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Review

The United Kingdom Children's Cancer Study Group—the First 20 Years of Growth and Development

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THE LATE 1960s and early 1970s were a time of rapid progress in the treatment of childhood cancer, particularly in North America and Western Europe. The impact of multicentre clinical trials run by the Children's Cancer Study Group (CCSG, now CCG) and Pediatric Oncology Group (POG) in the U.S. disseminated widely the benefits of the treatment advances pioneered in some of the individual major cancer centres. In Europe, the International Society of Paediatric Oncology (SIOP) drew together researchers from the main centres in the same way and provided an annual forum to update results from their own trials and the major U.S. trials, in particular those of the Intergroup (Wilms', rhabdomyosarcoma, Ewing's) studies. Young investigators interested in paediatric malignancy were able to use the contacts made within SIOP to arrange training opportunities across international boundaries and on their return to their home institution invigorated them with new ways of thinking about old problems. In the U.K. a few multicentre clinical trials took place under the auspices of the Medical Research Council (for leukaemias, Wilms' tumour and osteosarcoma) and some major centres contributed actively to SIOP trials on rhabdomyosarcoma and medulloblastoma. However, it became increasingly apparent that a new national organisation was required if children nationwide were going to benefit promptly from the advances being made.

On 14 January 1977, a meeting was held in the Birmingham Children's Hospital at which 14 members from 7 paediatric oncology units agreed to form the UKCCSG. This core group, which was augmented by invited representatives of 6 other units, was multidisciplinary and included paediatric oncologists, haematologists, surgeons, radiotherapists and pathologists. Half of its original members are still active participants of the group 20 years later. The membership of the UKCCSG now totals 220 full and associate members, 20 affiliates (consultants in shared care centres), 24 corresponding (overseas), 6 honorary and 17 junior members (trainees).

At that inaugural meeting, the aims of the group were agreed to include the establishment of cooperative groups and studies and the collection of epidemiological data with the formation of a tumour registry. The initial constitution included in its objectives the advancement of the study and knowledge of childhood cancer and the promotion and publication of collaborative research.

In the 20 years from 1977–1996, the group has grown to encompass 22 regional centres in the U.K. and Ireland and has registered more than 20 000 patients (Figure 1). A national Data Centre has been established in Leicester to handle these registrations and to service the clinical trials. Copies of the registration data are passed to the Childhood Cancer Research Group, which links them with the National Register of Childhood Tumours (NRCT), and also carries out an annual follow-up of patients who are not in UKCCSG studies. Data from the NRCT show that the percentage of children with malignant disease in the U.K. registered by the group has risen from 53% in the years 1977–1980 to 81% in the years 1993–1995 (Table 1), with several regions achieving more than 90% registration of all children with malignancy in their regions. These figures show a consistent though diminishing under-representation of teenagers and children with brain tumours when compared with the overall national data (Table 2).

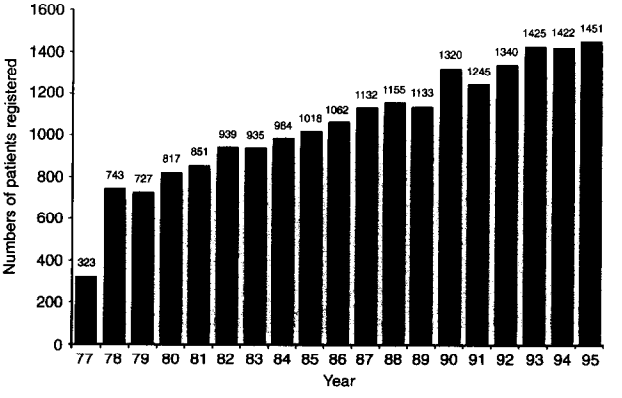

Figure 1. UKCCSG registrations per year for children aged under 15 years.

