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Trends in survival for childhood cancer in Britain diagnosed 1971–85

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Summary Survival rates were analysed for a population-based series of over 15,000 childhood cancers registered in Great Britain during 1971–85. There were highly significant improvements ($P < 0.001$ for trend) in survival for many major diagnostic groups. Between 1971–73 and 1983–85 the actuarial 5-year survival rates increased from 37% to 70% for acute lymphoblastic leukaemia, from 4% to 26% for acute non-lymphoblastic leukaemia, from 76% to 88% for Hodgkin's disease, from 22% to 70% for non-Hodgkin's lymphoma, from 61% to 72% for astrocytoma, from 24% to 42% for medulloblastoma, from 15% to 43% for neuroblastoma, from 58% to 79% for Wilms' tumour, from 17% to 54% for osteosarcoma, from 26% to 61% for rhabdomyosarcoma, from 59% to 94% for malignant testicular germ-cell tumours and from 43% to 77% for malignant ovarian germ-cell tumours. These increases in population-based survival rates reflect the substantial advances in treatment of a wide range of childhood cancers since 1970. The two principal diagnostic groups for which there was no evidence of any trend were retinoblastoma, which already had an excellent prognosis with a 5-year survival rate of over 85%, and Ewing's sarcoma, for which the survival rate remained below 45%.

Until now, the only detailed analysis of survival rates for childhood cancer using population-based data from the whole of Great Britain was that covering children registered during 1962–70, with a brief addendum for 1971–74 (Draper *et al.*, 1982). Survival rates during the 1960s were generally low. Of the major diagnostic groups, only retinoblastoma, Hodgkin's disease, astrocytoma, craniopharyngioma and fibrosarcoma had a 5-year survival rate of over 50%. The 5-year survival rate for childhood leukaemia was only around 10% towards the end of the decade. Since then, there have been advances in the treatment of many types of childhood cancer, which might be expected to result in markedly improved survival rates. For some diagnostic groups, improvements in survival have also been shown to be associated with increased centralisation of treatment (Stiller, 1988*a*; Stiller & Draper, 1989). Survival rates have been published from population-based childhood cancer registries in two Health Regions (Craft *et al.*, 1987; Birch *et al.*, 1988) but these regions are not typical as they both have very well-established patterns of centralised treatment for childhood cancer.

In this paper we present survival rates for Britain as a whole for children diagnosed during 1971–85. The reasons for trends in the survival rates for the various diagnostic groups will be discussed. Survival rates have also been published from a few population-based registries in other countries and these will be compared with the results from Britain.

Patients and methods

The National Registry of Childhood Tumours at the Childhood Cancer Research Group (CCRG) includes children who were domiciled in England, Scotland or Wales and aged under 15 at the time of diagnosis with a malignant neoplasm or certain other types of tumour. The principal sources of ascertainment are the National Cancer Registration Schemes which cover the whole of Britain through a network of regional registries. Children have also been ascertained from local population-based childhood cancer registries in several regions, from entries to the Medical Research Council leukaemia trials and, since 1977, from the register of patients treated by members of the United Kingdom Children's Cancer Study Group (UKCCSG). The Registry also receives death certificates for all deaths occurring in Britain under the age of 20 and with a neoplasm coded as the underlying cause.

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About 5 years from diagnosis the medical records of children in the Registry are checked in order to confirm the diagnosis and obtain a brief outline of treatment and follow-up. The survivors are flagged in the National Health Service Central Registers (NHSCR) so that CCRG will be notified of any further deaths and of embarkations resulting in loss to follow-up.

The patients included in the present study are all those children in the Registry who were diagnosed during 1971–85, except that those ascertained by death certificate alone have been excluded since unregistered survivors could not have been ascertained. Some cancer registrations for 1985 have not yet been received but we believe that over 90% of cases from that year have been ascertained. A few diagnoses from 1985 have also not yet been checked, though it is very unlikely that there are many major changes still to be recorded.

The diagnoses are coded according to the International Classification of Diseases for Oncology (ICD-O). Childhood tumours occur in a wide variety of histological types, several of which are seen only very rarely in adults. A classification based mainly on primary site such as the ICD is thus inappropriate for childhood cancer. We have used the classification scheme which was developed for a recent study of international childhood cancer incidence (Parkin *et al.*, 1988). The definitions of the individual categories by ICD-O codes are given in that volume and in a paper describing the scheme (Birch & Marsden, 1987). We have modified the scheme by combining categories in a few instances. (i) The very few cases of unspecified lymphoid leukaemia in the Registry are almost certainly acute lymphoblastic leukaemia (ALL) and they have been included with ALL here. There were no cases of chronic lymphatic leukaemia. (ii) Non-Hodgkin's, Burkitt's and unspecified lymphomas have been combined. The distinction between non-Hodgkin's and Burkitt's lymphoma is hard to make in the Registry, especially for earlier years of diagnosis. It was felt that cases of unspecified lymphoma were very unlikely to be Hodgkin's disease. (iii) 'Other glioma' and miscellaneous intracranial and intraspinal neoplasms have been combined. Many of these tumours have not been histologically confirmed and the distinction between unspecified, unverified glioma and unspecified, unverified tumour seemed artificial.

There are also a few well-defined histological types which are not allocated specific codes in ICD-O. We have assigned them to categories as follows: (i) Intracranial primitive neuroectodermal tumour (PNET) is classified with medulloblastoma, group III(c). (ii) Peripheral neuroectodermal tumours have been included with other soft-tissue sarcoma, group IX(c). There were no recorded cases of neuroectodermal tumours of bone. (iii) Rhabdoid renal tumour and bone-metastasing renal tumour of childhood have both been

classified with Wilms' tumour, group V(a). (iv) Pancreaticoblastoma has been included with other malignant neoplasms, group XII.

Acute megakaryocytic leukaemia (FAB M7) has been transferred from 'other and unspecified' to acute non-lymphocytic leukaemia. Histiocytosis X, or Langerhans Cell histiocytosis, has not been included because it is not currently regarded as a cancer and furthermore ascertainment is very incomplete.

The categories used in our analyses are listed in Table I. A few of the categories of other and unspecified tumours included some well-defined sub-groups of particular interest and these have also been considered separately.

