EUROPEAN JOURNAL OF CANCER 46 (2010) 1069–1078

available at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejconline.com

Comparison of self-reported late effects with medical records among survivors of childhood cancer

Naomi Taylor [a], *Kate Absolom* [b], *Gisela Michel* [c], *Tanya Urquhart* [d], *Mary Gerrard* [d], *Anna Jenkins* [d], *Vicki Lee* [d], *Ajay Vora* [d], *Christine Eiser* [c,*]

[a] *University of Sheffield Medical School, Beech Hill Road, Sheffield, UK*
[b] *Psychosocial Oncology and Clinical Practice Research Group, Bexley Wing, St. James's Institute of Oncology, Beckett Street, Leeds, UK*
[c] *Department of Psychology, University of Sheffield, Western Bank, Sheffield, UK*
[d] *Sheffield Children's Hospital, Department of Haematology/Oncology, Western Bank, Sheffield, UK*

ARTICLE INFO

Article history:
Received 22 July 2009
Received in revised form 10 December 2009
Accepted 15 January 2010
Available online 17 February 2010

Keywords:
Childhood cancer
Survivors
Follow-up care
Late effects

ABSTRACT

Background: Survival rates following childhood cancer have increased, but survivors experience significant late effects. Long-term follow-up is recommended but imposes an increasing burden on health services. We report prevalence of morbidity in a cohort of survivors from South Yorkshire based on: (i) case-note analysis and (ii) self-reported late effects (parent-reported for under-16s).

Methods: Treatment information was taken from case-notes. Comparisons were made between late effects described in notes and reported by 108 survivors aged >16 years, and 45 parents of survivors (12–15 years).

Findings: Of 892 patients diagnosed with childhood cancer and some benign conditions registered on hospital databases from January 1990 to December 2005, 337 (37.8%) met eligibility criteria. Ninety-one survivors (⩾16) (84.3%, confidence interval [CI]: 76.0–90.6) reported one or more late effects (mean = 3.5; CI: 3.0–4.1), significantly higher than the number of late effects documented in medical notes (mean = 0.7; CI: 0.5–0.9; $t = -11.26$, $p < 0.001$). Thirty-five parents (77.8%, CI: 65.1–90.4) reported late effects for their children (mean = 2.7; CI: 2.0–3.4), again higher than medical notes (mean = 0.7; CI: 0.4–1.1; $t = 7.18$, $p < 0.001$). More than 30 specialties were involved in survivor care (mean = 1.5; CI: 1.4–1.6; range 0–6). Those with more late effects saw more specialties ($r = 0.51$, $p < 0.001$).

Interpretation: We confirm the wide range of late effects experienced by survivors of child cancer, significantly greater than those recorded in medical notes, and requiring care from a range of specialties. Decisions about follow-up need to take account of patient-reported morbidity and concerns.

1. Introduction

Survival rates following childhood cancer currently approach 80%[1–3] but long-term health problems as a consequence of the original tumour or treatment are common,[4,5] depending on tumour type and on treatment received. Both physical[6] and psychological[7] late effects have been described and can occur decades after treatment completion.[8] Consequently, there have been calls for regular follow-up for survivors.[9] Decisions about follow-up need to take into account

* *Corresponding author:* Tel.: +44 114 222 6621; fax: +44 0114 276 6515.
E-mail address: c.eiser@sheffield.ac.uk (C. Eiser).
0959-8049/$ - see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.ejca.2010.01.022

Table 1 – Proposed levels of follow-up by Wallace et al.[11]

Level	Treatment	Method of follow-up	Frequency	Examples
1	Surgery alone Low risk Chemotherapy	Post or telephone	1–2 years	Wilm's tumours stage I or II Langerhans call histocytosis (single system disease) Germ cell tumours (surgery only)
2	Chemotherapy Low dose cranial irradiation (<24 Gy)	Led by nurse or primary care doctor	1–2 years	Most patients (e.g. ALL in first remission)
3	Radiotherapy except low-dose cranial irradiation	Medically supervised Late effects clinic	Annual	Brain tumours HSCT Patients with stage IV tumours (any type)

increasing numbers of survivors, the time-course of late effects and the need for early detection and treatment.