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Table 1. Percentage of children with malignant neoplasms registered with UKCCSG, 1977–1995, by age and year of diagnosis

Age at diagnosis (years)	Year				
	1977–80	1981–84	1985–88	1989–92	1993–95
0–9	57	70	77	81	85
10–12	49	62	64	66	74
13–14	32	41	47	55	58
Total	53	64	71	76	81

Table 2. Percentage of children with malignant neoplasms by diagnostic group and period of diagnosis registered with UKCCSG 1977–1995

Diagnostic group	Year				
	1977–80	1981–84	1985–88	1989–92	1993–95
Leukaemia	64	77	84	87	88
Lymphoma	64	75	81	85	84
CNS	31	36	43	56	73
Sympathetic nervous system	72	89	91	94	91
Retinoblastoma	10	35	76	90	88
Renal tumours	68	88	93	92	89
Hepatic tumours	61	70	81	82	90
Bone tumours	44	57	63	68	80
Soft tissue sarcomas	58	79	81	85	84
Germ cell and gonadal	48	53	69	72	83
Epithelial	27	27	18	18	22
Other		47	35	8	27
Total	53	64	71	76	81

Registry data (Figure 2 and Table 3) show a steady and consistent improvement in the overall survival of successive cohorts of children with an average improvement in 5-year survival rates of approximately 1% per annum for the 20-year period. The improvements in survival for individual tumour groups have been detailed in the published reports (see selected list of publications [1–38]) of the numerous randomised trials and non-randomised studies (Table 4) undertaken by the group often in association with other organisations e.g. SIOP, EORTC, ENSG, CESS, SFOP, CCG; these include the leukaemia trials undertaken under the auspices of the Medical Research Council. This trend for improved survival is reflected in population-based surveys [1]. Also, several studies have shown a survival advantage for children treated at specialist centres or entered in national trials in the U.K. [1, 3, 6]. Overtreatment with attendant increased risk of late effects has been shown to occur at non-specialist centres [22].

Table 3. Three-year actuarial survival rates for UKCCSG patients (%)

Tumour type	1977–81	1982–86	1987–90	1991–94	x^2 (1df) for trend
ALL	66	76	81	88	171.0
ANLL	22	35	45	58	75.4‡
Hodgkin's	92	94	93	98	4.49*
NHL	56	73	77	78	33.3‡
Neuroblastoma	33	46	49	54	27.2‡
Nephroblastoma	83	84	86	81	0.09
Hepatoblastoma	32	46	40	73	10.9‡
Osteosarcoma	43	59	63	64	9.55†
Ewing's sarcoma	46	55	72	71	13.5‡
Rhabdomyosarcoma	57	61	66	68	6.81†
Gonadal germ cell	85	94	97	98	6.13‡