For this study, follow-up of survivors through flagging at NHSCR and the routine receipt of death certificates was virtually complete to the end of 1988.

Survival rates were calculated by standard actuarial methods. Differences between the survival curves were tested by log-rank tests and the χ^2 test for linear trends.

Results

Table I shows the total numbers of registrations analysed for each major diagnostic group together with the actuarial 5-year survival rates for children registered in the five successive triennia from 1971–73 to 1983–85 and the result of a χ^2 test for linear trend in the survival curves. While for some childhood cancers 5-year survival may be regarded as almost equivalent to cure, for others there is an appreciable risk of death for many years after diagnosis. We have therefore also calculated 10-year survival rates for children diagnosed during 1971–79 and 15-year rates for those diagnosed during 1971–73; these rates are given in Table II. Actuarial survival curves for the five triennia of diagnosis for selected diagnostic groups are shown in Figures 1–12.

Leukaemia

There was a highly significant improvement in the survival rate for ALL (Figure 1). Girls have generally had a better prognosis than boys, and children aged 2–9 also had a higher survival rate. As shown in Table III, both sexes and all age groups shared in the improvement in survival. By 1983–85 the difference in 5-year survival between the sexes had disappeared. There was a substantial number of deaths among children with ALL more than 5 years after diagnosis; the improvement in survival during the 1970s persisted until at least 10 years after diagnosis.

Survival rates for acute non-lymphocytic leukaemia (ANLL) were consistently lower than for ALL (Figure 2). There was nevertheless a significant trend towards higher rates for children diagnosed more recently, with the largest improvement occurring between 1974–76 and 1977–79. For children diagnosed before 1977 there was, however, hardly any mortality more than 4 years from diagnosis, whereas for

Table I 5-year actuarial survival rates for children diagnosed in successive 3-year periods, with result of test for trend on survival curves

Diagnostic group	*Total registrations*	*5-year survival rate (%) for years of diagnosis*					χ^2 *(1 d.f.) for trend*
		1971–73	*1974–76*	*1977–79*	*1980–82*	*1983–85*	
I *Leukaemias*							
(a), (b) Acute lymphocytic and other lymphoid leukaemias	4993	37	47	53	65	70	302.1
(c) Acute non-lymphocytic leukaemia	1052	4	7	18	20	26	53.7
(d) Chronic myeloid leukaemia	145	22	18	17	17	41	0.9
(e) Other and unspecified leukaemia	141	6	9	19	18	48	11.0
II *Lymphomas*							
(a) Hodgkin's disease	857	76	83	88	90	88	21.9
(b), (c), (d) Non-Hodgkin's, Burkitt's and unspecified lymphomas	1128	22	28	39	56	70	145.3
III *CNS and miscellaneous intracranial and intraspinal neoplasms*							
(a) Ependymoma	523	38	32	29	37	54	5.0
(b) Astrocytoma	1606	61	54	61	65	72	15.2
(c) Medulloblastoma	899	24	30	36	37	42	14.2
(d), (e) Other and misc. intracranial and intraspinal neoplasms	1380	36	40	39	47	45	4.9
IV *Sympathetic nervous system tumours*							
(a) Neuroblastoma and ganglioneuroblastoma	1106	15	19	25	37	43	104.8
V *Retinoblastoma*	504	87	88	89	86	91	0.6
VI *Renal tumours*							
(a) Wilms' tumour	1088	58	64	76	76	79	32.5
VII *Hepatic tumours*							
(a) hepatoblastoma	120	8	21	17	30	40	4.8
VIII *Malignant bone tumours*							
(a) Osteosarcoma	519	17	24	28	34	54	36.4
(c) Ewing's sarcoma	373	39	38	34	34	42	1.5
IX *Soft-tissue sarcomas*							
(a) Rhabdomyosarcoma, embryonal sarcoma and soft-tissue Ewing's tumour	769	26	40	46	48	61	47.5
(b) Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms	171	69	37	54	71	63	0.7
(c) Other soft-tissue sarcoma	236	38	46	61	54	44	3.2
X *Germ-cell, trophoblastic and other gonadal neoplasms*							
(a) Gonadal germ-cell and trophoblastic neoplasms							
(i) Testicular	144	59	63	69	84	94	14.4
(ii) Ovarian	135	43	45	74	85	77	12.3
XI *Epithelial neoplasms*							
(b) Thyroid carcinoma	76	100	100	94	100	100	0.8
(c) Nasopharyngeal carcinoma	60	67	33	75	63	60	0.2

Table II Ten and 15-year actuarial survival rates for children in successive 3-year periods

Diagnostic group	10-year survival rate (%) for years of diagnosis 1971–73	1974–76	1977–79	Fifteen year survival rate (%) 1971–73
I *Leukaemias*				
(a), (b) Acute lymphocytic and other lymphoid leukaemias	29	39	46	28
(c) Acute non-lymphocytic leukaemia	3	6	15	3
(d) Chronic myeloid leukaemia	9	5	4	6
(e) Other and unspecified leukaemia	6	9	10	6
II *Lymphomas*				
(a) Hodgkin's disease	68	77	84	66
(b), (c), (d) Non-Hodgkin's, Burkitt's and unspecified lymphomas	20	27	36	20
III *CNS and miscellaneous intracranial and intraspinal neoplasms*				
(a) Ependymoma	35	28	26	32
(b) Astrocytoma	57	51	56	54
(c) Medulloblastoma	19	26	30	16
(d), (e) Other gliomas and misc. intracranial and intraspinal neoplasms	33	36	37	32
IV *Sympathetic nervous system tumours*				
(a) Neuroblastoma and ganglioneuroblastoma	14	18	25	14
V *Retinoblastoma*	84	88	87	84
VI *Renal tumours*				
(a) Wilms' tumour	57	63	73	56
VII *Hepatic tumours*				
(a) Hepatoblastoma	8	21	17	8
VIII *Malignant bone tumours*				
(a) Osteosarcoma	15	22	26	15
(c) Ewing's sarcoma	29	32	29	28
IX *Soft-tissue sarcomas*				
(a) Rhabdomyosarcoma, embryonal sarcoma and soft-tissue Ewing's tumour	24	38	43	24
(b) Fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms	62	37	49	59
(c) Other soft-tissue sarcomas	32	46	55	32
X *Germ-cell, trophoblastic and other gonadal neoplasms*				
(a) Gonadal germ-cell and trophoblastic neoplasms				
(i) testicular	59	63	69	55
(ii) ovarian	43	45	71	43
XI *Epithelial neoplasms*				
(b) Thyroid carcinoma	93	100	94	93
(c) Nasopharyngeal carcinoma	67	27	66	67