Based on national practice guidelines,[10] Wallace et al.[11] described a risk stratification approach to define the appropriate content of follow-up (Table 1). This recognises that some survivors need intensive follow-up while others may well be served through primary care. Based on the treatment received, survivors at low risk of late effects can be followed by post or telephone, those at moderate risk by primary care or by specialist nurses and those at higher risk would require follow-up at least annually within a specialist late effects clinic. Preliminary work has shown that survivors can be reliably categorised to one of the three levels and those categorised to higher level report more symptoms and late effects.[12]

However, such stratification systems do not take account of survivors' views about their illness or need for care. Survivors differ in their understanding of the cause and prognosis of their cancer,[13] and their views about the reasons for follow-up care.[14,15] Furthermore, a significant sub-group of survivors experience PTSD (post-traumatic stress disorder) and other anxiety disorders.[16,17] Survivors may be reluctant to be discharged from oncology-based care, and question the competence of primary care doctors.[18] Decisions to change the frequency or intensity of the follow-up therefore need to take into account survivors' views about follow-up and emotional consequences of the illness.

The general aims of this study were to inform current debates about provision of different models of care by considering the appropriateness of stratification based on case-notes analysis and survivor- (or parent-) reported late effects. Specifically, we report (1) a case-note analysis of patients treated at Sheffield Children's Hospital, South Yorkshire, UK between 1st January 1990 and 31st December 2005 and (2) a questionnaire survey of self-reported late effects, with the aims to determine

(i) Prevalence of morbidity (number and type of late effects and medication) and the range of expertise currently involved in the provision of care as documented in medical notes.
(ii) Self-reported late effects (parent-reported for under-16s).
(iii) The association between morbidity reported in medical case-notes and those reported by survivors (or parents of under 16-year olds).
(iv) Associations between risk stratification level, follow-up and late effects.

2. Methods

In Sheffield, all survivors under 16 years are seen in clinics in the Children's Services. This includes a specialist late effects clinic, and transition at approximately 16 years to a specialist Late Effects Service organised at a local adult hospital.[19,20] This is organised by a paediatric oncologist, adult endocrinologist, adult haematologist and clinical nurse specialist in late effects supported by specialists in reproductive medicine and psychiatry. Follow-up care is informed by national guidelines.[10,21] Decisions about the timing of transition are taken on grounds of physical and social maturity and are not based on risk stratification level. Survivors not under the care of Haematology/Oncology (e.g. benign tumours) are followed-up elsewhere.

2.1. *Procedure*

Ethics and other approvals were obtained and eligible patients were identified from databases at Sheffield Children's Hospital. These databases included all the patients diagnosed with childhood cancer and some benign conditions registered on the National Childhood Cancer Register.

2.2. *Case-note analysis*

2.2.1. *Inclusion criteria*

Diagnosis of childhood cancer between 1st January 1990 and 31st December 2005; treatment completed at least 2 years previously; aged $\leqslant$16 years at diagnosis and between 12 and 35 years on 1st February 2008.

2.2.2. *Exclusion criteria*

Recent relapse (within 2 years) or palliative care, Langerhans' cell histiocytosis (LCH) or benign teratomas, no local treatment or follow-up (children < 12 were not recruited as late effects are unlikely to be evident).

Treatment summaries for eligible survivors were written from medical notes up to the most recent clinic letter. Information included diagnosis, date of diagnosis, treatment [(surgery, radiotherapy, chemotherapy and haematopoietic stem

cell transplantation (HSCT)); problems during treatment; end of treatment date; relapses or SMNs (second malignant neoplasms)] and current late effects, medication and consultation with healthcare professionals. The treatment summaries produced for each patient highlight recommended follow-up investigations.

Risk stratification levels based on completed treatment summaries were assigned to each survivor[11] by two coders (N.T.; T.U.). In cases of disagreement, an independent consultant paediatric oncologist made the final decision.

2.3. Survivor-reported late effects

Survivors meeting the eligibility criteria defined above were identified from case-note analysis.

Survivors aged 16–35 years under regular follow-up in secondary care were posted a covering letter and an information sheet, a consent form, a questionnaire and a freepost envelope for return (Fig. 1). For survivors discharged or lost to follow-up, letters were sent to the GP requesting information about their address, health status and ability to give consent. Where appropriate information was obtained, survivors were sent information as described above. Those who did not return the questionnaire within 3 weeks were sent a reminder. To meet ethics requirements, parents of survivors aged 12–16 years were approached by the late-effects specialist nurse (T.U.) or a medical student (N.T.) during a scheduled clinic visit and were asked to participate.

Nine survivors attending clinics within the recruitment period who were not on the databases (because they were initially treated elsewhere) were included. Treatment summaries were written for these patients based on current case-notes. Survivors who had never undergone treatment, who had learning or language difficulties and were unable to complete the questionnaire or who had transferred to another area were excluded.

Treatment summaries were written for these survivors based on current case-notes.