*$P < 0.05$; †$P < 0.01$; ‡$P < 0.001$

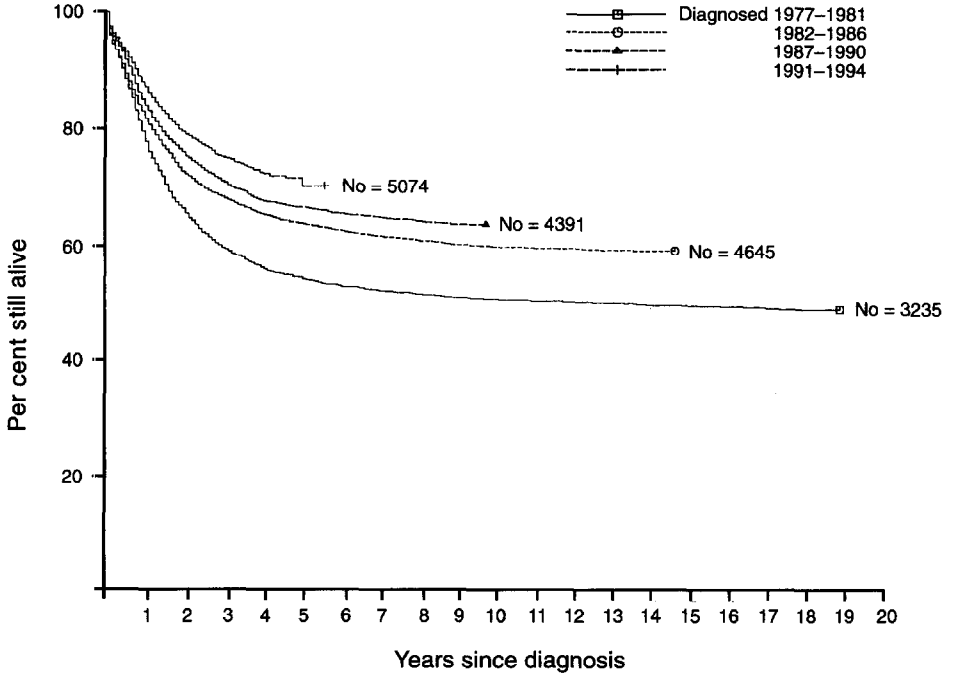

Figure 2. Survival of UKCCSG patients, 1977–1994.

Table 4. UKCCSG studies

Bone	
ET 7802	(ET - 1)
ET 8701	(ET - 2)
ET 9302*	(EICESS 92 MRC/UKCCSG/CESS)
OS 8302	(MRC/UKCCSG 80831)
OS 8602	(MRC/UKCCCSG 80861)
OS 8803	(MRC/UKCCSG/EORTC 80862)
OS 8804*	(MRC/UKCCSG/EORTC 80871)
OS 9303*	(MRC/UKCCSG 80931)
Brain	
CNS 7801	(First brain study)
CNS 8402	(SIOP Medullo)
CNS 8905	(Astrocytoma) (BT - 2)
CNS 8906	(Brain stem glioma) (BT - 3)
CNS 9006*	(Brain stem glioma)
CNS 9102*	PNET - 3
CNS 9204*	Infant brain tumours
CNS 9501*	High-grade astrocytoma
Germ cell	
GC 7901	(GC - 1)
GC 8901*	(GC - 2)
Histiocytoses	
LCH 9103	Langerhans cell histiocytosis (LCHI)
HLH 9505*	Haemophagocytic lymphohistiocytosis
LCH 9605*	Langerhans cell histiocytosis (LCHII)
Hodgkin's	
HD 8201	(HD - 1)
HD 9201*	(HD - 2)
Late effects	
LEG 9008	(Pregnancy and offspring)
LEG 9202	Ifosfamide toxicity
Liver	
LT 8907	(SIOPEL - 1)
LT 9510*	SIOPEL 2 Pilot
New agents	
NAG 8702	(NAG - I Carboplatin) (Not neuroblastoma)
NAG 8801	(MIBG) (NAG - 2)
NAG 8802	(VP - 16 for Wilms') (NAG - 3)
NAG 9007	(GM-CSF) (NAG - 5)
NAG 9009	(Targetting NHL/ALL) (NAG - 6)
NAG 9010	(Targetting monoclonal relapsed Medullo/PNET) (NAG - 7)
NAG 9203	(Etoposide) (NAG - 8)
NAG 9012	(Thiotepa) (NAG - 4)
NAG 9401	(Temozolomide) (NAG - 9)
NAG 9402*	(Carboplatin pharmacokinetics) (NAG - 10)
NAG 9504*	(Thiotepa Phase II) (NAG - 11)
NAG 9509*	(AG 337) (NAG - 12)
NHL	
NHL 7701	(NHL - 1)
NHL 8501	(NHL - 2 low stage)
NHL 8502	(NHL - 2 macho)
NHL 8503	(NHL - 2 T cell)
NHL 9001	(low stage)
NHL 9002	(advanced B cell–CNS)
NHL 9003	(advanced B cell + CNS)
NHL 9004	(T cell)
NHL 9404*	(LPD) Lymphoproliferative disease
NHL 9503*	(T cell)
NHL 9601*	(B cell - Group A)
NHL 9602*	(B cell - Group B)
NHL 9603*	(B cell - Group C, CNS –ve)
NHL 9603	(CNS)* (B cell - Group C, CNS +ve)
Neuroblastoma	
NB 8202	(ENSG - 1)
NB 8403	(ENSG - 2)
NB 8504	(ENSG 3a)
NB 8505	(ENSG 3b)
NB 8506	(ENSG 3c)
NB 8904*	(ENSG 4) (Retinoic acid)
NB 9011*	(ENSG 5)
NB 9205*	(ENSG 8) (Infant neuro)
NB 9301	(ENSG 6) (Stage 2b/3 pilot)
NB 9304	(ENSG 7) (Stage1/2A)
NB 9305*	Tyrosine hydroxylase
NB 9502*	(ENSG 9) (Stage 2B/3)
NB 9506*	LNESG (Low stage neuroblastoma)
NB 9508*	mIBG in neuroblastoma (pilot)
NB 9604*	Constitutional karyotype analysis
Soft tissue sarcoma	
STS 8102	(IRS II)
STS 8401	(IRS III)
STS 8902	(SIOP MMT - 89)
STS 8903	(European Stage IV)
STS 9507*	(SIOP MMT - 95)
Supportive care	
SC 9403	(Central venous catheter)
SC 9606*	(Central venous catheter—mechanical problems)
Wilms'	
WT 7702	(MRC)
WT 8001	(WT - 1)
WT 8601	(WT - 2)
WT 9101*	(WT - 3)
Other	
ALL 8101	(Relapsed ALL)
ALL 8301	(Relapsed ALL)

