

**Department of Health (DH) Policy Research Programme (PRP):
Final report on current 5 year Unit Contract 2006-2010**

From the

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Unit contract held by Dr MFG Murphy, Consultant Epidemiologist and CCRG Director, University of Oxford, Department of Paediatrics, in conjunction with the other principal researcher in the CCRG, Mr Charles Stiller, Director of the National Registry of Childhood Tumours (NRCT) housed within the CCRG

Programme Start Date: 01/01/06 to 31/12/07. Extended with variation to contract 01/01/08 to 31/12/10. Further extension with 4 months variation to contract from 01/01/11 – 30/04/11 inclusive

Budget

2006-07	£1,241,018
2008-10	£2,036,294
2011	£165,596

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Abbreviations/Acronyms

ART	Assisted Reproduction Technology
BTEC	Brain Tumor Epidemiology Consortium
CCLG	Children's Cancer and Leukaemia Group
CCRG	Childhood Cancer Research Group
CHECT	Childhood Eye Cancer Trust
CLIC	Childhood Leukaemia International Consortium
COMARE	Committee on Medical Aspects of Radiation in the Environment
CNS	Central nervous system
CRUK	Cancer Research UK
CTYA	Children and Teenagers/Young Adults
CwL	Children with Leukaemia
DBS	Dried Blood Spots
DH	Department of Health
ECRIC	Eastern Cancer Registry and Information Centre
EMF	Electromagnetic fields
HES	Hospital Episode Statistics
HFEA	Human Fertilisation and Embryology Authority
HPA	Health Protection Agency
IACR	International Association of Cancer Registries
IGF	Intrauterine growth factors
ISET	International Study of non-CNS Embryonal Tumours
JAMA	Journal of the American Medical Association
NACCPO	National Alliance of Childhood Cancer Parent Organisations
NCIN	National Cancer Intelligence Network
NRCT	National Registry of Childhood Tumours
NWCIS	North West Cancer Intelligence Service
PBC	Paediatric Blood and Cancer
PRP	Policy Research Programme
RCPCH	Royal College of Paediatrics and Child Health
RPR	Radiation Protection Research
SES	Socioeconomic status
SIOP	International Society of Paediatric Oncology
SSCRG	Site Specific Clinical Reference Group
TYA	Teenage Young Adult
UKACR	United Kingdom Association of Cancer Registries

CCRG Staff members in Post between 2006-10

Funded by DH (in whole or in part)

Anita Bayne
Pat Brownbill (left 2007)
Kathryn Bunch
Nicole Diggins
Liz Eatock
Jackie Gerenscer
Elaine Kemp
Janette King
Martin King
Mary Kroll
Angela MacCarthy
Michael Murphy
Karen O'Brien
Jane Passmore
Anita Rich (left 2007)
Anita Sabin (left 2007)
Charles Stiller
Tim Vincent
Jean Williams (left 2008)

Funded wholly from other sources

Tom Keegan 2007-09, Children with Leukaemia (CwL)
Kate O'Neil 2010 – current, Daphne Jackson Fellowship
Anjali Shah 2009 – current, CwL Fellowship

Additional external funding awarded during 2006-10

CwL Programme Grant	to 2012
DH Radiation Protection Research Grant (RX123)	to 2011
Scottish Executive annual allocation	to 2011
National Cancer Intelligence Network (NCIN) comorbidity grant	to 2012
CwL International Study of non-CNS Embryonal Tumours (ISET) Pilot study	to 2012
CwL Retinoblastoma study	to 2013
Cancer Research UK (CRUK) Human Fertilisation and Embryology Authority (HFEA)/NRCT linkage study	to 2012

Plain English/lay summary

The report describes the objectives and achievements of the Childhood Cancer Research Group (CCRG) over the five year period 2006-10. The CCRG is part of the University of Oxford Department of Paediatrics and houses the National Registry of Childhood Tumours (NRCT). The NRCT aims to collect a restricted set of data on every child normally resident in the UK at the time of their diagnosis under 15 years of age, with any type of malignancy or central nervous system tumour (whether malignant, benign or whose behaviour as a tumour is uncertain). The NRCT is one of the most important and longstanding specialist childhood cancer registries in the world. Use of the data it holds forms the basis of much of the CCRG's research, as well as widespread dissemination to professional organisations and the general public of childhood cancer intelligence for the UK and constituent countries. It is the lead organisation for these purposes in the UK. It provides data that helps to improve further the impact that the organisation and provision of clinical services for children with every type of cancer have on the outcomes of treatment for them and their families, and researches the causes of childhood cancer that may be preventable or reducible.