2.4. Measures: late effects

Survivors (over 16) and parents of younger survivors were given a list of 16 common late effects (see Appendix)[14] and asked 'Although many may not be relevant for you, do you now have any of these problems?'

2.5. Data analysis

Data were double entered into Microsoft Excel and were converted to an SPSS database (version 15.0). SPSS and STATA 10.0 were used for all statistical analyses. Descriptive statistics were used to describe the frequency of late effects,

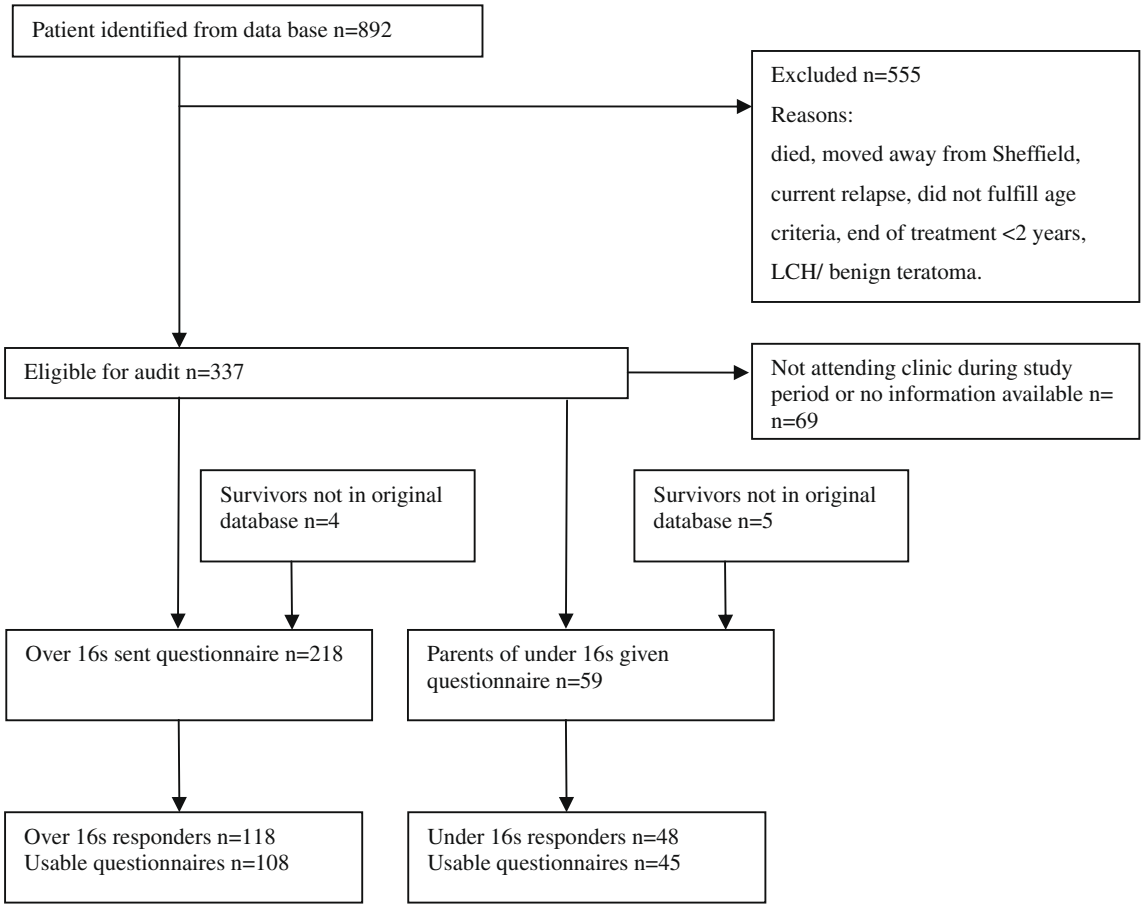

Fig. 1 – Study participation.

number of medications and type of follow-up. Correlations and ANOVAs were used to investigate associations between the number of late effects and other variables. Descriptive analyses, ξ^2- and *t*-tests were used to describe the sample and frequency of survivor/parent-reported late effects. *t*-Tests and ANOVAS were used to compare the survivor/parent-reported late effects. Agreement between late effects documented in medical notes and those reported by survivors/parents were analysed using McNemar tests (where sample sizes were adequate).

