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Childhood cancer survival in Ireland: Temporal, regional and deprivation-related patterns

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ABSTRACT

Survival after childhood cancer varies across Europe, but national or regional studies have so far shown no survival differences related to socio-economic disparity. The relationship of childhood cancer survival to disparity has not been studied in Ireland. We assessed observed survival for Irish children (ages 0–14 years) diagnosed with cancer during the period 1994–2005, overall (for all cancers included in the 3rd edition of the International Classification of Childhood Cancer) and for three main diagnostic groups – leukaemias, lymphomas, and central nervous system tumours. Comparisons were made between two diagnosis periods (1994–1999 and 2000–2005), between four regions of residence, and between five area-based deprivation categories. Regional patterns of treatment were examined to help assess the impact of centralisation of services. There was only limited evidence of improvements in survival over time. No clear evidence was found of deprivation-related influences on childhood cancer survival in Ireland, overall or for the three main diagnostic groups examined, although a weak trend was apparent for lymphoid leukaemias. Regional variation in survival was likewise not clear-cut, with the possible exception of CNS tumours (significantly higher survival amongst patients resident in the Western region). The absence of clear trends or patterns for regional or deprivation-related variation in survival may reflect a high degree of coordination and uniformity of treatment (and perhaps diagnostic) services, and application of standard treatment protocols nationally.

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1. Introduction

In Ireland, five-year survival after childhood cancers diagnosed during 1994–2000 was almost 80% for both males and females.[1] This compared favourably with survival figures from Europe and the United States. Childhood cancer survival is steadily increasing in Europe.[2–4] However, significant disparities in cancer survival, both for adults and for children, have been noted between eastern and western Europe. For childhood cancer, the ACCIS study reported average five-year survival of 64% for Eastern Europe compared with 75% in the west.[3] The EUROCARE-3 study reported five-year survival ranging 45–66% for individual eastern European countries compared with 71–90% (mainly 71–81%) for western European countries based on 1990–1994 cases.[2] Such geographical differences in survival after childhood cancer across Europe have been attributed to the need for more coordination, systematisation and standardisation in diagnosis, referral and treatment. Also, within regions, a number of studies have noted significant and persistent survival disparities related to socio-economic status for cancers amongst adults.[5–9] Possible explanations or mechanisms involve factors relating to

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the tumour (e.g. stage), the patient, and access to healthcare, and interactions between these.[7] In contrast to adults, studies of children have shown only limited or no evidence of a survival disparity related to deprivation.[5,10–13]

Survival disparities after childhood cancer may exist within Ireland, but have not been evaluated previously. We developed two hypotheses regarding regional or deprivation-based influences on survival after childhood cancer here. First, cancer services are centralised in the east of the country, in Dublin, so children from more distant regions might be expected to have less favourable survival. A second hypothesis was that relative deprivation would influence survival rates.

To test our hypotheses we used data from the Irish National Cancer Registry to assess variation in survival between larger geographical regions and between area-based deprivation strata. We also assessed time-trends in survival trends, updating an earlier analysis.[1] Our primary focus was on the three most common diagnostic groups – leukaemias, lymphomas and related neoplasms, and central nervous system (CNS) or intracranial neoplasms.

2. Materials and methods

2.1. Cases and incidence

National data on the incidence and treatment of childhood and adult cancers in Ireland are registered by National Cancer Registry (NCR) staff from patients' records, pathology reports and other sources provided by hospitals or clinics, supplemented by death certificate registrations for some cases. Analyses presented here are based on the third edition of the International Classification of Childhood Cancer (ICCC),[14] covering neoplasms in children below age 15. Neoplasms that are explicitly excluded from the ICCC were excluded from analysis (principally tumours of benign or uncertain behaviour). However, for intracranial and intraspinal sites, benign tumours and tumours of uncertain behaviour fall within the ICCC and were included in analyses.

Case numbers and incidence rates reported here excluded neoplasms flagged as duplicates by the IARCcrgTools programme (www.iacr.com.fr/iarccrgtools.htm) i.e. if second or subsequent neoplasms were considered sufficiently 'similar' by the programme. Otherwise, individuals with more than one primary cancer may have been included once for each new primary neoplasm of a different type (but only the first neoplasm was included in survival analyses). Incidence rates were standardised to the traditional World standard,[15] using age-groups 0–4, 5–9 and 10–14. Irish population data for each year 1994–2005 were derived from census data for 1991, 1996, 2002 and 2006, and official interpolations for intermediate years, provided by Central Statistics Office Ireland (CSO) (www.cso.ie). Trends in age-standardised incidence rates were assessed using the Joinpoint programme (srab.cancer.gov/joinpoint).[16]

2.2. Region of residence and region of treatment

Patients were assigned to one of four regions of residence, based on the Health Service Executive (HSE) administrative areas – Dublin/North–East, Dublin/Mid-Leinster, South and West – and this region was used both in descriptive analyses and in Cox regression (Section 2.4). To summarise the extent to which treatment may have been centralised, regions where each patient was treated were also identified. We allocated all recorded tumour-directed treatments (aimed at removing or destroying tumour) within one year of diagnosis to the region where the hospital or other treatment centre was located. Some patients received treatment (usually of different modalities) in more than one region, or multiple treatments in the same region, and we counted each region once per patient for (a) all relevant treatments combined and also separately for (b) surgery, (c) radiotherapy and (d) medical oncology treatments. A small number of first-course treatments initiated later than six months after diagnosis may have been under-recorded, particularly for earlier diagnosis years, but the broad geographical patterns of treatment should be unaffected.