The most recent 5 year Programme has:

- Allowed an annual assessment of the incident cancer burden and improvement in survival for every type of childhood tumour. The pattern of occurrence of secondary primary tumours following initial treatment has also been assessed in a major collaboration for surviving children registered on the NRCT prior to the 1990s. We participated in a Europe wide comparison of childhood cancer outcomes in different countries, identifying how well the UK was then performing.
- Allowed studies demonstrating important relationships between growth in the womb and risks of many (but by no means all) childhood cancers, which we will develop further. Studies of risks associated with occupational exposures to which the child's father may be subject have been more or less uniformly negative. However we have demonstrated relatively consistent relationships of risk of a variety of tumours with the socioeconomic status of the family.
- Allowed studies of the ways in which exposures to common infections may be implicated in increasing risk of a number of different childhood tumours, reinforcing the belief that the pattern of such exposure may be important.
- Allowed studies of risk of childhood tumours (in particular leukaemia) in relation to possible exposure to ionising radiation (natural environmental, medical exposure or that might be released from nuclear installations) and non-ionising radiation (namely very low frequency electromagnetic fields of the type that are produced by the distribution networks supplying electricity to domestic addresses). We have found some evidence that exposure to medical treatments and natural environmental sources of ionising radiation may be important, but not that risk is raised by possible exposures from nuclear installations, or from overhead powerlines supplying electricity to homes.

Brief executive summary of the Unit's work programme

Oversight/funding

The most recent quinquennial review of the CCRG took place in 2004. Continued Policy Research Programme (PRP) funding was agreed initially for 2006 and 2007, and subsequently to the end of 2010. A further extension was granted for the first 4 months of 2011. During these discussions a separation of the CCRG's functions was defined into (a) childhood cancer registration, descriptive epidemiology and the production of national intelligence (UK wide) about childhood cancer (b) related research (based on the NRCT) together with additional analytical research into childhood cancer causes. The separate funding basis for each of these two strands became increasingly well defined, though overlap remains, and they remain interlinked.

Objectives

The CCRG's objectives have always been:

- to provide information, analysis and the basis for further research into how to improve the impact clinical services for children with cancer in the UK and Ireland have on outcomes.
- to provide analysis of routinely available data, and data available from special studies for which the NRCT may provide the basic childhood cancer registration data, in order to provide insight into the causes of childhood cancer which may be preventable or reducible.

Programme

The research programme has consisted of investigations in 4 main areas:

- The efficient and complete accumulation of data within the NRCT to study cancer incidence (including second primary tumours), mortality and survival. This provides the basis for descriptive epidemiology/cancer intelligence for the UK, utilising the NRCT database linked to other available datasets, principally HES for England. This has constituted a substantial proportion of the DH funded work and enabled comparisons of cancer burden and treatment outcome with other countries, particularly in Europe.
- The investigation of prenatal/intrauterine exposures and childhood cancer risk. We have conducted a number of studies, including analysing the single largest dataset in the world (UK and USA), demonstrating robust relationships between intrauterine growth (birthweight) and risk of a variety of childhood tumours. We intend to take forward field studies, involving family interviews and tissue collection (based on sampling amongst NRCT identified cases) to understand the biological mechanisms (genomic and proteomic) more precisely. This will extend to attempts to detect evidence of intrauterine exposure to infection as a cause of leukaemias in particular. We have also systematically examined the evidence that paternal occupational exposures increase risk of childhood tumours. We have found little evidence this is so for the embryonal tumours, leukaemias and central nervous system (CNS) tumours. We have however provided robust evidence that socioeconomic status is associated with the risk of some tumours and this raises important questions for the successful conduct and interpretation of specific exposure/risk assessments.
- The investigation of the relationship between infection contact and childhood tumour risks. We have undertaken a variety of studies (tumour clustering in space and time, relationships with variables which might indicate an altered level of infection contact, estimates of population mixing of susceptibles and infectious contacts, and time-trend analyses of tumour occurrence in relation to demonstrable epidemics of infection) which bear on this issue. We have also undertaken

laboratory studies to define the feasibility of making direct measurement of intrauterine infection contact and tumour risk.