3. Results

3.1. *Case-note analysis*

Eight hundred and ninety two patients were registered between 1st January 1990 and 31st December 2005. After applying inclusion and exclusion criteria, 337 (37.8%) remained eligible. Eligible survivors (35.6%, $n = 120$) had been treated for leukaemia, 13.9% ($n = 47$) for lymphoma, 26.7% ($n = 90$) for CNS tumours and 23.1% ($n = 78$) for other solid tumours. Demographic and other medical information are shown in Table 2.

3.1.1. *Prevalence of morbidity from case-notes*

3.1.1.1. Number and type of late effects. For 47 (13.9%) cases, no information about late effects was recorded. Among the remainder ($n = 290$), 54.1% (95% confidence interval (CI): 48.2–60.0; $n = 157$) were recorded as having late effects (mean = 1.4; CI: 1.2–1.6; range = 0–10). Significantly more late effects were recorded for CNS tumour survivors (mean = 2.8; CI: 2.1–3.5) than others (leukaemia: mean = 1.1, CI: 0.7–1.4; lymphoma: mean = 0.8, CI: 0.4–1.3; solid tumours; mean = 0.8, CI: 0.6–1.0; $F = 18.4$; $p < 0.001$).

3.1.1.2. Current medications. No information was available for 14.8% of the sample ($n = 50$). For the remainder ($n = 287$), 39.7% (CI: 34.0–45.6; $n = 114$) were taking regular medication (mean = 1.0; CI: 0.8–1.2; range 0–15). Survivors with more late effects were prescribed more medications ($r = 0.67$, $p < 0.001$).

3.1.1.3. Follow-up. Sixty-one survivors (18.1%) were not receiving secondary care locally (formally discharged to primary care $n = 12$; moved house $n = 12$; previously seen in late effects clinic but no appointments in last 2 years $n = 15$; previously seen by neurosurgeons $n = 8$; no information $n = 14$). The majority of the remaining survivors were receiving follow-up from an oncologist or haematologist, with 55% attending the adult late effects clinic.

After excluding twelve patients who had been formally discharged, most survivors were seen annually ($n = 131$; 48.2%) with 49 (18.0%) seen less frequently and 80 (29.4%) more frequently (Table 5). The information regarding frequency of follow-up was not available for 65 survivors (19.3%). Follow-up was less frequent the longer the time since end of treatment ($r = -0.37$, $p < 0.001$).

A wide range of specialties was involved in survivor care (mean = 1.5; CI: 1.4–1.6; range 0–6). Those with more late effects saw more specialties ($r = 0.51$, $p < 0.001$), but longer since treatment completion was associated with fewer specialties ($r = -0.18$, $p = 0.003$).

Table 2 – Sample demographics.

	Total survivor group		Adult survivors completing questionnaire		Parents completing questionnaire	
	N	%	*N*	%	*N*	%
Total	337		108		45	
Gender: male	191	56.7	51	47.2	22	48.9
Diagnosis						
Leukaemia	120	35.6	38	35.2	23	51.1
Lymphoma	47	13.9	24	22.2		
CNS tumours	90	26.7	24	22.2	8	17.8
Other solid tumours	78	23.1	22	20.4	14	31.1
Treatment						
Chemotherapy	259	76.9	90	83.3	40	88.9
Radiotherapy	94	27.9	30	27.8	15	33.3
Surgery	165	49.0	48	44.4	20	44.4
HSCT[a]	19	5.6	6	5.6	3	6.7
Relapse/SMN[b]	27	8.0	8	7.4	4	8.9
	Mean (95% CI[c])	Range	Mean (95% CI)	Range	Mean (95% CI)	Range
Mean age	19.5 (19.0–20.0)	12.3–34.1	20.8 (20.0–21.5)	16.0–32.6	13.7 (13.4–14.0)	12.0–15.9
Mean age at diagnosis	8.0 (7.6–8.5)	0–16.1	9.0 (8.1–9.8)	0.0–16.0	5.1 (4.2–6.0)	0.2–11.5
Mean time since end of treatment	10.1 (9.7–10.6).	2.5–18.1	10.5 (9.7–11.3)	2.1–18	6.7 (5.8–7.6)	2.9–13.9

[a] HSCT: haematopoietic stem cell transplantation.
[b] SMN: second malignant neoplasm.
[c] 95% CI: 95% confidence interval.

3.1.2. *Self-reported late effects (parent-reported for under-16s)*

3.1.2.1. *Survivors >16 years*. A total of 218 survivors were eligible (214 from case-note analysis) and 118 (54.1%) responded. Ten (4.6%) replied indicating they did not wish to participate. The remaining 108 survivors completed the questionnaires (Table 2). There was no significant difference between responders and non-responders in the number of late effects documented in medical notes ($t = -1.31$, $p = 0.19$), chronological age, age at diagnosis, time since treatment completion or diagnostic group but significantly more females (65.6%) than males (46.1%) returned the questionnaires ($\xi^2 = 8.31$, $p = 0.004$).