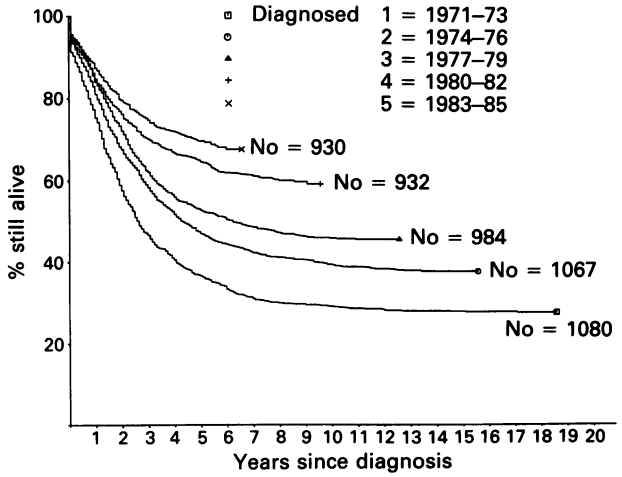

Figure 1 Actuarial survival curves for children with acute lymphocytic leukaemia diagnosed 1971–85.

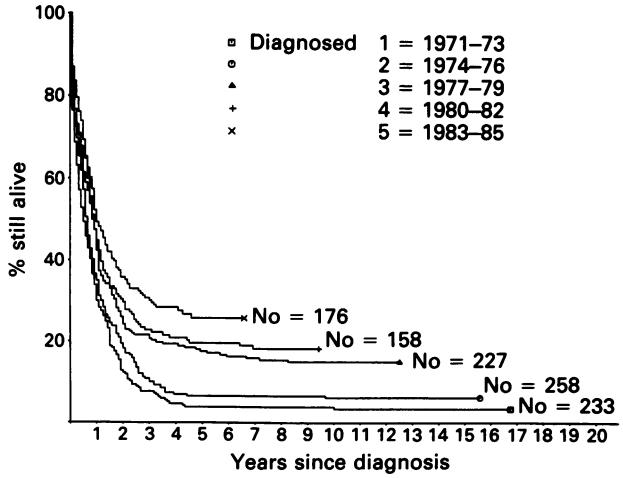

Figure 2 Actuarial survival curves for children with acute non-lymphocytic leukaemia diagnosed 1971–85.

Table III 5-year actuarial survival rates for children diagnosed as having acute lymphocytic leukaemia in successive 3-year periods

		5-year survival rate (%) for years of diagnosis					χ^2 (1d.f.)
Registrations		*1971–73*	*1974–76*	*1977–79*	*1980–82*	*1983–85*	*for trend*
(a) *Stratified by sex*							
Sex							
Male	2881	32	42	52	61	69	220.6
Female	2112	43	54	54	69	70	86.0
(b) *Stratified by age at diagnosis*							
Age							
0	151	16	0	8	35	26	8.8
1	379	33	42	52	61	63	20.5
2–4	2099	43	50	60	74	82	200.0
5–6	748	40	49	60	70	74	49.8
7–9	729	35	54	47	61	66	29.2
10–14	887	24	41	44	51	54	37.4

those diagnosed more recently a substantial risk of death persisted for at least two further years. There was little difference in prognosis between the sexes. Infants aged under 1 year had a lower survival rate but their outlook also improved during the 15 years under review.

There was no significant trend in survival rates for chronic myeloid leukaemia; around a fifth of the children survived for 5 years but the longer term survival was very low indeed.

Most of the remaining 141 children had leukaemia of unspecified cell type. There was considerable variation in the numbers registered during successive triennia. The survival rate was markedly higher for the children diagnosed most recently. There was little difference in prognosis between the sexes. As with ALL and ANLL, the rate was particularly low for infants aged under 1 year.

Lymphoma

Survival rates for Hodgkin's disease improved significantly from 75% at 5 years for children diagnosed in 1971–73 to around 90% for those diagnosed from 1977 onwards. Overall, boys had a better prognosis than girls, largely because the lymphocyte predominant subtype, which has a good prognosis, was more common in boys; however, the survival rate for girls showed a greater improvement and had slightly exceeded that for boys by 1983–85. Children aged under 5 years or 12 years and over had a worse prognosis, but the improvement in survival rates took place in all age groups. There were substantial numbers of deaths more than 5 years after diagnosis, but among 5-year survivors the risk of death during the following 5 years was halved between 1971–73 and 1977–79.

Survival rates for non-Hodgkin's lymphomas (NHL) were markedly lower than for Hodgkin's disease, but there was a very highly significant improvement over the 15-year period which was especially marked from 1977 onwards (Figure 3). Survival rates were similar for the two sexes and all age groups except for infants under 1 year of age, who had a lower survival rate. There were only 22 registrations for this age group, with no clear trend.

Central nervous system (CNS) tumours

There were significant trends in survival rates for all categories of CNS tumours. Overall, survival rates were unchanged until the mid 1970s (Figure 4). Thereafter there was a steady improvement, especially in survival rates more than a few months after diagnosis.

For ependymoma there was little change until 1983–85; children diagnosed during these years showed a substantial improvement, with a particularly pronounced reduction in mortality beyond 3 years after diagnosis.

The trend for astrocytoma was predominantly among younger children, and especially infants, though the prognosis for this age group was still worse than for older children by the end of the study period.