- The investigation of the relationship between exposure to radiation (ionising and non-ionising) and tumour risk. We have made major contributions to the work of the Committee on Medical Aspects of Radiation in the Environment (COMARE), in particular in its evaluation of possible risks posed by the existence of nuclear installations of different types. We have separately contributed to characterising the risks of childhood tumours arising from exposure to natural sources of background radiation and medical uses. Building on work previously supported by DH, we have assembled the resources to investigate further whether exposure to power frequency electromagnetic fields (EMFs), defined either in terms of physical distance from the powerline distribution system or predicted exposure from line loads/voltages, is associated with increased childhood tumour risk.

Relevance to DH policy

- Comparison of the UK childhood cancer burden, and the outcomes which are largely defined by provision and organisation of NHS clinical services for this patient group, in relation to the performance of other countries.
- Advice to government about the size of childhood cancer risk that may be attributable to the generation of electricity in nuclear power plants, its transmission via the powerline distribution network, or from naturally occurring radiation exposure. The policy implications are with respect to methods of energy generation and housing policy with respect to both old and new housing, in terms of location and construction.
- The work on prenatal/postnatal growth and results suggesting risk associations with birthweight may have implications for pregnancy nutrition policy, obstetric practice, infant feeding and childhood nutrition and monitoring of childhood growth. If growth factor exposure were shown to have a direct impact on risk, then the development further of chemotherapy based on chemical antagonists of insulin-like growth factors (IGF) may be of interest.
- Our work on infection contact and risk may have future implications for vaccination policies, daycare provision as a matter of social policy, and parenting practice.

Brief update since last progress report

Our most recent interim report covered the 21 month period April 2008-December 2009, and was delivered at the start of February 2010. This report covers the period January – December 2010. This period included some important administrative and research developments.

Administrative/financial

- Consolidation of our position at a new location on the Old Road Campus of the University of Oxford alongside the majority of cognate academic units, and physically closer to paediatric oncology clinical colleagues in the NHS Children's Cancer and Leukaemia Group (CCLG) Principal Treatment Centre at the John Radcliffe Hospital.
- The appointment of a new Action Research Professor of Paediatrics (Georg Holländer) within the CCRG's host department.
- Negotiated agreement over future National Cancer Intelligence Network (NCIN)/DH funding for the NRCT, to take effect from January 2011. The NRCT is the lead NCIN registry for childhood tumours and supports joint initiatives with the NCIN Teenage Young Adult (TYA) Registry (based at the North West Cancer Intelligence Service in Manchester). Their joint work is overseen by the NCIN CTYA Site Specific Clinical Reference Group (SSCRG).
- Additional project grant funding was obtained for: studies of the influence of comorbidity upon outcome (from NCIN); collaborative involvement in studies of the influence of Assisted Reproduction Technology (ART) on childhood cancer risk (from CRUK); collaborative involvement in the International Study of non-CNS Embryonal Tumours (ISET) UK pilot (from CwL); studies of the way in which mutations in the retinoblastoma gene affect tumour risk (from CwL). All take effect from 2011.
- A Daphne Jackson Fellowship (Kate O'Neill) to train in molecular epidemiology started in May 2010.

Research (4 areas)

- National childhood cancer intelligence. This includes basic childhood cancer descriptive epidemiology, technical developments in relation to how the NRCT collects and assimilates its data, and the production of material based on linked NRCT datasets.
- Intrauterine growth and childhood cancer risk.
- Infection contact and childhood cancer risk.
- Radiation exposure (all types), genetic susceptibility and childhood cancer risk.

National Childhood Cancer Intelligence

- The NRCT is complete to registration year 2007, with 2008/09 in prospect because of the continued cooperation of the Children's Cancer and Leukaemia Group (CCLG) clinicians across the UK and Ireland.
- A BTN3/NHSnet connection has been established, facilitating childhood cancer registrations by CCLG members, and NRCT access to NHS datasets which might help to accelerate the registration process, and enrich the data available about children with cancer on the NRCT. We

have used the NRCT link to Hospital Episode Statistics (HES) to study end of life care for children with cancer who die, as part of a series of pieces of work exploiting these links.