2.3. Deprivation: The SAHRU index

The standard measure of area-based deprivation currently used in Ireland is the SAHRU (Small Area Health Research Unit) Deprivation Index, derived from socioeconomic data collected for c3400 Electoral Divisions (EDs) as part of the 2002 Census of Ireland.[17] The census variables used in the index cover unemployment, social class, type of housing tenure, car ownership and overcrowding.[18] The index is similar in design to the Carstairs and Townsends indices widely used in the UK.[19,20] The SAHRU index was available for 89% of all childhood cancer cases during 1994–2005, those for whom address data were precise enough to allow assignment of EDs. The ten-point index (1–10) was re-grouped for analysis into five broader categories (1–2 to 9–10). The index is known to be strongly correlated with the incidence of cancers amongst Irish adults, with clear associations between higher deprivation and higher risk of lung and stomach cancers and between lower deprivation and higher risk of breast cancer and melanoma.[18]

2.4. Survival

Follow-up of Irish cancer cases by the NCR was based on matching of personal details against national death certificate data provided by the CSO and the General Registrar's Office and updated four times each year. Clinical data on deaths were also used where available. Observed survival is presented, as the standard approach for children in western populations, and has been estimated by life-table methods using the *strs* command in Stata (www.pauldickman.com/rsmodel/stata_colon/). Cohort estimates of five-year and ten-year survival are presented for 1994–2005, and five-year survival for the diagnosis periods 1994–1999 and 2000–2005, based on follow-up to the end of 2006. 'Hybrid' estimates are also presented for the period 2000–2005, based on all cases diagnosed during those years and longer-term follow-up of cases diagnosed in earlier years supplemented by one-year follow-up of cases diagnosed in 1999. This approach and related 'period' approaches provide an empirically validated basis for more up-to-date assessment of longer-term survival.[21,22] Estimates were not standardised for age (but

Table 1 – Summary of patient characteristics and data-quality indicators for incident childhood cancers (first malignancy per patient), Ireland, 1994–2005.

	1994–2005		1994–1999		2000–2005		EUROCARE-4
	Cases	%	Cases	%	Cases	%	%
All cases (valid ICCC)	1452		679		773		
Boys	787	54	367	54	420	54	
0–4 years of age at diagnosis	631	44	282	42	349	45	[c]46
5–9 years	386	27	183	27	203	26	[c]26
10–14 years	435	30	214	32	221	29	[c]28
Microscopic verification	1354	93	639	94	715	93	[d]96
Unspecified cases[a]	74	5.1	39	5.7	35	4.5	[d]3.8
Death-certificate- or autopsy-only[b]	4	0.3	2	0.3	2	0.3	[d]0.4
Other death = diagnosis date[b]	3	0.2	2	0.3	1	0.1	
Second or subsequent tumours[b]	5	0.3	2	0.3	3	0.4	
Cases for survival analysis[b]	1440	100	673	99	767	99	
Follow- up <10 years	1099	76	332	51	767	100	
Follow-up <5 years	508	35	0	0.0	608	66	
Follow-up <1 years	0	0.0	0	0.0	0	0.0	

[a] Unspecified cases: cases assigned to non-specific ICCC categories Ie, IIe, IIIf, VIc, VIIc, VIIIe, IXe or XIIb.
[b] DCO and autopsy-only cases, other cases with <1 day survival, and second or later tumours were excluded from survival analyses.
[c] EUROCARE-4 figures for European cases 1995–2002.[4]
[d] EUROCARE-4 figures for European cases 1995–2002, ages 0–24 years combined.[4]

model-based comparisons were adjusted for age – see below). Conditional survival (e.g. survival to five years assuming survival through the first year) was also examined, by diagnosis period and deprivation category, to allow assessment of possible late influences on survival (details presented in Appendices Table A2 and Table A3).

Possible regional variations in survival were examined by area of residence, and fuller address data were also used to assign patients to Electoral Divisions (ED), allowing assignment of ED-based deprivation. Formal comparisons of survival between diagnosis cohorts, areas of residence or deprivation categories were made by Cox regression, adjusted for sex, five-year age-group and case-mix. For regional and deprivation-category analyses (included in a single model), diagnosis period – 1994–1999 or 2000–2005 – was also adjusted for. For all cancers combined, the case-mix categories used were (following EUROCARE-4):[4] lymphoid leukaemias (ICCC Ia); acute myeloid leukaemias (Ib); Hodgkin lymphomas (IIa); non-Hodgkin lymphomas (IIb); CNS tumours (III); kidney (ICD10 C64–C65); eye and orbit (C69); bone (C40–C41); soft tissues (C49); and other sites. Within groups I–III, categories Ia–e, IIa–e and IIIa–f were used, respectively. Proportionality of hazards was assessed by testing the effect of including interactions between covariates and follow-up time in the Cox model (www.ats.ucla.edu/stat/stata/faq/test_proportionality.htm). If there was significant interaction, the final model used was stratified by the relevant covariate(s) (mainly case-mix and age).

3. Results

3.1. *Patient characteristics and data quality indicators*

Data on 1452 newly diagnosed cases of childhood cancer (within the ICCC groups I–XII) in Ireland during 1994–2005, an average of 121 per year, are summarised in Table 1. The percentage of cases microscopically verified and the percentage of cases assigned to non-specific tumour morphologies were broadly similar to recent figures for Europe as a whole.[4] After excluding second malignancies and cases with same diagnosis and death date, 1440 patients were included in survival analyses. All patients diagnosed during 1994–1996 (24% of total) had potential follow-up of a full ten years to the end of 2006, whilst those diagnosed during 1994–2001 (65%)

Table 2 – Percentage distribution by deprivation category (area of residence) of childhood cancer cases included in survival analyses, Ireland, 1994–2005, in relation to baseline population percentages for the same period. Patients from unknown deprivation category (11% of cases) are not tabulated.