*Studies currently open.

As well as undertaking many clinical trials resulting in improved survival rates as outlined above, the UKCCSG has been active in a number of other areas. The group has fostered laboratory research activity within many of the centres and has facilitated the sharing of ideas and biological samples, and collaboration with scientists, thereby advancing knowledge of the biology and behaviour of tumours (see selected list of publications [1–38]). The UKCCSG has also facilitated the national epidemiological study of childhood cancers, the U.K. Childhood Cancer Case-Control Study, which has recruited 1500 cases of acute lymphoblastic leukaemia and 2300 cases of other cancers. In addition, the UKCCSG has held annual scientific meetings where young clinicians and scientists have described their work and competed for the McElwain Prize, given in memory of one of our distinguished members, the late Professor Tim McElwain.

The UKCCSG has worked hard to establish paediatric oncology as a recognised specialty in the U.K. with an appropriate training programme, adequate numbers and quality of training posts and a career structure. This involved gaining the support of the British Paediatric Association, the British Association of Paediatric Surgeons and the Royal College of Physicians [39,40] and discussions with the Department of Health. Representatives of the UKCCSG also contributed to the recommendations of the SIOP Committee on Standards of Care and Training in Paediatric Oncology [41]. The UKCCSG remains deeply involved in the training of paediatric oncologists through its Education and Training Committee, which has recently drawn up for the Royal College of Paediatrics and Child Health revisions to the Training Programme in accordance with the recommendations of the Calman report [42] and has prepared in draft form a curriculum record ('log book') for trainees.

It has also been necessary for the UKCCSG to provide evidence to support requests around the nation for better funding, staffing and other facilities for the care of children with cancer [39,43] and this has led to considerable improvements, although many centres still have to rely on substantial help from charitable sources.

The UKCCSG is now looking forward to building on the progress of the last 20 years. Our priorities will be to try to achieve 'cure for all' at the least possible cost to the patients in terms of both immediate and late toxicity and to increase our understanding of the causes, prevention and biological behaviour of childhood cancers. It is likely that progress in research will be hastened by increasing the trend towards international collaboration. At the same time the provision of high standards of care of all children with cancer in the U.K. must be maintained and appropriate facilities must be provided for all adolescents as well. We look forward to the 21st century with confidence.

This is a selection of UKCCSG publications; the full list is available from the UKCCSG Data Centre, University of Leicester, Department of Epidemiology and Public Health, 22-28 Princess Road West, Leicester LW1 6TP, U.K., on request.

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