- We have a paper in press about the completeness of childhood cancer registration data on the NRCT (again involving the use of HES data). Several other related papers are in production. All draw on the work for Mary Kroll's DPhil thesis, which was successfully examined in 2010.
- We have coordinated with the North West Cancer Intelligence Service (NWCIS) in Manchester over the production of initial NCIN bulletins relating to both children and teenagers/young adults (TYA). These will cover survival and end of life care.
- We have coordinated with the Eastern Cancer Registry and Information Centre (ECRIC) the NCIN lead registry for brain tumours, over the improved collection of data for brain tumours at all ages and the analyses of these epidemiological data. For the latter Mary Kroll provided data from her DPhil thesis about time trends in childhood brain tumour occurrence, for the Brain Tumour Epidemiology Consortium (BTEC) meeting held in Cambridge (April 2010).
- We contributed to the CRUK Childhood Cancer Statistics Bulletin, published at the end of 2010.

Intrauterine exposures and childhood cancer risk

- A paper about the risk of childhood leukaemia (subtype) in relation to birthweight in England and Wales has been submitted to Paediatric Blood and Cancer (PBC)
- A paper about the risk of every type of childhood tumour in relation to birthweight (based on both UK and USA data), will be submitted to a special Journal of the American Medical Association (JAMA) edition on cancer.
- CwL funded work on the measurement of proteins in neonatal dried blood spots (DBS) has progressed. This includes infection-related antibodies and proteins forming part of the growth factor pathway which might be incriminated in the birthweight risk relationship.
- We have analysed data on socioeconomic status (SES) at the time of birth (and diagnosis) of childhood cancer cases. We will report consistent evidence (geographical area-based indicators of SES, and paternal occupation at birth measures) for leukaemia occurrence, and less consistent evidence of the same association for CNS tumours. Paternal occupational exposures specifically do not appear to be important for either leukaemia (subtype) or CNS (subtype) risk, and these studies will also be reported.

Infection contact

- A paper based on Mary Kroll's DPhil thesis about the way in which infection death rates and undiagnosed leukaemia may interact will be submitted.
- Our CwL funded laboratory work on markers of intrauterine infection contact which can be measured in neonatal dried blood spots has progressed. It is possible to demonstrate the results of wideranging nucleic acid scans for evidence of virus presence in dried blood spots, but difficult to do so when looking for immunological (protein) evidence .

Radiation exposure

- We have contributed extensively to the forthcoming COMARE report evaluating the implications for this country of the KiKK Study results for Germany.
- With the assistance of DH RPR RX123 grant we have nearly completed analyses of the degree to which cancer excesses in the vicinity of the Sellafield and Dounreay nuclear installations can be seen to persist. This will form the basis of published papers and a further COMARE report.
- We have completed a case-control analysis of environmental radon and gamma exposure and childhood tumour risk and will publish it.
- With support from CwL we have made substantial progress towards evaluating the risk of childhood tumours in relation to powerline electromagnetic field (EMF) exposure using NRCT data 1996 onwards.
- In 2010 we contributed to/published 3 papers and a letter on powerline-frequency EMFs and childhood cancer risk of different types.

Key achievements 2006-10

a) Examples of work influencing policy/practice

Of the 100 or so publications we have produced in the period 2006-10 listed below about 30 are related to ionising/non-ionising radiation exposure and risk, or to risks associated with radiotherapy/chemotherapy for a primary tumour. 14 are related to international comparisons of incidence/survival or specific studies in the UK of these features for particular tumours. 6 are related to infection contact and risk, and 4 are about growth or genetic influences on risk. 5 are related to parental occupational exposures and risk, and the remainder about childhood cancer are general reviews, including a book, published in 2007. 26 papers listed are only indirectly related to childhood cancer, since they largely concern tobacco dependence/smoking, though this may be relevant in terms of causation (intrauterine and postnatal exposure to tobacco smoke products) and in terms of health behaviours adopted by childhood cancer survivors.