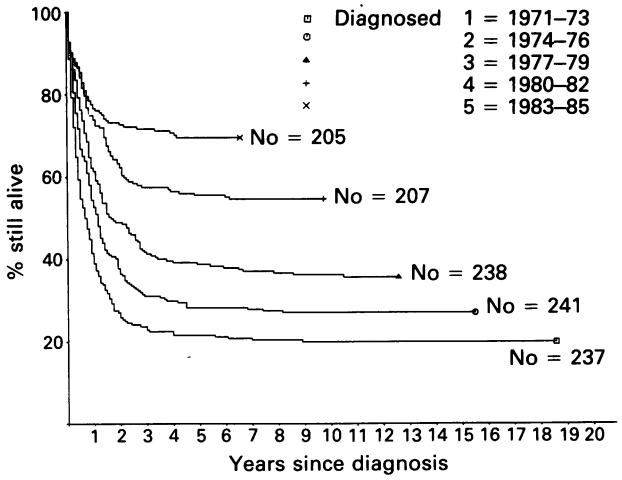

Figure 3 Actuarial survival curves for children with non-Hodgkin's, Burkitt's and unspecified lymphoma diagnosed 1971–85.

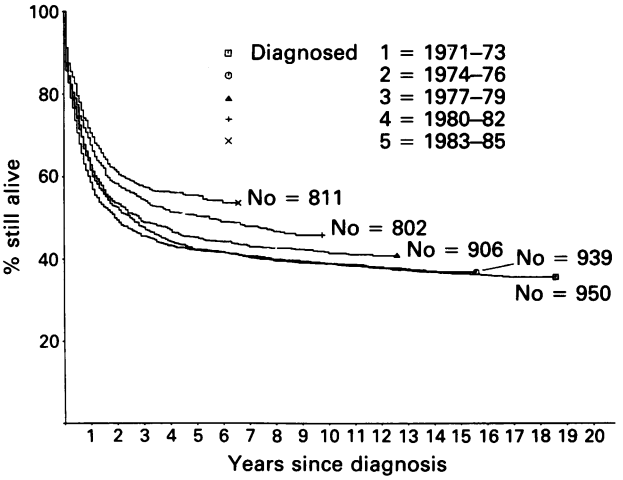

Figure 4 Actuarial survival curves for children with CNS and miscellaneous intracranial and intraspinal neoplasms diagnosed 1971–85.

Survival rates for medulloblastoma were higher among older children. The prognosis was especially poor for infants and, in contrast to older children, there was no improvement in their survival rate until 1983–85; the numbers of registrations at age under 1 year were small and the trend was not significant.

The small but significant improvement in survival for the

heterogenous category of other gliomas and miscellaneous intracranial and intraspinal tumours was confined to boys. Within this diagnostic group, there are several well-defined types of tumour. For gliomas and unspecified tumours of the brain stem, survival rates were generally low (under 20% at 5 years) and, although the prognosis had improved in the latter years of the study, the trend was not significant. The prognosis for craniopharyngioma was much better and improved further during the period under review (5-year survival rates were 89% for 1983–85 as opposed to 65% for 1971–73). For pineal tumours, although the survival rates fell in the middle years of the study, there was very little overall change: 5-year survival rates were 50% for 1971–73 and 52% for 1983–85.

Sympathetic nervous system

There was a highly significant improvement in survival rates for neuroblastoma and ganglioneuroblastoma (Figure 5), although by 1983–85 the prognosis was still poor in comparison to those for many other diagnostic groups. As shown in Table IV, the prognosis worsened with increasing age at diagnosis but there was a significant trend in survival during the study period for all age groups.

There were 22 registrations for miscellaneous other malignant tumours of the sympathetic nervous system (eight medulloepithelioma or neuroepithelioma, six olfactory tumours, four paraganglioma and four phaeochromocytoma); their 5-year survival rate was 46%.

Retinoblastoma

Survival rates were already high by 1971 and there was no further improvement during the study period.

Renal tumours

Survival rates for Wilms' tumour rose significantly, especially in the period before 1980 (Figure 6). The prognosis was significantly better for boys and children aged under 5 years. The improvement in survival rates applied to both sexes and all ages except possibly for the small number of children aged 10–14.

There were 22 registrations for renal carcinoma, with a 5-year survival rate of 55%. There were only four registrations for other and unspecified renal tumours.

Hepatic tumours

For hepatoblastoma there was a significant trend in survival rates with year of diagnosis. No deaths have been observed more than 5 years after diagnosis. There were 38 registrations for hepatocellular carcinoma. The 5-year survival rate was 13%, with no evidence of any trend. There were no registrations for other and unspecified hepatic tumours.

Malignant bone tumours

There was a highly significant increase in survival rates for osteosarcoma, with the improvement being especially marked between 1980–82 and 1983–85 (Figure 7). For Ewing's sar-

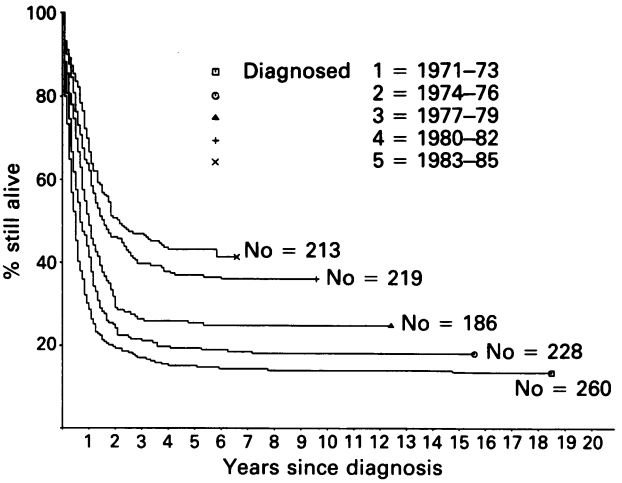

Figure 5 Actuarial survival curves for children with neuroblastoma and ganglioneuroblastoma diagnosed 1971–85.

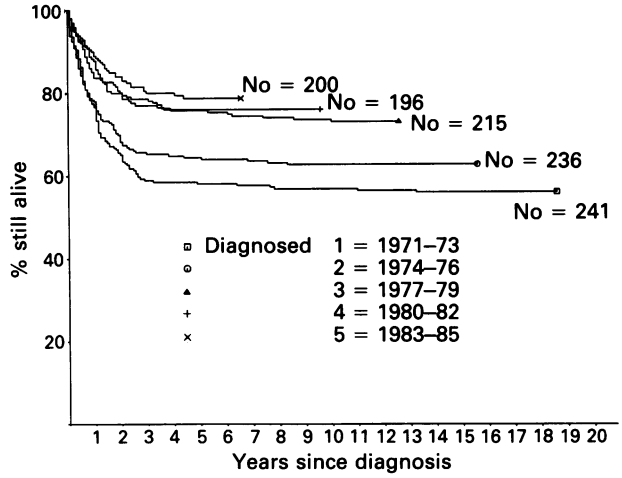

Figure 6 Actuarial survival curves for children with Wilms' tumour diagnosed 1971–85.

