analysis of the ALL group over the 39-year period may not be informative, but nevertheless the increase in incidence rate of the whole leukaemia group is of interest. We looked separately at the estimated annual change in incidence rate of ALL during 1978–1998, and found no significant change. In the USA, both total leukaemia and ALL incidence rates increased from 1977 to 1995 by 0.9% per year [21].

The incidence of all lymphomas in Swedish children increased annually during 1960–1998 by an average of +1.87%. Hodgkin's disease and the 'other lymphoma' group, but not NHL, increased significantly in Swedish children. The 'other lymphoma' group is a heterogeneous group of NHL, including, e.g. reticulosis and the

increase in incidence rate might be due to different coding practices over time. An increasing incidence rate of NHL by 2.9% per year 1970–1989 was observed in the Greater Delaware Valley [17]. In nine European countries an annual 0.76% increase in NHL incidence rate was seen between 1970 and 1990 [22]. The NHL incidence 1975–1995 presented by the SEER programme [23] did not change significantly. In north-west England an average annual increase of 1.2% from 1954 to 1998 was seen for Hodgkin's disease but no significant change was seen for NHL [24]. The incidence rate of Hodgkin's disease among children in Norway 1971–1995 [25] and in the Greater Delaware Valley mentioned above was stable, while in the USA 1975–1995 a slight decline was seen [7]. The increasing incidence rate of Hodgkin's disease seen in Sweden is believed to be true and not due to changes in diagnostic procedures. A pathological review of cases 1975–1994 in western Sweden showed good agreement with the initial diagnosis [26].

For brain tumours in Swedish children 0–14 years old, an average annual increase in incidence rate of 2.6%, and for astrocytoma 3.0%, has been reported for the period 1973–1992 [27]. Another Swedish study showed an average annual increase in brain tumour incidence rate of 3.0% from 1978 to 1992 in the 0–19 year age group [28]. In our study, for all CNS tumours from 1960 to 1998 in the 0–14 year age group, the average annual increase in incidence rate was +1.45%. Excluding the benign brain tumours we still found an increase in the incidence rate. In the USA it was estimated that benign brain tumours contributed with 28% of the total increase of the incidence rate of brain tumours [29].

An increase in incidence rates for brain tumours in children has also been reported from other countries. In the USA, a significant increase was seen from 1975 to 1995, though most of the increase was seen from 1983 to 1986 [7]. Trends in the USA from 1977 to 1995 were analysed and for both high- and low-grade glioma combined, the incidence rates increased by an average of 1.8% per year, but during the last decade the rates stabilised and even declined slightly [30]. In Sweden, computed tomographic scans became available in the mid-1970s and magnetic resonance imaging (MRI) in the mid-1980s, making it easier to image pathological changes in the brain. A steep increase in incidence rates of brain tumours during the mid-1980s was reported from USA and a 'jump model' of incidence rates was postulated [31]. Using this model, the steep increase that occurred during the mid-1980s can be assigned to better case ascertainment with the introduction of MRI. This model and explanation have been widely discussed [32–35].

In our study we found a significantly increased incidence rate only for low-grade astrocytoma and benign brain tumours, which might be explained by better diagnostic methods. The average annual incidence rate of CNS tumours in the 1960s (benign excluded) was 2.90/100,000 py, in the 1970s 3.23/100,000 py, in the 1980s 3.62/100,000 py and during 1990–1998 3.73/100,000 py. For the benign brain tumours, the change was more striking; the average annual incidence rate was in the 1960s 0.44/100,000 py, in the 1970s 0.56/100,000 py, in the 1980s 0.92/100,000 py and in 1990–1998 1.16/100,000 py. The Swedish Registry groups the gliomas into two main groups, low grade or high grade. The new imaging techniques, especially MRI, make it easier to discover especially low-grade glioma [30,36]. Excluding both benign and low-grade glioma, no significant trend in incidence was found during the study period. Thus better diagnostic methods may in part explain the increasing incidence rate of low-grade glioma and benign brain tumours.