Our work is most likely to have influenced policy/practice in the field of radiation protection. We have contributed extensively to COMARE's work and hence advice to government, particularly about risks that may be associated with the activity of nuclear installations.

Our work contributing to international comparisons of incidence/survival has demonstrated a firm foundation for using data for Britain for statistical comparison of childhood cancer data between countries. It has led to a particular interest being taken in the possibility that the poorer survival of children in the UK than in some countries in Western Europe seen in the 1990s may be related to a tendency to later diagnosis at a slightly more advanced stage in this country. Attention and efforts to investigate this possibility further have ensued.

The three publications of note that are attached are number 2, number 33 and number 27 (a link to a book).

b) Publications 2006-2010

2006

Childhood cancer

1. Stiller CA, Passmore SJ, Kroll ME, Brownbill PA, Wallis JC, Craft AW. Patterns of care and survival for patients aged under 40 years with bone sarcoma in Britain, 1980-94. **Br J Cancer** 2006;**94**:22-29
2. Kroll ME, Draper GJ, Stiller CA, Murphy MFG. Childhood leukaemia incidence in Britain, 1974-2000: time trends and possible relation to influenza epidemics. **JNCI** 2006;**98**:417-420
3. McNally RJ, Alexander FE, Bithell JF. Space-time clustering of childhood cancer in Great Britain: a national study 1969-93. **Int J Cancer** 2006;**118**:2840-2846
4. Rao A, Hills RK, Stiller CA, Gibson BE, de Graaf SN, Hann IM, O'Marcaigh A, Wheatley K, Webb DKH. Treatment for myeloid leukaemia of Down syndrome: population based experience in the United Kingdom and results from the Medical Research Council AML 10 and AML 12 trials. **British Journal of Haematology** 2006;**132**:576-83

5. Wall BF, Kendall GM, Edwards AA, Bouffler S, Muirhead CR, Meara JR. What are the risks for medical x-rays and other low dose radiation? **British Journal of Radiology** 2006;**79**:285-94
6. MacCarthy A, Draper GJ, Steliarova-Foucher E, Kingston JE. Retinoblastoma incidence and survival in European children (1978–1997). Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2092-2102
7. Sankila R, Martos Jiménez MC, Miljus D, Pritchard-Jones K, Steliarova-Foucher E, Stiller C. Geographical comparison of cancer survival in European children (1988-1997): Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:1972-1980
8. Spix C, Pastore G, Sankila R, Stiller CA, Steliarova-Foucher E. Neuroblastoma incidence and survival in European children (1978-1997): Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2081-2091
9. Steliarova-Foucher E, Stiller CA, Pukkala E, Lacour B, Plesko I, Parkin DM. Thyroid cancer incidence and survival among European children and adolescents (1978-1997): Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2150-2169
10. Stiller CA, Bielack SS, Jundt G, Steliarova-Foucher E. Bone tumours in European children and adolescents, 1978–1997. Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2124-2135
11. Stiller CA, Desandes E, Danon SE, Izarzugaza I, Ratiu A, Vassileva-Valerinova Z et al. Cancer incidence and survival in European adolescents (1978–1997). Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2006-2018
12. Stiller CA, Marcos-Gragera R, Ardanaz E, Panelli F, Almar Marqués E, Cañada Martínez A et al. Geographical patterns of childhood cancer incidence in Europe, 1988–1997. Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:1952-1960
13. Stiller CA, Pritchard J, Steliarova-Foucher E. Liver cancer in European children: Incidence and survival, 1978–1997. Report from the Automated Childhood Cancer Information System project. **European Journal of Cancer** 2006;**42**:2115-2123
14. Pritchard-Jones K, Kaatsch P, Steliarova-Foucher E, Stiller CA, Coebergh JWW. Cancer in children and adolescents in Europe: Developments over 20 years and future challenges. **European Journal of Cancer** 2006;**42**:2183-2190
15. Kendall G, Hughes JS, Oatway WB, Jones AL. Variation in radiation exposures of adults and children in the UK. **Journal of Radiological Protection** 2006;**26**:257-76
16. Scott RH, Stiller CA, Walker L, Rahman N. Syndromes and constitutional chromosomal abnormalities associated with Wilms tumour. **Journal of Medical Genetics** 2006;**43**:705-715
17. Swanson J, Vincent T, Kroll M, Draper G. Power-frequency electric and magnetic fields in the light of Draper *et al* 2005. **Annals NYAS** 2006;**1076**:318-330