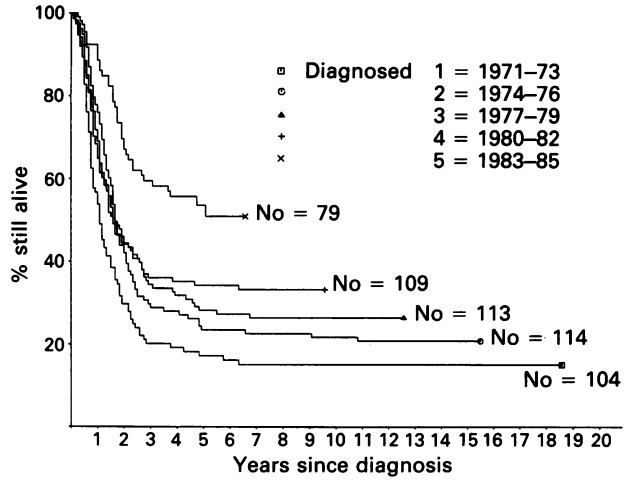

Figure 7 Actuarial survival curves for children with osteosarcoma diagnosed 1971–85.

Table IV 5-year actuarial survival rates for children with neuroblastoma, classified by age at diagnosis

Age (years)	*Total registrations*	*5-year survival rate (%) for years of diagnosis*					χ^2 *(1d.f.) for trend*
		1971–73	*1974–76*	*1977–79*	*1980–82*	*1983–85*	
0	280	30	52	56	68	77	36.6
1	183	21	15	21	31	39	10.8
2	182	7	10	18	23	28	26.8
3	133	12	11	14	13	23	8.7
4	94	6	5	0	18	25	8.7
5–9	164	8	7	15	26	24	15.5
10–14	70	7	13	19	67	44	9.7

Table V 5-year actuarial survival rates for children with rhabdomyosarcoma, classified by primary site

Primary site	Total registrations	5-year survival rate (%) for years of diagnosis					χ^2 (1d.f.) for trend
		1971–73	1974–76	1977–79	1980–82	1983–85	
Orbit	68	46	64	77	85	94	5.9
Nasopharynx	62	0	38	14	42	54	14.0
Head and neck	183	30	38	33	53	65	13.4
Upper limb	27	22	100	43	83	100	7.8
Lower limb	74	33	25	33	36	31	0.1
Bladder	56	33	38	55	46	82	4.4
Male genital	54	44	78	80	86	85	4.4
Female genital	28	17	67	100	33	88	6.7
Other pelvic	86	21	41	47	39	35	1.3
Thoracic	56	14	25	30	23	36	1.8
Other	75	16	17	13	25	52	11.5

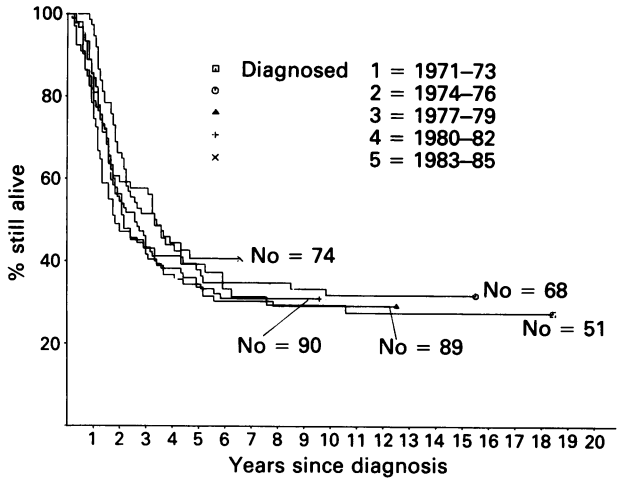

Figure 8 Actuarial survival curves for children with Ewing's sarcoma of bone diagnosed 1971–85.

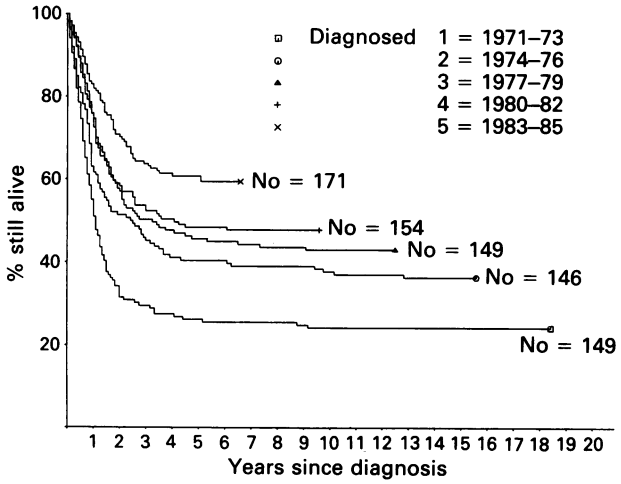

Figure 9 Actuarial survival curves for children with rhabdomyosarcoma, embryonal sarcoma and soft tissue Ewing's tumour diagnosed 1971–85.

coma (Figure 8) there was no change in survival rates, which remained between 34% and 42% at 5 years throughout the study period; there were substantial numbers of deaths beyond 5 years, and the 10-year survival rate overall was 31%. There were 22 registrations for chondrosarcoma, with a 5-year survival rate of 50%. Other bone tumours, mostly of unspecified cell type, were registered in 37 children; the 5-year survival rate was 32%.

Soft-tissue sarcomas

Rhabdomyosarcoma, the commonest childhood soft-tissue sarcoma, showed a highly significant improvement in survival (Figure 9). The survival rates for individual primary sites are shown in Table V. Significant increases were seen for all sites except the lower limbs, pelvis (non-genital) and thorax. The improvement was most marked for tumours of the nasopharynx and head and neck.