In the USA, mortality rates for childhood CNS tumours decreased significantly by 1.1% per year from 1975 to 1995 and the absence of increase of mortality in children with CNS tumours was used as an argument against a true increase in incidence rates [7,30]. It is possible to live for a long time with a low-grade tumour [36], tumours may be diagnosed earlier with new techniques, and treatment becomes more aggressive, often combing surgery with radiotherapy and chemotherapy. Perhaps it is too early to draw any conclusions from the mortality in brain tumours that we see today about whether there has been a true increase in the occurrence of the disease or not.

A significant increase in the incidence rate of neuroblastoma was seen in 1970–1989 in the Greater Delaware Valley [17] and among infants in the USA in 1980–1990 [37]. No significant trend in children under 15 years (1975–1995) was observed in the SEER programme, except for increasing rates among infants in the latest year [38]. The incidence rate of sympathetic nervous system tumours increased significantly in Sweden, although no screening programme has been conducted.

Hepatic tumours were few but showed increasing incidence rates. Similar findings are reported from north-west England 1954–1998 [6]. The incidence rate of hepatoblastoma increased while that of hepatocellular cancer decreased in the USA, 1975–1995 [39]. The incidence rate of germ cell and gonadal tumours increased by an average of 1.21% per year. Similar results have been reported for testicular cancer among boys in England and Wales 1962–1995 [40], the increase of all germ cell tumours was 2.6% each year in north-west England 1954–1998 [6].

In summary this study showed a significant increase in the incidence rate of childhood malignancies during 1960–1998 in Sweden. New diagnostic tools have become available; classification has changed for some of the tumour types; case ascertainment might differ between the periods and this can affect the incidence rates. Increases in incidence rates are seen in several Western

societies, which is of concern. The treatment of cancer may improve but the therapeutic arsenal we have today, consisting mainly of chemotherapy and radiotherapy, is toxic and may have long-term side-effects. Further research to identify risk factors is necessary so that preventive measures can be taken and hopefully we will see less of childhood cancer in the future. Of interest are perinatal risk factors, such as exposure to certain persistent organic pollutants [41,42], ionising radiation [43] and genetic factors.