SAHRU deprivation index	All cancers (%)	Leukaemias and related (%)	Lymphomas and related (%)	CNS and related (%)	Population (ages 0–14) (%)
1–2 (least deprived)	23	25	20	23	23
3–4	16	17	18	16	15
5–6	13	13	14	13	14
7–8	18	18	19	19	18
9–10 (most deprived)	30	27	29	29	30

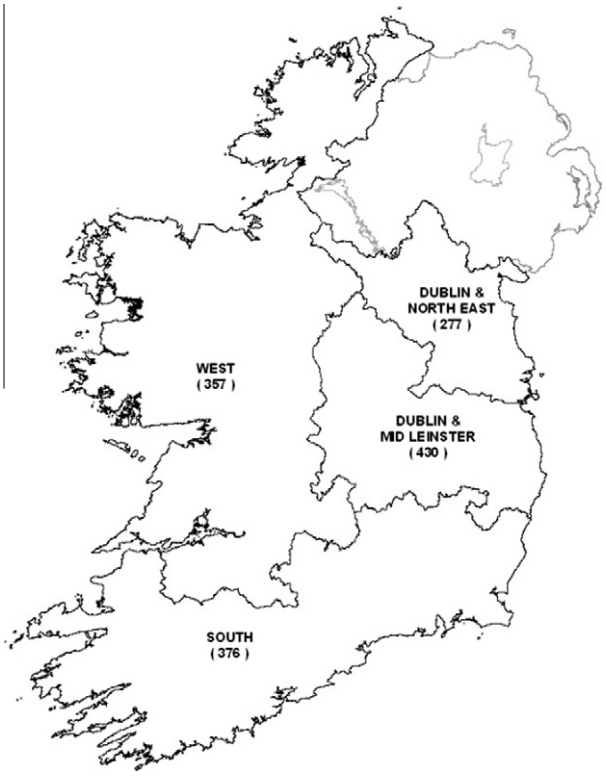

Fig. 1 – Irish regions (Health Service Executive areas) used for geographical analysis of childhood cancer survival, with regional case-totals shown by region of residence (1994–2005).

had potential follow-up of five years. The remainder had between one and five years of follow-up, but no patients were known to have been lost to follow-up.

Of all cancer patients, 30% were resident in areas of highest deprivation (category 9–10), similar to the distribution of the childhood population at risk (Table 2). The distribution of patients by deprivation category within specific diagnostic groups was also broadly similar to the overall distribution.

3.2. *Region of treatment in relation to region of residence*

Regardless of region of residence (Fig. 1), a high proportion of patients had tumour-directed treatment (within a year of diagnosis) in the Dublin/Mid-Leinster (DML) region: 72% overall, ranging from 61% of patients resident in the Southern region to 79% of those resident in DML (Table A1). For leukaemias, lymphomas and related neoplasms, in particular, 85% of patients had treatment (mainly chemotherapy) in DML. Treatment of CNS tumours was more evenly split between DML (39% of patients, mainly for radiotherapy and medical oncology) and Dublin/North–East (48%, mainly surgery).

3.3. *Incidence by diagnostic group and diagnosis period*

Overall, the rate of childhood cancer increased from 137 per million during 1994–1997 to 158 per million during 2002–2005, with an average percentage increase of 1.5% each year (Table 3). Leukaemia rates increased from 43 per million to 50, and lymphoma rates from 13 to 16, over the same period. Rates of tumours of the CNS showed little change from 40 per million during 1994–1997 to 39 during 2002–2005. However, trends during 1994–2005 as a whole were not statistically significant for any group or overall (Fig. 2).

3.4. *Survival estimates and time-trends in survival*

Five-year survival for all cancers of childhood averaged 79% for 1994–2005 as a whole, and varied little over time (79% for 1994–1999, 80% for 2000–2005) (Table 4). Leukaemias and related neoplasms also showed little change in survival between diagnosis periods (overall figure 77%), as did tumours of the central nervous system (73%). Average five-year survival for lymphoma patients did show an apparent increase, from 87% in 1994–1999 to 96% in 2000–2005 (overall 91%).

However, model-based comparisons, adjusted for age, sex and case-mix, found no significant changes in survival between the diagnosis periods 1994–1999 and 2000–2005, either overall or for any of the 12 specific diagnostic groups within the International Classification of Childhood Cancer (Table 4, data for groups IV–XII not shown). Lymphomas showed the strongest indications of improvement (hazard ratio 0.35, 95% CI 0.09–1.31, $P = 0.119$).

Conditional survival after the first year following diagnosis was high, as most deaths occurred in the first year. As with total five-year survival, there was little evidence of an upward trend in conditional five-year survival (Table A2). Estimates of ten-year survival were, in general, only slightly lower than the

Table 3 – Childhood cancer incidence rates, Ireland, by broad diagnosis period, 1994–2005.

Description and ICCC group	World age-standardised rates (per million children per year)								
	1994–1997			1998–2001			2002–2005		
	Rate	95% CI		Rate	95% CI		Rate	95% CI	
All childhood cancers (ICCC groups I–XII)	137	124	150	153	139	167	158	144	171
I. Leukaemias, myeloproliferative diseases, and myelodysplastic diseases	43	36	51	48	40	56	50	43	58
II. Lymphomas and reticuloendothelial neoplasms	13	9	17	18	13	22	16	11	20
III. CNS and miscellaneous intracranial and intraspinal neoplasms	40	33	47	34	27	40	39	32	45