For fibrosarcoma and related tumours (mostly malignant fibrous histiocytoma and neurofibrosarcoma) there was no overall trend in survival rates (Figure 10). The 5-year survival rate for 1974–76, however, was substantially lower than those for earlier or later years of diagnosis.

There were 36 registrations for synovial sarcoma, with a 5-year survival rate of 58%. For the 24 children with liposarcoma the survival rate was 79% at 5 years, while for the 20 with leiomyosarcoma it was 55%. There were 156 children with other, mainly unspecified, soft-tissue sarcomas. Their 5-year survival rate was 40%, with no evidence of any trend.

Germ-cell, trophoblastic and other gonadal neoplasms

The patterns of occurrence of gonadal germ-cell tumours differ markedly between the sexes. Testicular tumours of childhood are predominantly yolk-sac tumours occurring at ages under 5 years, whereas ovarian tumours exhibit a wider range of histological types and have their highest incidence in the 10–14 age range. There were significant improvements in survival rates for gonadal germ-cell tumours in both boys (Figure 11) and girls (Figure 12). For testicular tumours the improvement was greatest in the age range 1–2 years, while for ovarian tumours it was most marked among girls aged

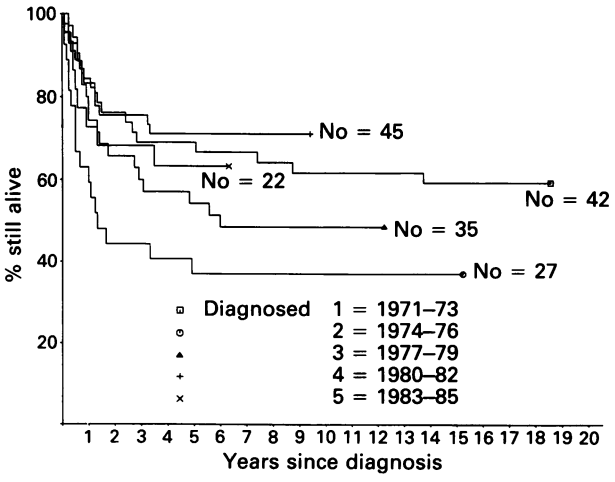

Figure 10 Actuarial survival curves for children with fibrosarcoma, neurofibrosarcoma and other fibromatous neoplasms diagnosed 1971–85.

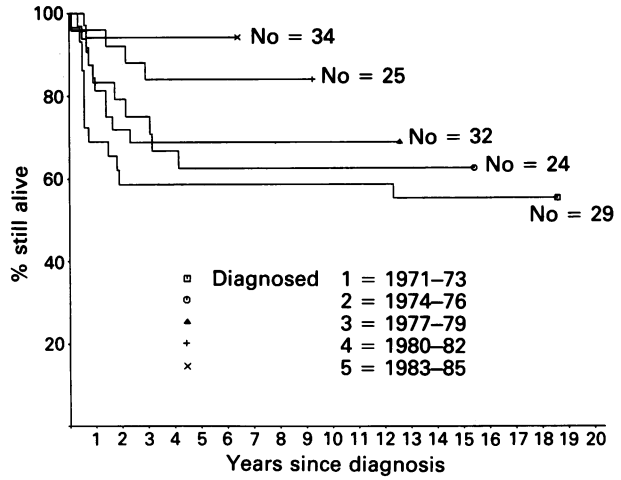

Figure 11 Actuarial survival curves for boys with malignant testicular germ-cell tumours diagnosed 1971–85.

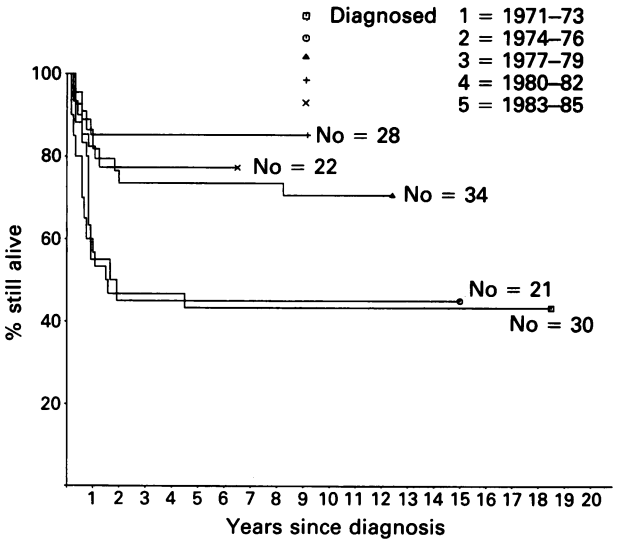

Figure 12 Actuarial survival curves for girls with malignant ovarian germ-cell tumours diagnosed 1971–85.

13–14. The trend in survival for ovarian tumours was largely attributable to a dramatic improvement occurring in girls diagnosed around 1976–77.

The most common extragonadal sites for germ-cell tumours were the CNS and the sacrococcygeal region. There was no trend in survival for the 93 children with intra-cranial tumours, but the results are difficult to interpret as the numbers of registrations increased substantially from 1977 onwards. There was a highly significant trend among the 51 children with malignant sacrococcygeal tumours ($\chi^2 = 18.0$ on 1 d.f., $P < 0.0001$), with 5-year survival rates improving from 10% in 1971–73 to 100% in 1983–85. No other sites for germ-cell tumours had sufficient numbers for analysis.

There were only 5 boys and 12 girls with gonadal carcinoma and one boy and 10 girls with other malignant gonadal tumours.

Epithelial neoplasms

Survival rates for thyroid carcinoma were uniformly high. Nasopharyngeal carcinoma had a lower survival rate but there was no sign of a trend; the unusually low 5-year survival rate of 33% for patients with this tumour diagnosed in 1974–76 was based on only 15 registrations. The 5-year survival rate for the 37 children with adrenocortical carcinoma was 19%, with little evidence for any trend. Among the 94 registered cases of skin carcinoma, only one death has been recorded. The only other carcinomas occurring in substantial numbers were those of miscellaneous other sites in the head and neck. There were 45 registrations, predominantly for tumours of the salivary glands. The 5-year survival rate was 79%, and no later deaths have so far been recorded.

Survival rates for malignant melanoma were not calculated as the diagnosis has yet to be verified in a large proportion of cases.