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References

1. The National Board of Health and Welfare. Yearbook of health and medical care 2000, Stockholm, Sweden, Socialstyrelsen, 2000.
2. Ries LAG, Eisner MP, Kosary CL, *et al*. SEER cancer statistics review, 1973–1999. Bethesda (MD), National Cancer Institute, 2002, Also available from: URL:. Available from: http//:www.seer.cancer.gov/CSR/1973_1999 [accessed 2003, September 15].
3. Baron JA, Bergstrom R, Lindgren C, Teppo L, Storm H, Adami HO. Trends in non-epithelial cancer incidence in Denmark, Finland, and Sweden, 1961–1990. *Int J Cancer* 1996, **67**(5), 648–652.
4. Ericsson JL, Karnstrom L, Mattsson B. Childhood cancer in Sweden, 1958–1974. I. Incidence and mortality. *Acta Paediatr Scand* 1978, **67**(4), 425–432.
5. Cotterill SJ, Parker L, Malcolm AJ, Reid M, More L, Craft AW. Incidence and survival for cancer in children and young adults in the North of England, 1968–1995: a report from the Northern Region Young Persons' Malignant Disease Registry. *Br J Cancer* 2000, **83**(3), 397–403.
6. McNally RJ, Kelsey AM, Cairns DP, Taylor GM, Eden OB, Birch JM. Temporal increases in the incidence of childhood solid tumors seen in Northwest England (1954–1998) are likely to be real. *Cancer* 2001, **92**(7), 1967–1976.
7. Linet MS, Ries LAG, Smith MA. Cancer surveillance series: recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst* 1999, **91**, 1051–1058.
8. Adami HO, Glimelius B, Sparen P, Holmberg L, Krusemo UB, Ponten J. Trends in childhood and adolescent cancer survival in Sweden 1960 through 1984. *Acta Oncol* 1992, **31**(1), 1–10.
9. Mattsson B, Wallgren A. Completeness of the Swedish Cancer Register. Non-notified cancer cases recorded on death certificates in 1978. *Acta Radiol Oncol* 1984, **23**(5), 305–313.
10. The National Board of Health and Welfare. Socialstyrelsens föreskrifter om anmälan till cancerregistret. The National Board of Health and Welfare regulation on reporting to the Cancer Register, Stockholm, Sweden, Socialstyrelsen, 1984 [In Swedish].
11. WHO. International classification of diseases. 7 rev ed. Geneva: World Health Organization; 1957.
12. Kramarova E, Stiller CA. The international classification of childhood cancer. *Int J Cancer* 1996, **68**(6), 759–765.
13. IARC. Cancer incidence in five continents, vol VII. Lyon (France): International Agency for Research on Cancer; 1997.
14. Checkoway H, Pearce NE, Crawford-Brown DJ. Research methods in occupational epidemiology. New York, Oxford University Press, 1989.
15. SAS. In: Cary NC, editor. SAS. 6.06 ed.: SAS Institute Inc.; 1987.
16. Parkin DM, Kramárová E, Draper GJ, *et al*., eds. *International incidence of childhood cancer*, vol. II. Lyon (France), International Agency for Research on Cancer, 1998.
17. Bunin GR, Feuer EJ, Witman PA, Meadows AT. Increasing incidence of childhood cancer: report of 20 years experience from the greater Delaware Valley Pediatric Tumor Registry. *Paediatr Perinat Epidemiol* 1996, **10**(3), 319–338.
18. Gurney JG, Davis S, Severson RK, Fang JY, Ross JA, Robison LL. Trends in cancer incidence among children in the U.S. *Cancer* 1996, **78**(3), 532–541.
19. Bennett JM, Catovsky D, Daniel MT, *et al*. Proposals for the classification of the acute leukaemias. French–American–British (FAB) co-operative group. *Br J Haematol* 1976, **33**(4), 451–458.
20. Miller RW. Childhood leukemia and neonatal exposure to lighting in nurseries. *Cancer Causes Control* 1992, **3**(6), 581–582.
21. Smith MA, Gloeckler Ries LA, Gurney JG, Ross JA. Leukemia. In Ries LAG, Smith MA, Gurney JG, *et al*., eds. *Cancer incidence and survival among children and adolescents: United States SEER program 1975–1995*. Bethesda (MD), National Cancer Institute, 1999.
22. Weidmann C, Black RJ, Masuyer E, Parkin DM. Incidence of non-Hodgkin's lymphoma in children between 1970 and 1990 in nine European countries. *Eur J Cancer* 1999, **35**(8), 1235–1237.
23. Percy CL, Smith MA, Linet M, Gloekler Ries LA, Friedman DL. Lymphomas and reticuloendothelial neoplasms. In Ries LAG, Smith MA, Gurney JG, *et al*., eds. *Cancer incidence and survival among children and adolescents: United States SEER program 1975–1995*. Bethesda (MD), National Cancer Institute, 1999.
24. McNally RJ, Cairns DP, Eden OB, Kelsey AM, Taylor GM, Birch JM. Examination of temporal trends in the incidence of childhood leukaemias and lymphomas provides aetiological clues. *Leukemia* 2001, **15**(10), 1612–1618.
25. Foss Abrahamsen A, Egeland T, Hansen S, Langholm R, Holte H, Kvaloy S. Hodgkin's disease in a national and hospital population: trends over 20 years. *Eur J Cancer* 1997, **33**(14), 2380–2383.
26. Samuelsson BO, Ridell B, Rockert L, Gustafsson G, Marky I. Non-Hodgkin lymphoma in children: a 20-year population-based epidemiologic study in western Sweden [see comments]. *J Pediatr Hematol Oncol* 1999, **21**(2), 103–110.
27. Hjalmars U, Kulldorff M, Wahlqvist Y, Lannering B. Increased incidence rates but no space-time clustering of childhood astrocytoma in Sweden, 1973–1992: a population-based study of pediatric brain tumors. *Cancer* 1999, **85**(9), 2077–2090.
28. Hardell L, Tondel M, Flodin U, *et al*. [Increased incidence of brain tumors. A study of Swedish children and adolescents aged 0–19 [In Swedish]. *Lakartidningen* 1997, **94**(9), 728–731.
29. Gurney JG, Wall DA, Jukich PJ, Davis FG. The contribution of nonmalignant tumors to CNS tumor incidence rates among children in the United States. *Cancer Causes Control* 1999, **10**(2), 101–105.
30. Legler JM, Ries LA, Smith MA, *et al*. Cancer surveillance series [corrected]: brain and other central nervous system cancers: recent trends in incidence and mortality [published erratum appears in J. Natl. Cancer Inst. 1999, 91(19);1693] [see comments]. *J Natl Cancer Inst* 1999, **91**(16), 1382–1390.
31. Smith MA, Freidlin B, Ries LA, Simon R. Trends in reported incidence of primary malignant brain tumors in children in the United States [see comments]. *J Natl Cancer Inst* 1998, **90**(17), 1269–1277.
32. Black WC. Increasing incidence of childhood primary malignant brain tumors–enigma or no-brainer? [editorial; comment] [see comments]. *J Natl Cancer Inst* 1998, **90**(17), 1249–1251.

