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Risk of second malignant neoplasms after childhood central nervous system malignant tumors: an international study

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Childhood central nervous system (CNS) cancer

- 2nd most common malignancy in children (0-14 years) after leukemia
- ~ 20% of all childhood tumors
- commonest cause of cancer-related death in children

Childhood CNS cancer

Incidence rates

Europe: 30 per million child-years in 1988-97
annual percent change: 1.7% in 1978-97

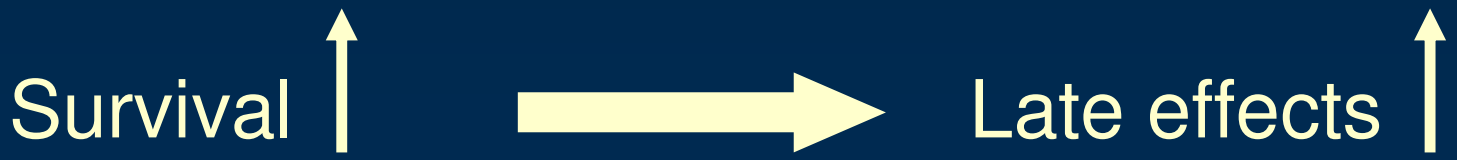
US: 37 per million child-years in 2001-2004
annual percent change: 1.1% in 1975-2004

5-year survival rates

Europe: from 40% in the 1970s to 64% in the 1990s

US: ~ 71% in 1996-2003
from 47% for gliomas to 84% for astrocytomas

Childhood CNS cancer



Second malignant neoplasms (SMN)

Malignant tumors of the CNS are the most frequent SMNs affecting childhood CNS cancer survivors

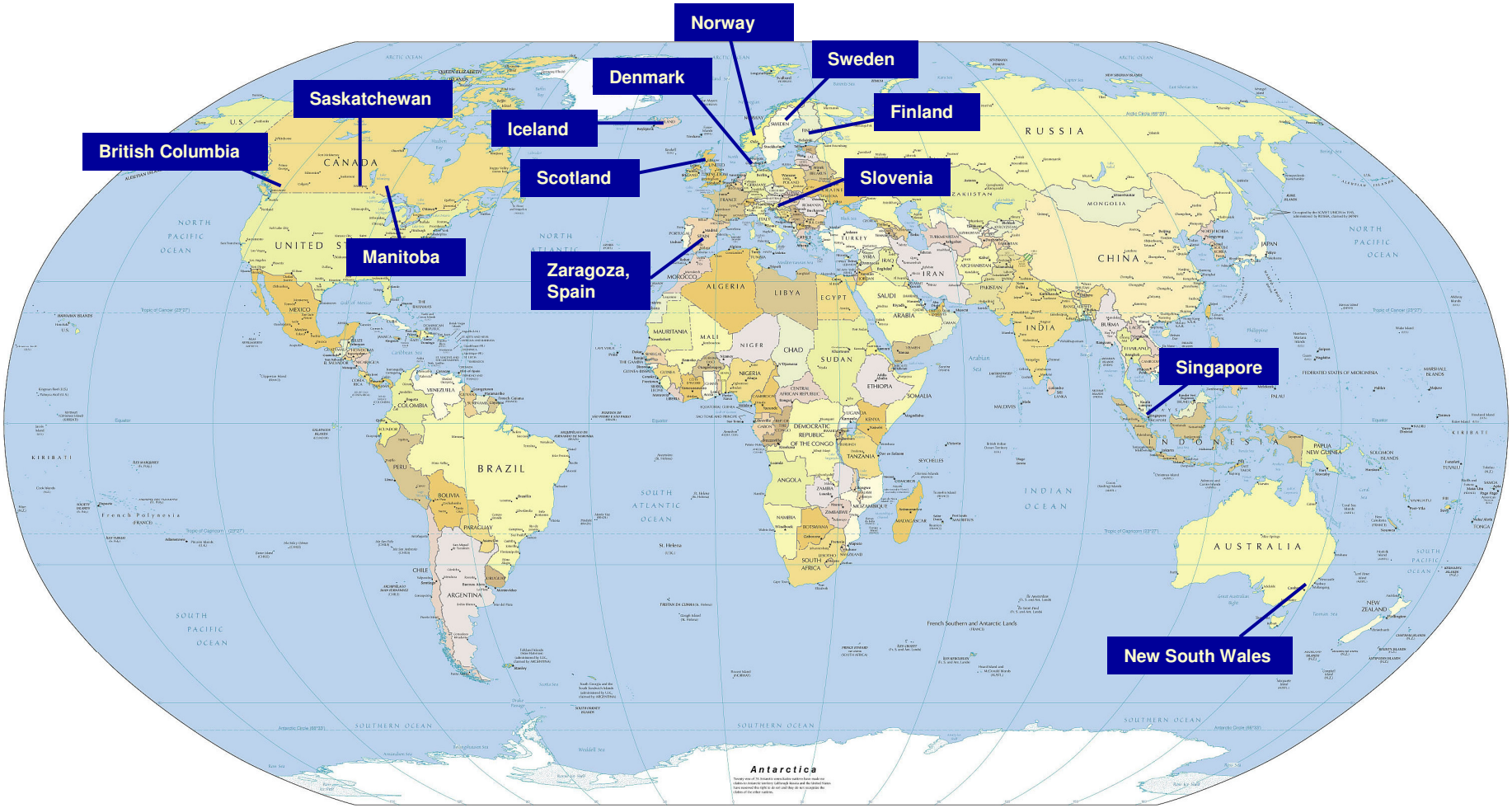
Study	Area	Period of 1st CNS cancer	Cohort size	Risk of 2nd CNS cancer
Inskip & Curtis. Int J Cancer 2007	US (SEER)	1973-2002	25,965	n=8, SIR=13 (5.4-25) after astrocytoma n=8, SIR=45 (19-88) after PNET
Neglia et al. JNCI 2006	US-Canada	1970-1986	14,361	n=8, SIR=14 (6.5-27)
Olsen et al. BMJ 1993	Nordic countries	1943-1987	30,880	n=27, SIR=13 (8.7-19)