Discussion

Over the 15-year period covered by this study there were substantial, statistically significant improvements in the prognosis for most diagnostic groups, encompassing the great majority of cases of childhood malignant disease.

For most diagnostic groups there are few comparable data from large population-based registries in other countries. The largest series outside Britain is that of the United States SEER Program for children diagnosed during 1973–81 (Young *et al.*, 1986). In Table VI, 5-year survival rates for several diagnostic groups from that series are compared with those from the present study.

For children with ALL, the most common childhood cancer, the probability of surviving 5 years from diagnosis almost doubled between the early 1970s and mid 1980s. The data relating to ALL have been discussed in more detail elsewhere (Stiller & Draper, 1989). Over half of the children treated during the study period were entered in the Medical Research Council UKALL trials. Within the trials there was little increase in survival rates during the 1970s, but a substantial improvement occurred during the 1980s (MRC, 1986*a*). The continuing improvement in the national series throughout 1971–85 is attributable to an increase in the proportion of children with ALL who were entered in the trials or treated at hospitals seeing large numbers of children with this disease (Stiller & Draper, 1989).

Survival rates during the 1970s were somewhat lower than those observed in the United States; the 5-year survival rate in the SEER Program was 59%, while for New York State during 1973–78 the corresponding figure was 55% (Poledna k, 1986). More recently, however, results in Britain have been similar to those in other countries. Whites in the SEER Program had a 3-year survival rate of 77% during 1981–84 (Steinhorn & Gloeckler Ries, 1988). In the Nordic countries children diagnosed during 1981–85 had an actuarial survival rate of 65% at 4½ years from diagnosis after the exclusion of the small, poor-prognosis subgroups of children with B-cell ALL and infants aged under 1 year (Gustafsson *et al.*, 1987). In a large clinical trial series comprising more than half the children with ALL in Italy during 1976–86, again omitting B-cell ALL and infants as well as children with CNS involvement at diagnosis, the 5-year survival rate was 65% (Paolucci *et al.*, 1989).

Table VI 5-year survival rates (%) for childhood cancer in Britain and the United States, 1973–81

	Britain (present study)	*United States (Young et al., 1986)*
Leukaemia	43	51
ALL	51	59
ANLL	12	20
Hodgkin's disease	86	84
NHL	36	51
Ependymoma	30	32
Astrocytoma	60	66
Medulloblastoma	33	41
Neuroblastoma[a]	24	50
Retinoblastoma	87	88
Renal tumours	70	76
Osteosarcoma	27	43
Ewing's sarcoma	36	48
Rhabdomyosarcoma[b]	42	54

[a]US data may include up to two cases of paraganglioma. [b]US data exclude embryonal sarcoma.

In many large series, boys with ALL have been found to have a worse prognosis than girls (Miller *et al.*, 1983; Steinhorn & Gloeckler Ries, 1988; Gustafsson *et al.*, 1987). This difference between the sexes was also observed in our data until the most recent period; there had been a proportionately greater improvement in survival rates for boys so that by 1983–85 there was little difference between the sexes in the proportions surviving 5 years. It has previously been reported that the influence of sex on survival is greatest during the first 15 months of complete remission but that boys also suffer an excess of late relapses (Sather *et al.*, 1981). In the present series there was relatively little difference between the sexes in the 1-year and 2-year survival rates. The difference between the sexes in longer-term survival has, however, persisted: among children diagnosed during 1980–82 who had survived 5 years, the mortality during the next 4 years was 10% for boys but only 4% for girls. The outlook for very young children aged under 2 with ALL, and especially for infants diagnosed before the first birthday, has always been poor (Cangir *et al.*, 1975; Miller *et al.*, 1983; Leiper & Chessells, 1986). Although the relatively low survival rates for this age group persisted throughout the study period, they did nevertheless show some improvement. This improvement in survival with more intensive treatment has also been reported from clinical studies (Reaman *et al.*, 1987). Since 1981 the UKALL trials have included larger numbers of very young children, who thus now receive more intensive chemotherapy than they did formerly, though with CNS irradiation postponed until age 2.

Survival has been considerably lower among children with ANLL, although there have been improvements, particularly since the mid 1970s. Children with ANLL who were treated at non-teaching hospitals during 1977–84 had a lower survival rate (Stiller, 1988*a*) and it is likely that the trend towards treatment in specialist centres with widening availability of bone marrow transplantation has contributed to the improved survival rate nationally. Five-year survival rates in the United States SEER registries were substantially higher than in Britain for both 1973–76 (19%) and 1977–80 (25%) (Steinhorn & Gloeckler Ries, 1988).

Hodgkin's disease already had a relatively good prognosis by 1971, and a significant further improvement has since taken place. The survival rate nationally was slightly less than the 94% at 5 years reported from two large oncology centres during 1974–82 (Robinson *et al.*, 1984). During 1970–84, 68 children with Hodgkin's disease were included in the British National Lymphoma Investigation, a study in which most of the patients are adults; the 5-year survival rate for those children was 87% (Makepeace *et al.*, 1987), very similar to that nationally. Survival rates in Britain during 1973–81 were similar to those in the United States (Table VI).

Clinical studies of childhood NHL, have been conducted in Britain by the UKCCSG since 1977 (Mott *et al.*, 1984*a*,*b*). The most marked improvement in the prognosis for NHL occurred from that date onwards. Since survival rates at hospitals outside the UKCCSG have lagged behind those at paediatric oncology centres (Stiller, 1988*a*), much of this improvement can be ascribed to the UKCCSG studies. The survival rate during the 1970s was markedly lower than in the United States (Table VI).

The increase in survival rates from medulloblastoma between 1971 and 1977 has been reported previously (Stiller & Lennox, 1983), and was attributed to improvements in post operative survival and increase in doses of radiotherapy. The trend in survival rates since 1977 has been more modest. The survival rates in the national series are appreciably lower than those reported from large clinical trials (Allen *et al.*, 1986) but the trials did not include patients who died without undergoing surgery or post-operatively. The population-based survival rate was, however, also lower in Britain than in the United States (Table VI) for medulloblastoma. For ependymoma and astrocytoma, rates in the two countries were very similar.