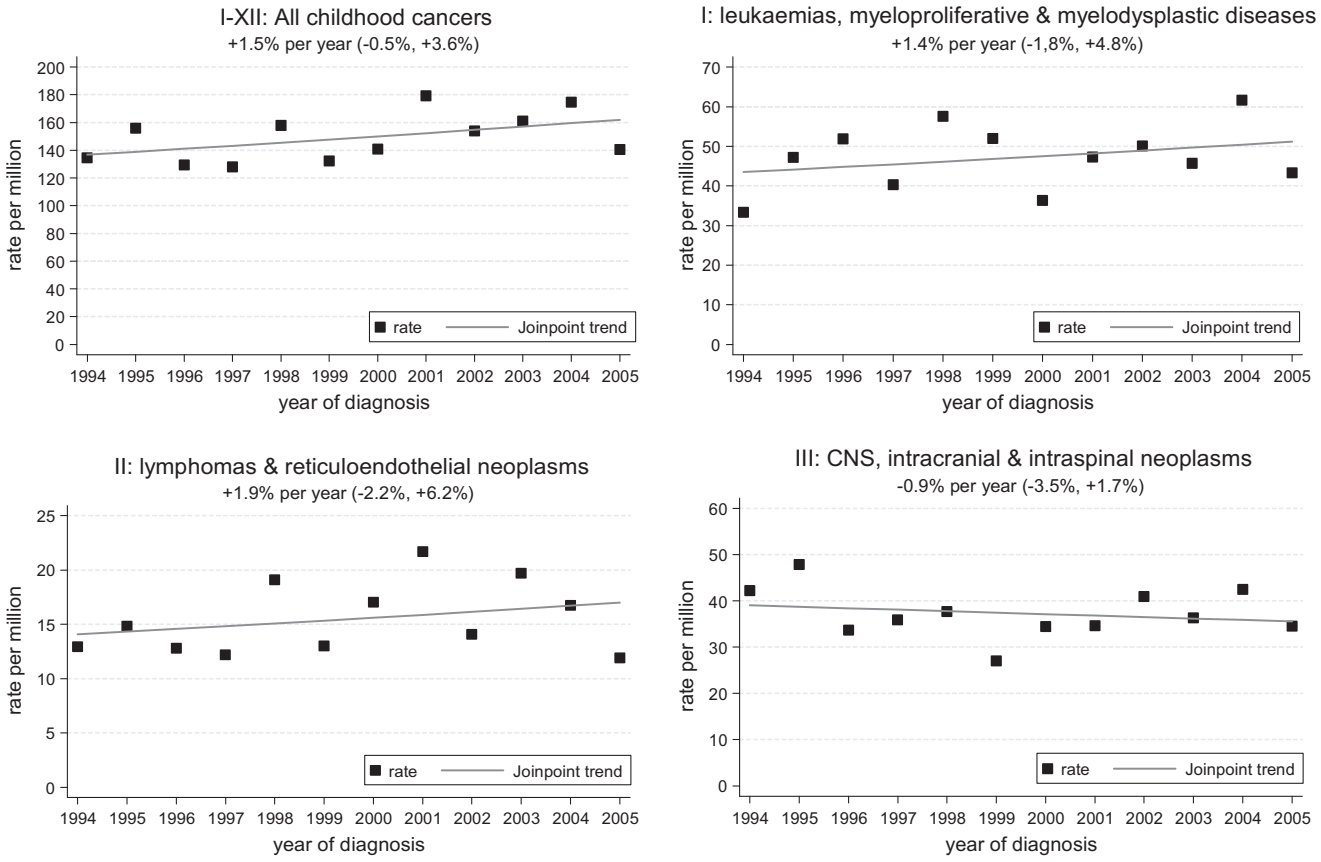

Fig. 2 – Trends in annual incidence (world age-standardised rates per million) of childhood cancer in Ireland, 1994–2005.

five-year estimates (Table 4). Conditional ten-year survival (for children who survived five years) was very high – 96% for all cancers combined and for leukaemias and related neoplasms, 99% for lymphomas and related neoplasms, and 95% for CNS, intracranial and intraspinal neoplasms (Table A2).

3.5. *Survival variation by region of residence*

When survival was evaluated according to region of residence there were relatively minor differences across the four regions (Table 5). Neither of the Dublin regions had better results than the Southern or Western regions. In fact, children from other regions seemed to do better than those from Dublin and adjacent counties, comparing childhood cancers as a whole, although the differences were not statistically significant (having adjusted for age, sex, diagnosis period, case-mix and deprivation category).

Within specific diagnostic groups, there were some indications of variation in five-year or ten-year survival between the regions, but with little indication of consistency across cancer types. Survival from CNS tumours was significantly higher amongst patients resident in the Western region (adjusted hazard ratio 0.51, 95% CI 0.29–0.91) compared with Dublin/Mid-Leinster. Otherwise variation was not statistically significant.

Restriction of survival comparisons to the first six months of follow-up after diagnosis accentuated regional variation in survival after CNS tumours: adjusted hazard ratio 0.21 (0.05–0.93, $P = 0.040$) for the Western region compared with Dublin/Mid Leinster. But early mortality did not vary significantly between regions for cancers as a whole or for leukaemias (details not presented), and could not be compared for lymphoma because of few early deaths.

3.6. *Survival variation by deprivation category*

Across the five deprivation categories examined, midpoint estimates of five-year survival during 1994–2005 varied between 75% (categories 7–8) and 83% (categories 3–4) for all childhood cancers combined (Table 5). There was no clear trend across deprivation categories in the unadjusted figures for five-year or ten-year survival, or for conditional survival (Table A3), overall or for specific diagnostic groups. Likewise there was no significant variation comparing more deprived with the least deprived areas, having adjusted for age, sex, diagnosis period, case-mix and region of residence (Table 5).

4. Discussion

4.1. *Time-trends in survival*

Our analysis indicates only modest (if any) improvement in survival over time, with no statistically significant trends and some apparent small declines. These minor trends seem

Table 4 – Observed five-year survival and ten-year survival of childhood cancer patients in Ireland by year of diagnosis.