18. Kroll M, Draper G, Stiller CA, Murphy MFG. RESPONSE: Re: Childhood Leukemia Incidence in Britain, 1974-2000: Time Trends and Possible Relation to Influenza Epidemics. **JNCI** 2006;**98**:1746-1747

Paediatric

19. Murphy MFG, Neale R, Hey K, Seagroatt V, Goldacre M, Vessey M, Willis B, Ellis JD, Barlow D. Pregnancy outcome amongst twins conceived after subfertility treatment compared with natural twins: a population based study. **Twin Research and Human Genetics** 2006;**9**:279-84
20. Pyper C, Bromhall L, Dummett S, Altman DG, Brownbill P, Murphy M. The Oxford Conception Study design and recruitment experience. **Paediatric and Perinatal Epidemiology** 2006; **20**(Supplement 1):51-59
21. Munafo MR, Wileyto EP, Murphy MFG, Collins BN. Maternal smoking during late pregnancy and offspring smoking behaviour. **Addictive Behaviors** 2006;**31**:1670-1682

Other

22. Clark T, Murphy MFG, Hey K, Drury M, Cheng KK, Aveyard P. Does smoking influence survival in cancer patients through effects on respiratory and vascular disease mortality. **Eur J Cancer Prev** 2006;**15**:87-90
23. Bhatia M, Howard SC, Clark T, Neale R, Qizilbash N, Murphy MFG, Rothwell P. Apolipoproteins as predictors of ischaemic stroke in patients with a previous transient ischaemic attack. **Cerebrovascular Diseases** 2006;**21**:323-328
24. Munafo MR, Murphy MFG, Johnstone EC. Smoking cessation, weight gain and DRD4-521 genotype. **Am J Med Genet (Neuropsychiatric Genetics)** 2006;**141**:398-402
25. Johnstone E, Benowitz N, Cargill A, Jacob R, Hinks L, Day I, Murphy MFG, Walton R. Determinants of the rate of nicotine metabolism and effects on smoking behavior. **Clin Pharmacol Ther** 2006; **80**:319-330

2007

Childhood cancer

26. Taylor AJ, Winter DL, Stiller CA, Murphy MFG, Hawkins MM. Risk of breast cancer and other second malignancy neoplasms in female survivors of childhood Hodgkin's disease in Britain: a population-based study. **Int J Cancer** 2007; **120**:384-391
27. Childhood cancer in Britain: incidence, survival, mortality. Ed: Stiller, CA. Oxford: Oxford University Press; 2007

Chapter 1 - Introduction. Draper GJ

Chapter 2 - Methods. - Vincent TJ, Bayne AM, Brownbill PA, Stiller CA

Chapter 3 - Incidence of Childhood Cancer 1991-2000. Stiller CA, Kroll ME, Eatock EM

Chapter 4 - Time Trends in Incidence 1966-2000. Kroll ME, Stiller CA

Chapter 5 - Survival from Childhood Cancer. Stiller CA, Kroll ME, Eatock EM

Chapter 6 - Childhood Cancer Mortality. Bunch KJ, Stiller CA

Chapter 7 - Uses of the NRCT. Murphy MFG, Bayne AM

28. Jenkinson HC, Winter DL, Marsden HB, Stovall MA, Stevens MCG, Stiller CA and Hawkins MM. A study of soft tissue sarcomas after childhood cancer in Britain. **Br J Cancer** 2007;**97**:695-699
29. Kendall G, Murphy M. Natural environmental radiation and childhood cancer. *Environmental Radon Newsletter* 2007; Autumn(52):1
30. Arndt V, Lacour B, Steliarova-Foucher E, Spix C, Znaor A, Pastore G, Stiller C, Brenner H. Up-to-date monitoring of childhood cancer long-term survival in Europe: tumours of the sympathetic nervous system, retinoblastoma, renal and bone tumours, and soft tissue sarcomas. **Annals of Oncology** 2007;**18**:1722-1733
31. Stiller CA. International patterns of cancer Incidence in adolescence. Invited article. **Cancer Treatment Reviews** 2007;**33**:631-645
32. Kendall GM, Phipps AW. Effective and organ doses from thoron decay products at different ages. **Journal of Radiological Protection** 2007;**27**:427-435
33. Pritchard-Jones K, Stiller CA. What can we learn from geographical comparisons of childhood cancer survival? **Br J Cancer** 2007;**96**:1493-7
34. Neale RE, Carriere P, Murphy MFG, Baade P. Testicular cancer in twins: a metaanalysis. **Br J Cancer** 2007;**98**:171-173