Compared with other diagnostic groups there was an unusually high mortality many years after diagnosis for patients with CNS tumours, with no sign of a plateau in the survival curves. Of the 52 deaths so far recorded among 10-year survivors, death certificates indicated that 36 (71%) were due to recurrent tumour, four (8%) to a second neoplasm and 11 (22%) to other causes. These proportions are very similar to those found among 112 deaths occurring 10–19 years after diagnosis in childen who had CNS tumours diagnosed before 1971 (Hawkins *et al.*, 1990); the causes of death, determined from medical records, were recurrent tumour in 82 (73%), second neoplasm in six (5%) and other causes in 24 (21%).

Survival rates for children with neuroblastoma were still low in comparison with most other childhood cancers by 1983–85, despite the substantial improvements which had taken place, especially since 1980. This was a time which saw intensive research into treatment for neuroblastoma using different combinations of cytotoxic drugs with, in some instances, radiotherapy and/or high dose chemotherapy with autologous bone marrow rescue (Pinkerton, 1990), but no survival rates have been published from these studies for all stages combined. The increase in survival rates nationally might be attributable in part to a rise in the proportion of early stage tumours but this could not be checked in the Registry data. The 2-year survival rate of 32% in Denmark during 1970–80 (Carlsen *et al.*, 1986) was somewhat better than the 24% in Britain during 1971–79, but 5-year survival in the United States was appreciably higher than in either country (Table VI).

Survival rates for retinoblastoma were very high throughout the period and have been documented in greater detail elsewhere (Sanders *et al.*, 1988). The continuing mortality at more than 5 years after diagnosis is due largely to the occurrence of second primary tumours in survivors of bilateral retinoblastoma (Draper *et al.*, 1986; Hawkins, 1989).

Survival rates for Wilms' tumour showed a substantial improvement, particularly in the earlier part of the study period. Throughout 1971–85 there has been a succession of clinical trials and studies of Wilms' tumour in Britain, organised at first by the MRC (MRC, 1978; Morris Jones *et al.*, 1983) In the early 1970s, children included in the first MRC trial had a higher survival rate than eligible children who were not included (Lennox *et al.*, 1979). The category of Wilms' tumour in our series included children with bone-metastasising renal tumour of childhood (BMRTC) and rhabdoid renal tumour. We have identified 25 cases of BMRTC during the study period, nearly all of them from national clinical studies. The 3-year survival rate was 68% overall, and 91% for the 11 children diagnosed during 1980 onwards. These survival rates may well be over estimated as there could have been other, unidentified children with BMRTC outside the trials who may have died. Nevertheless, it is clear that this tumour, which originally had a very poor prognosis, is now eminently treatable. We have also recorded 14 cases of rhabdoid tumour, all but one of them diagnosed during 1979 or later. The survival rate 1 year after diagnosis was only 21%, and only one child has so far survived more than 5 years. This very grave prognosis is similar to that observed in the principal clinical trials (Weeks *et al.*, 1989).

The large increase in survival rates for osteosarcoma during the most recent triennium has been reported previously (Stiller, 1988*b*). The present results, based on a larger number of patients and an extended period of follow-up, confirm the trend noted in that preliminary report. The improvement in prognosis during 1981 onwards was attributable to the much greater improvement for children who were treated at paediatric oncology centres (Stiller, 1988*a*). Some children were entered in clinical trials organised by the Medical Research Council during 1975–81 (MRC, 1986*b*) and EORTC-SIOP during 1978–83 (Burgers *et al.*, 1988). Survival rates for children were not reported separately in either study. In the earlier trial, the 5-year survival rate was 27%, with no significant variation by age; in the latter, where children were stated to have a lower survival rate than adults, the rate for all ages combined was 43%. Thus the 5-year

rates for children in both studies were probably similar to the 25–35% in the present series during the same period. In comparison with the United States (Table VI), however, the survival for childhood osteosarcoma in Britain during the 1970s was poor.

The combination of a 5-year survival rate well under 50% and no increase in survival rates during the study period which was found in Ewing's sarcoma occurred for no other diagnostic group. Higher survival rates have been reported for clinical series in Britain (Graham-Pole, 1979). Population-based survival rates in the United States were also somewhat higher than in Britain (Table VI).

The increase in survival rates for rhabdomyosarcoma took place concurrently with large clinical trials in Europe and the United States in which various combinations of chemotherapy and radiotherapy were evaluated. The 5-year survival rates reported here were nevertheless appreciably lower than the 55% in the Intergroup Rhabdomyosarcoma Study (IRS)-I which was open during 1972–78 (Maurer *et al.*, 1988*a*), the 52% in the SIOP trial of 1975–82 (Rodary *et al.*, 1988) and the 62% in IRS-II of 1978–84 (Maurer *et al.*, 1988*b*). The American population-based survival rate was also higher than that in Britain (Table V), but very similar to those in IRS-I (Maurer *et al.*, 1988*a*). The 5-year survival rate for children treated at two large oncology centres in Britain during 1974–81 was 58% (Kingston *et al.*, 1983), higher than in the present series but similar to the American results (Table VI). The variation in survival rate between primary sites, with the best prognosis for tumours of the orbit and the genitourinary sites, was similar to that found in IRS-I and the SIOP trial (Maurer *et al.*, 1988*a*; Rodary *et al.*, 1988).

The improvements in survival for germ-cell tumours were the result of the use of increasingly effective chemotherapy regimes. The role of chemotherapy in ovarian tumours during the first half of the study period has been previously described (La Vecchia *et al.*, 1983). The improvements in more recent years were parallel with those in the UKCCSG germ-cell tumour studies (Mann *et al.*, 1989), in which many of the children analysed here were entered.

A detailed study of children with carcinomas diagnosed during 1971–80 has recently been published (McWhirter *et al.*, 1989). Carcinoma of the thyroid already had an excellent prognosis. The second most common site was the nasopharynx; there was no sign of any increase in survival rates, despite the recently reported improvement in prognosis for children treated with adjuvant chemotherapy in conjunction with radiotherapy (Roper *et al.*, 1986).

The improvements in survival rates for nearly all diagnostic groups described above took place during a period when increasing numbers of chilren were treated at specialist centres participating in national and international clinical trials and studies. It is hoped that this centralisation of care will provide the opportunity for further improvements in the prognosis for many childhood cancers.

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