	5-yr survival			[a]Hazard ratio	10-yr survival	
	1994–2005 complete (%)	1994–1999 cohort (%)	2000–2005 complete (%)	2000–2005 v 1994–1999	1994–2005 complete (%)	2000–2005 hybrid (%)
All ICCC3-classified neoplasms	79	79	80	[b]0.99	76	77
	77–81	75–82	76–83	0.79–1.25	74–79	74–80
All cases (age 0 only)	71	71	72	[b]1.05	71	72
	62–78	56–81	59–81	0.52–2.09	62–78	61–81
I. Leukaemias, myeloproliferative and myelodysplastic diseases	77	78	76	[b]1.05	74	74
	72–81	71–83	68–82	0.69–1.61	68–78	68–78
I. (age 0 only)	25	29	24	[b]1.48	25	32
	8.2–47	4.1–61	4.4–53	0.43–5.01	8.2–47	8.5–58
Ia. Lymphoid leukaemias	80	80	81	0.93	77	77
	76–85	73–85	73–87	0.55–1.56	71–82	71–83
Ia. (age 0 only)	22	20	25	0.80	22	26
	3.5–50	8.4–58	1.2–65	0.13–4.65	3.5–50	12–67
Ib. Acute myeloid leukaemias	65	65	61	1.13	63	64
	52–75	45–79	42–74	0.51–2.52	50–73	49–76
II. Lymphomas and reticuloendothelial neoplasms	91	87	96	[b]0.35	90	92
	86–95	7.0–93	89–99	0.09–1.31	84–94	85–96
IIa. Hodgkin lymphoma	91	86	97	0.31	88	89
	80–96	66–94	80–100	0.03–2.84	73–95	73–96
IIb. Non-Hodgkin lymphoma	93	89	97	[cd]0.50	93	95
	82–97	68–96	80–100	0.05–5.62	82–97	83–99
III. CNS and miscell. intracranial and intraspinal neoplasms	73	72	73	[c]0.88	69	71
	68–77	65–78	65–79	0.59–1.32	63–74	64–76
III. (age 0 only)	54	50	56	0.89	54	61
	34–70	23–72	25–78	0.29–2.68	34–70	34–80
IIIa. Ependymomas and choroid plexus tumours	61	60	64	0.95	43	44
	37–78	25–83	33–84	0.25–3.58	13–71	13–72
IIIb. Astrocytomas	81	79	83	[c]0.69	79	84
	75–86	70–86	72–90	0.35–1.36	72–85	75–90
IIIc. Intracranial and intraspinal embryonic tumours	52	49	59	0.74	47	51
	39–64	32–63	35–77	0.34–1.60	33–60	34–66

[a] Hazard-ratio comparisons between 1994–1999 and 2000–2005 are based on Cox regression, adjusted for age and sex (also case-mix within major groups).
[b] Cox regression includes interaction between casemix and follow-up time (non-proportionality of hazards) for this group.
[c] Interaction between age and time.
[d] Interaction between sex and time.

likely to reflect a combination of the small numbers of cases (or more particularly deaths) involved, and the already high survival for most childhood cancers in Ireland from 1994 onwards.[1] Across Europe, EUROCARE comparisons of childhood cancer survival for the periods 1990–1994, 1995–1999 and 2000–2002 have indicated continuing (though sometimes small) improvements for most diagnostic groups, including significant reductions for lymphoid leukaemias and for CNS tumours between the latter two periods.[2,4] A narrowing of differences between countries was also noted in more recent years compared with 1990–1994.[2,4]

4.2. *Deprivation-related and regional variation in survival*

We found no clear evidence of an influence of deprivation on childhood cancer survival, although there was some suggestion of an effect for leukaemias (especially lymphoid leukaemias). Nor was there substantial regional variation in survival, overall or for the leukaemias or lymphomas, although the Western region had significantly higher survival for tumours of the central nervous system. For leukaemias, these findings are broadly in line with those from other studies internationally. In general, published results showing a lack of influence of deprivation on childhood cancer contrast with findings for adult cancers.

The strongest evidence we found of a deprivation influence was for lymphoid leukaemias (ICCC diagnostic group Ia), which has been the focus of most other studies. Point estimates of five-year survival ranged from 83% in the least deprived category to 75% in the most deprived, and ten-year estimates from 83% down to 71% over the same deprivation range. But the overall adjusted trend was not statistically significant, nor were the adjusted mortality hazard ratios for specific higher-deprivation categories.

The observation that survival after CNS tumours was better in the Western region compared to Dublin/Leinster is in contrast to our hypothesis that residence at a greater distance from Dublin would be associated with poorer survival because of difficulties in accessing specialty care. We cannot explain this finding.

There was a high degree of centralisation of treatments for the cancer types we focused on here. This, in combination with application of standard treatment protocols nationally

Table 5 – Observed five-year and ten-year survival of childhood cancer patients in Ireland by area-based deprivation category and region of residence, 1994–2005.