Information on the risk of SMNs in organs other than the CNS is more limited

Assess the relative and absolute risk of other than CNS neoplasms after childhood CNS cancer in an international multicentre study

- Data on cases of CNS cancer occurring in children (0-14 years) and on subsequent SMNs from 13 population-based cancer registries
- The registries contributed data for different time periods in the years 1943-2000
- The mean follow-up time was 8.6 years

- SMNs standardized incidence ratios (SIRs) with 95% confidence intervals (CI), absolute excess risk (AER), cumulative incidence



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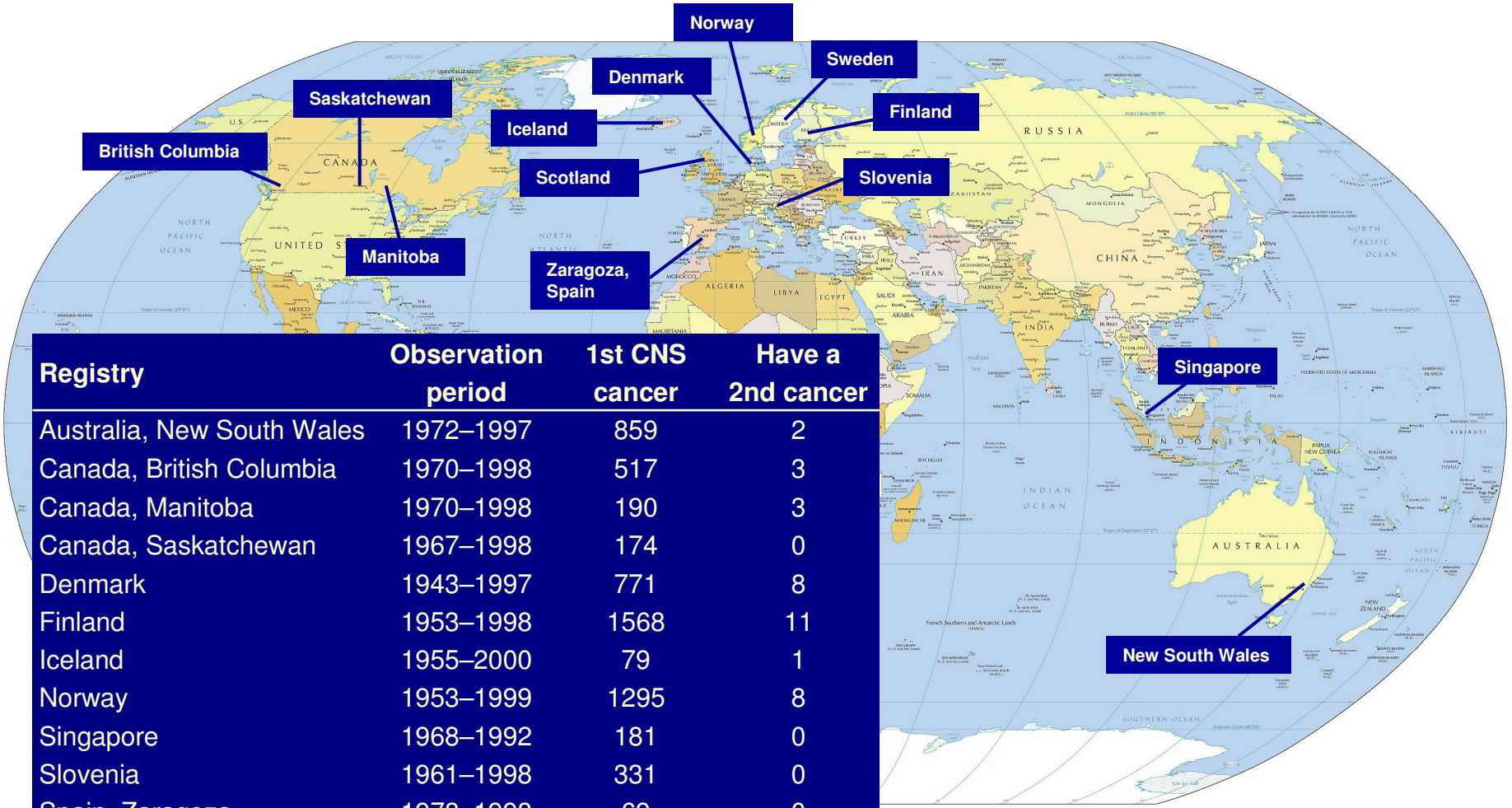


Registry	Observation period	1st CNS cancer	Have a 2nd cancer
Australia, New South Wales	1972–1997	859	2
Canada, British Columbia	1970–1998	517	3
Canada, Manitoba	1970–1998	190	3
Canada, Saskatchewan	1967–1998	174	0
Denmark	1943–1997	771	8