33. Gurney JG. Topical topics: brain cancer incidence in children: time to look beyond the trends. *Med Pediatr Oncol* 1999, **33**(2), 110–112.
34. Forman AD. Re: Trends in reported incidence of primary malignant brain tumors in children in the United States [letter; comment]. *J Natl Cancer Inst* 1999, **91**(7), 648–649.
35. Schechter CB. Re: Brain and other central nervous system cancers: recent trends in incidence and mortality [letter]. *J Natl Cancer Inst* 1999, **91**(23), 2050–2051.
36. Heideman RL, Packer RJ, Albright LA, Freeman CR, Rorke LB. Tumors of the central nervous system. In Pizzo PA, Poplack DG, eds. *Principles and practice of pediatric oncology*. 3rd ed. Philadelphia, Lippincott–Raven, 1997.
37. Kenney LB, Miller BA, Ries LA, Nicholson HS, Byrne J, Reaman GH. Increased incidence of cancer in infants in the U.S.: 1980–1990. *Cancer* 1998, **82**(7), 1396–1400.
38. Goodman MT, Gurney JG, Smith MA, Olshan AF. Sympathetic nervous system tumors. In Ries LAG, Smith MA, Gurney JG, *et al*., eds. *Cancer incidence and survival among children and adolescents: United States SEER program 1975–1995*. Bethesda (MD), National Cancer Institute, 1999.
39. Bulterys M, Goodman MT, Smith MA, Buckley JD. Hepatic tumors. In Ries LAG, Smith MA, Gurney JG, eds. *Cancer incidence and survival among children and adolescents: United States SEER program 1975–1999*. Bethesda (MD), National Cancer Institute, 1999.
40. dos Santos Silva I, Swerdlow AJ, Stiller CA, Reid A. Incidence of testicular germ-cell malignancies in England and Wales: trends in children compared with adults. *Int J Cancer* 1999, **83**(5), 630–634.
41. Hardell L, Dreifaldt AC. Breast-feeding and the risk of malignant diseases in childhood. *Eur J Clin Nutr* 2001, **55**, 179–185.
42. Hardell L, van Bavel B, Lindström G, *et al*. Increased concentrations of polychlorinated biphenyls, hexachlorobenzene and chlordanes in mothers to men with testicular cancer. *Environ Health Perspect* 2003, **111**, 930–934.
43. Axelson O, Fredrikson M, Åkberblom G, Hardell L. Childhood leukemia (0–19 years) and exposure to ionizing radiation in homes built from uranium containing alum shale concrete. *Epidemiology* 2002, **13**, 146–150.