		2002 SAHRU deprivation index[17]							Region of residence			
		1–2 Least deprived	3–4	5–6	7–8	9–10 Most deprived	Unknown	Overall trend[ab]	Dublin and Mid Leinster	Dublin and North East	South	West
All cancers	Cases	297	204	172	234	380	160		430	277	376	357
	5-yr	79%	83%	77%	75%	80%	82%		79%	77%	80%	81%
	95% CI	74–84%	77–88%	69–82%	69–80%	75–84%	74–88%		74–82%	71–81%	75–88%	77–85%
	10-yr	77%	79%	71%	72%	77%	82%		75%	75%	77%	77%
	95% CI	72–82%	71–85%	63–78%	64–78%	71–81%	74–88%		70–80%	69–80%	72–81%	72–82%
	HR[b]	1.00	0.79	1.36	1.25	1.01	0.81	1.03	1.00	1.12	0.89	0.87
	95% CI	–	0.52–1.21	0.92–2.02	0.86–1.80	0.72–1.42	0.51–1.29	0.96–1.11	–	0.81–1.54	0.65–1.21	0.63–1.19
All cancers (age 0 only)	HR[b]	1.00	1.30	1.93	1.54	1.71	0.38	1.12	1.00	0.72	0.69	1.42
	95% CI	–	0.30–5.65	0.41–9.16	0.46–5.18	0.63–4.59	0.04–3.28	0.89–1.42	–	0.24–2.12	0.24–1.93	0.49–4.12
I. Leukaemias and related	Cases	96	65	49	69	105	51		130	76	120	106
	5-yr	79%	77%	76%	77%	73%	81%		76%	77%	79%	74%
	95% CI	69–86%	64–86%	61–86%	64–85%	62–81%	64–90%		67–83%	65–85%	70–86%	64–82%
	10-yr	79%	73%	70%	72%	70%	81%		73%	77%	75%	70%
	95% CI	69–86%	57–84%	53–81%	59–82%	58–79%	64–90%		64–81%	65–85%	65–83%	59–79%
	HR	1.00	0.96	1.60	1.23	1.08	0.86	1.04	1.00	0.88	0.86	1.01
	95% CI	–	0.48–1.93	0.77–3.30	0.62–2.43	0.60–1.96	0.38–1.97	0.91–1.19	–	0.48–1.63	0.50–1.51	0.58–1.75
I. (age 0 only)	HR	–	–	–	–	–	–	1.10	–	–	–	–
	95% CI	–	–	–	–	–	–	0.82–1.47	–	–	–	–
Ia. Lymphoid leukaemias	Cases	78	48	46	55	74	45		101	62	100	81
	5-yr	83%	83%	81%	80%	75%	85%		78%	82%	83%	79%
	95% CI	72–90%	67–92%	65–90%	66–89%	62–84%	66–92%		67–86%	68–90%	74–90%	68–87%
	10-yr	83%	78%	74%	74%	71%	85%		74%	82%	79%	74%
	95% CI	72–90%	59–89%	56–85%	59–85%	55–82%	66–92%		63–83%	68–90%	67–87%	60–83%
	HR	1.00	1.05	1.55	1.45	1.42	0.91	1.10	1.00	0.71	0.70	0.90
	95% CI	–	0.43–2.56	0.66–3.63	0.65–3.24	0.69–2.95	0.34–2.40	0.93–1.30	–	0.33–1.52	0.36–1.35	0.47–1.72
II. Lymphomas and related	Cases	30	27	21	28	44	18		43	42	41	42
	5-yr	93%	96%	85%	89%	93%	89%		95%	84%	89%	98%
	95% CI	73–98%	76–99%	61–95%	69–96%	79–98%	43–98%		82–99%	68–93%	73–96%	84–100%
	10-yr	93%	96%	74%	89%	93%	89%		95%	79%	89%	98%
	95% CI	73–98%	76–99%	40–90%	69–96%	79–98%	43–98%		82–99%	59–90%	73–96%	84–100%
	HR	1.00	0.68	4.78	1.18	1.27	1.41	1.04	1.00	4.32	2.07	0.59
	95% CI	–	0.05–8.62	0.68–33.6	0.17–8.08	0.19–8.55	0.11–17.5	0.71–1.53	–	0.85–22.0	0.33–13.2	0.07–7.32
III. CNS and related	Cases	75	53	44	63	95	43		116	71	102	84
	5-yr	70%	78%	70%	69%	74%	74%		65%	76%	73%	79%
	95% CI	58–79%	63–87%	55–82%	54–80%	64–82%	58–85%		55–73%	64–84%	63–81%	68–87%
	10-yr	65%	73%	66%	65%	71%	74%		59%	76%	70%	74%
	95% CI	51–75%	57–84%	47–78%	48–77%	60–79%	58–85%		47–69%	64–84%	59–78%	61–83%
	HR	1.00	0.71	1.09	1.08	0.87	0.90	1.00	1.00	0.65	0.76	*0.51
	95% CI	–	0.34–1.45	0.55–2.13	0.57–2.01	0.49–1.53	0.43–1.86	0.88–1.14	–	0.36–1.16	0.46–1.24	0.29–0.91
III. (age 0 only)	HR	1.00	0.65	9.29	0.93	1.40	–	0.99	1.00	1.15	1.33	2.77
	95% CI	–	0.06–7.26	0.37–230.9	0.04–20.7	0.32–6.05		0.69–1.41	–	0.07–18.7	0.29–6.13	0.32–23.9

[a] Overall trend if deprivation category is treated as a continuous variable (1–5).

[b] Hazard ratios derived by Cox regression, including both deprivation and region of residence (adjusted for deprivation as a category) in the model, also adjusting for age, sex, diagnosis period and (within major groups) case-mix; includes adjustment for interaction between case-mix and follow-up time (non-proportionality of hazards) for all cancers combined, group I and group II; includes adjustment for interaction between age and follow-up time for group III.

Table A1 – Modality and region of tumour-directed treatment[a] in relation to region of residence for childhood cancer patients in Ireland, 1994–2005: all cases combined, and ICCG groups I–III.