Finland	1953–1998	1568	11
Iceland	1955–2000	79	1
Norway	1953–1999	1295	8
Singapore	1968–1992	181	0
Slovenia	1961–1998	331	0
Spain, Zaragoza	1978–1998	69	0
Sweden	1961–1998	1823	7
UK, Scotland	1975–1996	574	0
Total	*1943–2000*	*8431*	*43*

8431 CNS cancer survivors; 72,514 person-years at risk

SMN*	n	SIR	95% CI	AER†
All malignant (non CNS)	43	2.3	1.6-3.0	33
Soft tissue sarcoma	4	7.7	2.1-20	4.8
Thyroid gland	9	11	4.9-20	11
Lymphohematopoietic	12	2.6	1.3-4.5	10
Lymphomas	6	2.5	0.9-5.4	4.9
Non Hodgkin lymphoma	5	4.3	1.4-10	5.3
Leukemias	6	2.8	1.0-6.0	5.3

*SMNs with at least 4 observed cases

†per 100,000 person-years

4966 glioma survivors; 47,056 person-years at risk

SMN*	n	SIR	95% CI	AER†
All malignant (non CNS)	26	2.2	1.4-3.2	30
Soft tissue sarcoma	4	12	3.2-30	7.8
Thyroid gland	4	6.8	1.9-18	7.2
Lymphohematopoietic	8	2.7	1.2-5.3	11
Lymphomas	6	3.8	1.4-8.2	9.4
Non Hodgkin lymphoma	5	6.7	2.2-16	9.1