Paediatric

35. Fear N, Vincent T, Hey K, Murphy MFG. Paternal occupation and other risk factors for the occurrence of neural tube defects. **Paediatric and Perinatal Epidemiology** 2007;**21**:163-168.
36. Collins BN, Wileyto EP, Murphy MFG, Munafò MR. Adolescent environmental tobacco smoke exposure, not prenatal exposure to tobacco predicts adolescent academic achievement failure. **J Adolesc Health** 2007;**41**:363-70

Other

37. Johnstone EC, Elliot KM, David SP, Murphy MFG, Walton RT, Munafò MR. Association of *COMT* Val^{108/158} Met genotype with smoking cessation in a nicotine replacement therapy randomised trial. **Cancer Epidemiol Biomarkers Prev** 2007;**16**:1065-1069
38. Johnstone EC, Murphy MFG. Pharmacogenomics of nicotine dependence and impact on smoking cessation. **Current Pharmacogenomics** 2007;**5**:178-189
39. David SP, Munafò MR, Murphy MFG, Walton RT, Johnstone EC. The serotonin transporter *5-HTTLPR* polymorphism and treatment response to nicotine patch: follow-up of a randomized controlled trial. **Nicotine and tobacco research** 2007;**9**:225-231
40. Wright AJ, Aveyard P, Guo B, Brown K, Murphy MFG, Marteau TM. Is attributing smoking to genetic causes associated with a reduced probability of quit attempt success. **Addiction** 2007;**102**:1657-1664

41. Aveyard P, Brown K, Saunders C, Alexander A, Johnstone E, Munafo MR, Murphy M. Weekly versus basic smoking cessation support in primary care: a randomised controlled trial. **Thorax** 2007;62;898-903
42. Johnstone EC, Murphy MFG. Inter-individual differences in tobacco dependence: the impact of genetics. In: Why people smoke. Ed: Paloma Martin and Michael Forrest. **Brussels ENSP** 2007
43. Munafo MR, Elliot KM, Murphy MFG, Walton RT, Johnstone EC. Association of the Mu-opioid receptor gene with smoking cessation. **The Pharmacogenomics Journal** 2007;7;353-61

2008

Childhood cancer

44. Taylor AJ, Winter DL, Pritchard-Jones K, Stiller CA, Frobisher C, Lancashire ER et al. Second primary neoplasms in survivors of Wilms' tumour - a population-based cohort study from the British Childhood Cancer Survivor Study. **Int J Cancer** 2008; 122:2085-2093.
45. Windsor R, Stiller C, Webb D. Peripheral T-Cell Lymphoma in Childhood: Population-Based Experience in the United Kingdom Over 20 Years. **Pediatric Blood Cancer** 2008; 50:784-787.
46. Stiller CA, Kroll ME, Boyle PJ, Feng Z. Population mixing, socioeconomic status and incidence of childhood acute lymphoblastic leukaemia in England and Wales: analysis by census ward. **Br J Cancer** 2008;98:1006-1011
47. Walker DA, Bendel A, Stiller C, Byrne P, Sokal M. Central nervous system tumours. In: Bleyer A, Barr R (eds.), *Cancer in Adolescents and Young Adults*, Springer-Verlag, Heidelberg. 2008
48. Stiller, C.A. Epidemiology of Childhood Tumours. In: Carachi R et al (eds), *The Surgery of Childhood Tumours*, Springer-Verlag, Heidelberg. 2008
49. Murphy MFG, Bunch KJ, Chen B, Hemminki K. Reduced occurrence of childhood cancer in twins compared to singletons: 'protection' but by what mechanism? **Pediatric Blood & Cancer** 2008;51:62-65
50. Muirhead CR, O'Hagan JA, Kendall GM. Studies of occupational radiation exposure and health experience from the UK National Registry for Radiation Workers. **Radiation Biology. Radioecology.** 2008;48;212-217
51. Shah A, Stiller CA, Kenward MG, Vincent T, Eden TOB, Coleman MP. Childhood leukaemia: long-term excess mortality and the proportion 'cured'. **Br J Cancer** 2008; 99(1):219-223
52. Stiller CA, Kroll ME, Boyle PJ, Feng Z. Reply: Population change, population mixing and incidence of childhood acute lymphoblastic leukaemia in England and Wales. **Br J Cancer** 2008; 99:1192-1193.
53. FACT Collaboration (Stiller). Constitutional 11p15 abnormalities, including heritable imprinting center mutations, cause nonsyndromic Wilms tumor. **Nat Genet** 2008; 40:1329-34