Cancer type and region of residence	*n* (cases)	Tumour-directed treatment modality				Region(s) where tumour-directed treatment received			
		Any (%)	Surgery (%)	Radiotherapy (%)	Medical oncology (%)	DML (%)	DNE (%)	S (%)	W (%)
All childhood cancers									
Dublin (south) and Mid Leinster (DML)	431	91	40	18	69	79	23	0.0	0.0
Dublin (north) and North East (DNE)	278	90	37	19	67	73	30	0.0	0.0
South (S)	378	88	37	19	66	61	13	34	0.3
West (W)	360	88	40	21	70	73	20	1.7	13
Total	1447	89	39	19	68	72	21	9.4	3.2
I. Leukaemias and related neoplasms									
Dublin (south) and Mid Leinster (DML)	131	96	0.8	3.8	96	95	0.8	0.0	0.0
Dublin (north) and North East (DNE)	77	99	1.3	3.9	99	92	13	0.0	0.0
South	120	96	0.8	4.2	95	69	2.5	38	0.0
West	107	94	0.0	4.7	94	85	2.8	0.0	15
Total	435	96	0.7	4.1	96	85	3.9	10	3.7
II. Lymphomas and related neoplasms									
Dublin (south) and Mid Leinster (DML)	43	91	7.0	4.7	86	91	2.3	0.0	0.0
Dublin (north) and North East (DNE)	42	98	26	12	91	93	19	0.0	0.0
South	41	98	17	12	83	76	2.4	39	0.0
West	42	95	14	14	81	83	4.8	0.0	19
Total	168	95	16	11	85	86	7.1	10	4.8
III. CNS and related neoplasms									
Dublin (south) and Mid Leinster (DML)	116	80	58	32	34	48	58	0.0	0.0
Dublin (north) and North East (DNE)	71	70	54	25	18	34	55	0.0	0.0
South	102	71	52	28	23	30	23	39	0.0
West	84	79	63	33	36	43	60	3.6	3.6
Total	373	75	57	30	28	39	48	12	0.8

[a] Surgical excision, radiotherapy or medical oncology within 12 months following diagnosis. For patients who had treatment in more than one region, each region is counted.

or enrolment in clinical trials (although neither of these can be assessed directly from the NCR dataset), may account for the general lack of clear regional or deprivation-related variation in survival. It may be that children with cancer have access to uniform treatments regardless of means, since the private sector does not provide paediatric oncology services in Ireland.

A study of childhood leukaemia in the Netherlands (1973–1979 diagnoses of acute lymphoblastic and acute non-lymphoblastic leukaemia) likewise suggested that 'good access to diagnosis and treatment ... carried out with a high degree of national uniformity' may have explained, in part, the finding of only 'slight and equivocal' differences in survival in relation to parental education level.[10] Amongst UK children diagnosed with acute lymphocytic leukaemia during 1971–1990, there was little variation in survival between deprivation categories although some weak evidence that survival was poorest in the most deprived group.[12] One possible interpretation suggested was that access to treatment was similar across groups. However, significant variation in survival was noted amongst regions of residence, especially within the first six months after diagnosis, having adjusted for age, sex and deprivation.[12] A study of childhood cancer patients in Yorkshire during 1974–1995 noted significant declines in (unadjusted) survival across five deprivation strata for all cancers combined, leukaemias and central nervous system tumours, but not after adjustment for age, ethnicity and other factors.[11] Similarly, no significant socio-economic survival gradient was noted for children with cancer across England and Wales during 1971–1995.[5] This was considered likely to reflect the availability of effective chemotherapy for many childhood malignancies and a high degree of centralisation of treatment in specialist centres.

4.3. *Strengths and limitations of this study*

This study is based on full, population-based coverage of childhood cancers throughout Ireland. A further strength is that all relevant neoplasms, including benign tumours of CNS or intracranial sites, and haematological neoplasms not classed as 'malignant' in earlier editions of the International Classification of Childhood Cancers, have been registered by the National Cancer Registry throughout the study period (1994–2005). Routine collection of treatment data (modality, date and location) has also been underway since the NCR's establishment in 1994, which potentially aids interpretation of survival statistics here.

Limitations include the length of available follow-up – a full five years of follow-up was only available for patients diagnosed during 1994–2001, and ten years for 1994–1996. Comparisons between areas of residence and deprivation categories were made for multiple diagnostic groups, thus by chance some 'statistically significant' findings might be expected. On the other hand, the small numbers of incident

Table A2 – Observed conditional five-year survival and conditional ten-year survival of childhood cancer patients in Ireland by year of diagnosis.

	5-yr$^{(1yr)}$ Survival			10-yr$^{(5yr)}$
	1994–2005	1994–1999	2000–2005	1994–2005
All ICCC3-classified neoplasms	87% 85–89%	87% 84–90%	87% 84–90%	96% 94–97%
I. Leukaemias, myeloproliferative and myelodysplastic diseases	86% 81–89%	91% 86–94%	86% 78–91%	96% 91–98%
Ia. Lymphoid leukaemias	87% 82–90%	86% 79–90%	88% 79–93%	95% 90–98%
Ib. Acute myeloid leukaemias	85% 72–93%	87% 65–96%	83% 59–93%	100% –
II. Lymphomas and reticuloendothelial neoplasms	93% 87–96%	88% 79–94%	99% 91–100%	99% 91–100%
IIa. Hodgkin lymphoma	91% 80–96%	86% 66–94%	97% 80–100%	96% 75–99%
IIb. Non-Hodgkin lymphoma	94% 84–98%	89% 68–96%	100% –	100% –
III. CNS and miscell. intracranial and intraspinal neoplasms	86% 82–90%	89% 83–93%	83% 75–89%	95% 89–98%
IIIa. Ependymomas and choroid plexus tumours	66% 40–82%	67% 28–88%	68% 34–87%	71% 9.0–95%
IIIb. Astrocytomas	94% 88–97%	97% 89–99%	89% 78–95%	97% 90–99%
IIIc. Intracranial and intraspinal embryonic tumours	68% 51–79%	64% 44–79%	75% 43–90%	89% 63–97%

5-yr$^{(1yr)}$ survival: 5-year survival conditional on 1-year survival.
10-yr$^{(5yr)}$: 10-year survival conditional on 5-year survival.

cases and more particularly deaths in each region or deprivation category might not allow detection of real differences. Only limited information (insufficient for analysis) was available on stage or other prognostic factors for childhood cancers in this study, especially for leukaemias and CNS tumours (neither included in the 5th edition of the AJCC cancer staging scheme currently used by NCR).[23] A further limitation is the use of ecological rather than individual data for attribution of deprivation categories to patients. It would be preferable to have an indicator of socio-economic status for each patient; however, this information is not currently available to the cancer registry.