*SMNs with at least 4 observed cases

†per 100,000 person-years

2346 embryonal tumor survivors; 15,600 person-years at risk

SMN*	n	SIR	95% CI	AER†
All malignant (non CNS)	11	3.9	1.9-7.0	52
Thyroid gland	4	30	8.2-77	25

1089 other CNS cancer survivors; 9858 person-years at risk

SMN*	n	SIR	95% CI	AER†
All malignant (non CNS)	6	1.4	0.5-2.9	16

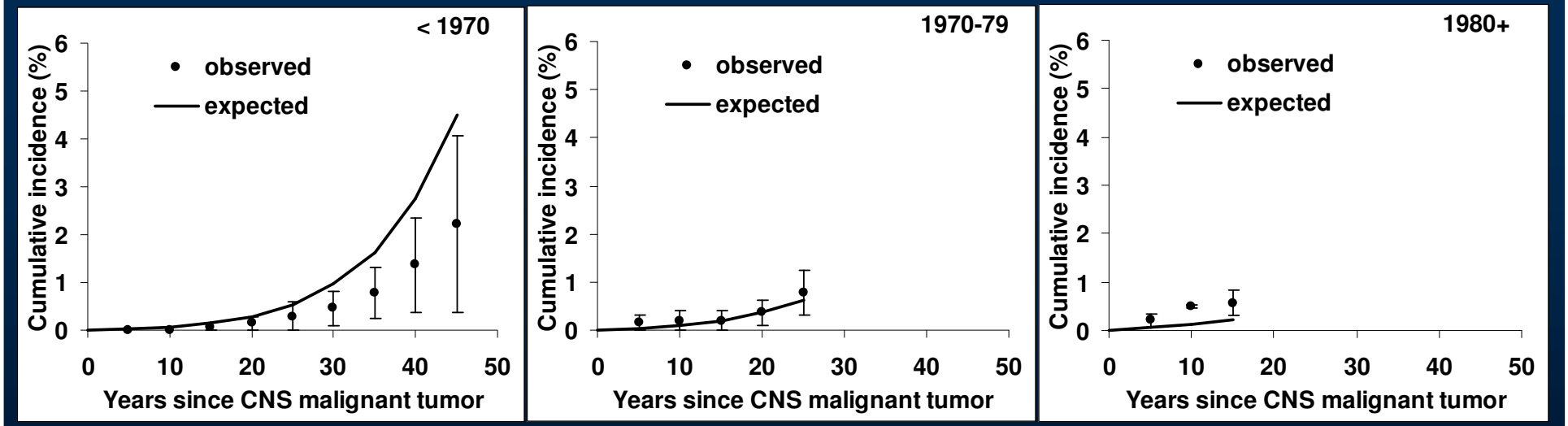
*SMNs with at least 4 observed cases

†per 100,000 person-years

All non-CNS SMNs after childhood CNS cancer, by length of follow-up after the first cancer diagnosis

Years since CNS cancer	Person-years	n	SIR	95% CI
Less than 1 year	7108	3	4.0	0.8-12
1-4 years	19,128	9	4.8	2.2-9.1
5-9 years	16,811	10	5.1	2.4-9.3
10-14 years	11,551	2	0.9	0.1-3.2
15-19 years	7735	4	1.6	0.4-4.1
20+ years	10,181	15	1.6	0.9-2.6

Cumulative incidence (%) of non-CNS SMNs after childhood CNS malignant tumor, by calendar period of 1st cancer diagnosis



- Survivors of childhood CNS cancer had an elevated risk of developing a non-CNS SMN
- Risk increased with the calendar period of CNS cancer diagnosis
- Risk was significantly higher after both glioma and embryonal malignant tumors
- Cumulative incidence within 15 years after CNS cancer for survivors' diagnosed after 1980 was more than twice the one expected in the general population
- Childhood CNS tumors still represent a therapeutic challenge. Whilst survival rates of some of the malignant varieties are still very poor, those of others have improved dramatically over the last decades, but the toll paid in terms of late consequences is still high