54. Stiller C A Pediatric Cancers. In: Kris Heggenhougen and Stella Quah, editors International Encyclopedia of Public Health, Vol 5. San Diego: Academic Press; 2008. pp. 28-40.
55. Bithell JF, Keegan TJ, Kroll ME, Murphy MFG, Vincent TJ. Childhood leukaemia near British Nuclear installations: methodological issues and recent results. **Radiat Prot Dosimetry** 2008;132:191-97
56. Draper G. Preconception exposures to potential germ-cell mutagens. **Radiat Prot Dosimetry** 2008;132:241-45

Paediatric - nil

Other

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c) Dissemination activities

- Contributions to Childhood Eye Cancer Trust (CHECT) and the National Alliance of Childhood Cancer Parent Organisations (NACCPO) conferences involving affected families in UK
- Contributions to CCLG annual winter and summer meetings involving most paediatric oncologists in UK
- Contributions to CwL conferences
- Contributions to United Kingdom Association of Cancer Registries (UKACR)/NCIN conferences
- Contributions to International Association of Cancer Registries (IACR) conferences
- Contributions to International Society of Paediatric Oncology (SIOP) conferences
- Contribution to DH Radiation Protection Research (RPR) seminars
- Contributions to Royal College of Paediatrics and Child Health (RCPCH) conferences
- Contributions to Record Linkage Scotland – Exploiting Existing Data for Health Research conferences
- Contributions to Health Protection Agency (HPA) conferences
- Contributions to the Childhood Leukaemia International Consortium (CLIC) meetings
- Contributions to the Brain Tumor Epidemiology Consortium (BTEC) meetings

Conclusion

The CCRG has achieved its objectives for the period 2006-10 inclusive. It is poised from 2011 to continue providing data which will inform decisions about the optimum configuration of (NHS) clinical services for children with cancer and the overlapping group of teenagers/young adults. It will also continue to provide insights into the potentially reducible causes of childhood cancer and possibilities for prevention.

Comparison with peer European countries has suggested that UK survival performance was not as good as some of the best in the 1990s. Work is in hand to understand whether any survival variation exists within the UK, the reasons for this if found, and how to change that situation. In addition we aim to shed light on whether outcomes other than survival have improved and can continue to be improved. We would like to undertake a more contemporary analysis of comparative outcomes in European countries to see if the UK has closed the gap with the best performing countries.

With regard to causes, we have demonstrated important progress in what is, or is not, likely to be importantly related to the occurrence of the range of childhood cancers, and aim to explore these factors further. A better understanding of how germline genetic mutations contribute to primary childhood cancer and second primary tumour risks will be gained through the studies in hand. Similarly we are developing studies to illuminate further the roles of prenatal infection contact and intrauterine growth on risk, since both are likely to be important. We believe that our studies to date exonerate paternal occupation exposure as a major cause of any risk. Certain forms of (potential) exposure to ionising radiation (from nuclear installations) are also unlikely to be causes of childhood cancer. However, other sources of exposure to ionising radiation (therapeutic irradiation; natural environmental) are incriminated as potential causes of some cancers. The role of non-ionising radiation as a cause of some childhood cancers is uncertain but under further investigation.