4.4. *Survival comparisons with Europe*

Of the cancers for which direct comparisons are possible with recent EUROCARE survival figures (Table A4),[4] Irish survival figures appear to be slightly lower for lymphoid leukaemias and some other diagnostic groups. Generally, however, Irish figures seem broadly comparable. A previous analysis of Irish survival data, covering 1994–2000 cases, noted relatively high five-year survival for acute non-lymphocytic leukaemias here (67% age-standardised) compared with EUROCARE-3 data from 1990–1994 for Europe as a whole (48%) and the Nordic countries (62%).[1] For the equivalent current ICCC grouping, acute myeloid leukaemias, Irish five-year survival during 2000–2005 was still moderately high (64% age-standardised) but now closer to or slightly lower than the EUROCARE-4 averages for Europe (67%) and northern European (average (68%) from 1995–2002 (Table A4). This seems to reflect improvements in European survival rates for these leukaemias between the two EUROCARE studies.[2,4]

4.5. *Conclusions*

With cancer incidence data now available comprehensively for Irish children back to 1994, there is increasing potential for detection of factors influencing late mortality. The present analysis did not find strong evidence of disparities in childhood cancer survival within Ireland, and medium-term survival figures are quite high in a European context. However, in the absence of precise information that can only be obtained by personal contact, it may not be possible to detect subtle influences of socio-economic status on long-term survival. Nevertheless, as the National Cancer Registry matures and years of long-term follow-up accrue, we will be able to produce useful information to inform policy and service provision for this growing population of patients.

Conflict of interest statement

None declared.

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Table A3 – Observed conditional five-year and ten-year survival of childhood cancer patients in Ireland in relation to area-based deprivation, 1994–2005.

		2002 SAHRU deprivation index[17]				
		1–2 Least deprived	3–4	5–6	7–8	9–10 Most deprived
All cancers	Cases	297	204	172	234	380
	5-yr^{1yr}	87%	89%	88%	83%	89%
	95% CI	82–90%	83–93%	81–92%	76–88%	85–92%
	10-yr^{5yr}	98%	95%	93%	96%	96%
	95% CI	93–99%	86–99%	84–97%	88–98%	91–98%
I. Leukaemias and related	Cases	96	65	49	69	105
	5-yr^{1yr}	91%	84%	87%	86%	82%
	95% CI	81–95%	70–92%	71–94%	73–93%	72–89%
	10-yr^{5yr}	100%	95%	91%	94%	96%
	95% CI	–	68–99%	69–98%	78–98%	74–99%
Ia. Lymphoid leukaemias	Cases	78	48	46	55	74
	5-yr^{1yr}	90%	87%	89%	87%	80%
	95% CI	79–95%	71–94%	73–96%	72–94%	67–89%
	10-yr^{5yr}	100%	94%	91%	93%	94%
	95% CI	–	64–99%	69–98%	74–98%	66–99%
II. Lymphomas and related	Cases	30	27	21	28	44
	5-yr^{1yr}	96%	100%	90%	89%	93%
	95% CI	74–99%	–	64–97%	69–96%	79–98%
	10-yr^{5yr}	100%	100%	87%	100%	100%
	95% CI	–	–	36–98%	–	–
III. CNS and related	Cases	75	53	44	63	95
	5-yr^{1yr}	82%	86%	91%	81%	89%
	95% CI	69–89%	71–93%	75–97%	64–90%	80–95%
	10-yr^{5yr}	93%	95%	93%	94%	95%
	95% CI	74–98%	68–99%	60–99%	62–99%	82–99%

5-yr^{1yr}: 5-year survival conditional on 1-year survival.
10-yr^{5yr}: 10-year survival conditional on 5-year survival.

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Appendix A

See Tables A1–A4.

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Table A4 – Comparison of observed five-year survival rates between Ireland and EUROCARE-4 results for Europe[4] for malignant cancers amongst children aged 0–14 (age-standardised to the EUROCARE-4 patient population for each diagnostic group unless otherwise noted).

ICCC group	Ireland 2000–2005[a]		Europe 2000–2002[a]		[b]Northern Europe 1995–1999[a]	
Ia. Lymphoid leukaemias	81%	76–86%	85%	84–87%	85%	83–87%
Ib. Acute myeloid leukaemias	64%	51–71%	67%	62–72%	68%	60–75%
IIa. Hodgkin lymphomas	[c]93%	80–98%	95%	93–98%	93%	89–98%
IIb. Non-Hodgkin lymphomas	[c]95%	83–99%	82%	78–87%	86%	80–91%
III. All CNS tumours[d]	63%	54–71%	63%	60–66%	61%	57–66%
IIIa. Ependymomas and related[d]	[c]62%	36–80%	62%	56–68%	66%	53–78%
IIIb. Astrocytoma[d]	76%	61–90%	63%	57–69%	63%	52–74%
IIIc. Embryonal CNS tumours	59%	43–75%	66%	61–71%	56%	47–66%

[a] Irish 2000–2005 and European 2000–2002 figures here are period or hybrid estimates, thus the Irish figures differ from cohort analyses presented in Table 4 (further differences may reflect age-standardisation or different inclusion criteria).
[b] Northern Europe comprises Denmark, Finland, Iceland, Norway and Sweden.
[c] Irish survival estimates for these diagnostic groups not age-standardised, because of insufficient data (or 100% survival in some age-groups).
[d] These diagnostic groups strictly include some CNS or intracranial tumours of benign or uncertain behaviour, but as non-malignant cases are not included in the European survival data quoted here, invasive cases have also been excluded from Irish data in these comparisons.

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