Ninety-one survivors (84.3%, CI: 76.0–90.6) reported late effects. There were no differences depending on diagnosis (leukaemia: mean = 3.2; CI: 2.1–4.2; lymphoma: mean = 3.5; CI: 2.4–4.5; CNS tumours: mean = 4.9; CI: 3.7–6.1; solid tumours: mean = 2.8; CI: 1.6–3.9; $F = 2.53$; $p = 0.061$).

3.1.2.2. *Survivors <16 years*. Fifty-nine eligible families (54 from case-note analysis) attended clinic during the recruitment period and 48 completed the questionnaires (81.36%). There were no differences between responders and non-responders depending on gender ($\xi^2 = 0.66$; $p = 0.415$), chronological age ($t = 1.64$; $p = 0.108$), age at diagnosis ($t = 0.60$; $p = 0.550$) or number of late effects as documented in medical notes ($t = -0.24$; $p = 0.81$). The data from 3 families were incomplete. Thus, the information for the final sample was based on 45 parents (40 mothers; 88.9%; Table 2). Thirty-five parents reported late effects in their children. The parents of CNS tumour survivors (mean = 4.4; CI: 2.6–6.2) reported more late effects than the parents of leukaemia (mean = 2.6; CI: 1.6–3.7) or solid tumour survivors (mean = 1.8; CI: 0.7–2.8; $F = 3.4$; $p = 0.043$).

3.1.3. *Relationship between late effects in case-notes and self- or parent report*

3.1.3.1. *Survivors >16 years*. Since a wider range of late effects was recorded in medical notes compared with those of the survivor checklist, comparisons were made only for the overlapping items. Among those over 16 years, 91 survivors reported late effects (mean = 3.5; CI: 3.0–4.1; range 0–16) significantly higher than those documented in medical notes (mean = 0.7; CI: 0.5–0.9; range 0–5; $t = -11.26$, $p < 0.001$) (Fig. 2).

3.1.3.2. *Survivors <16 years*. Thirty-five parents reported late effects in their children (77.8%, CI: 65.1–90.4, $m = 2.7$; CI: 2.0–3.4; range = 0–8), significantly higher than those documented in medical notes (mean = 0.7; CI: 0.3–1.1; range 0–5; $t = 7.18$; $p < 0.001$) (Fig. 3).

3.1.4. *Associations between risk stratification level, follow-up and late effects*

Insufficient information was available to assign a risk stratification level to two survivors (0.6%), and they were therefore excluded from subsequent analyses ($n = 335$). Excellent inter-rater agreement was achieved for 92.6% ($n = 312$) of the sample. An independent paediatric oncologist assigned levels for the remaining 23 survivors (6.8%).

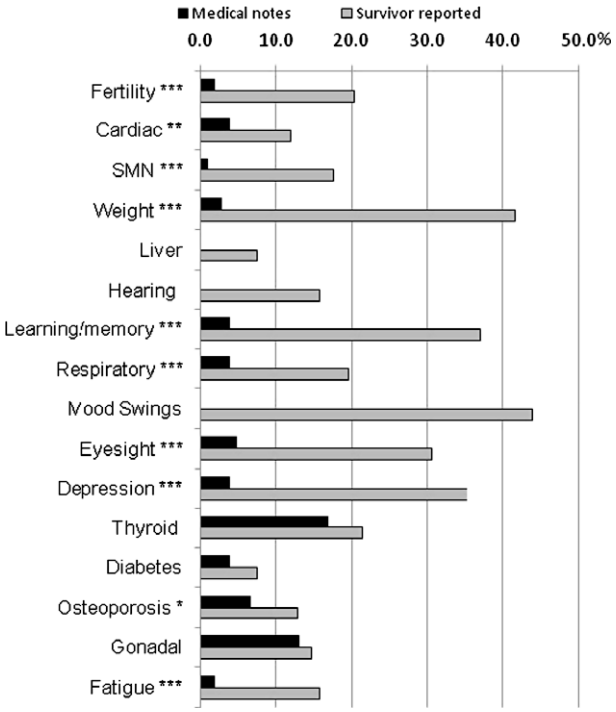

Fig. 2 – Comparison of self-reported late effects and late effects documented in medical notes (over 16s, $n = 108$). McNemar test: $^{*}p < 0.05$; $^{**}p < 0.01$; $^{***}p < 0.001$.

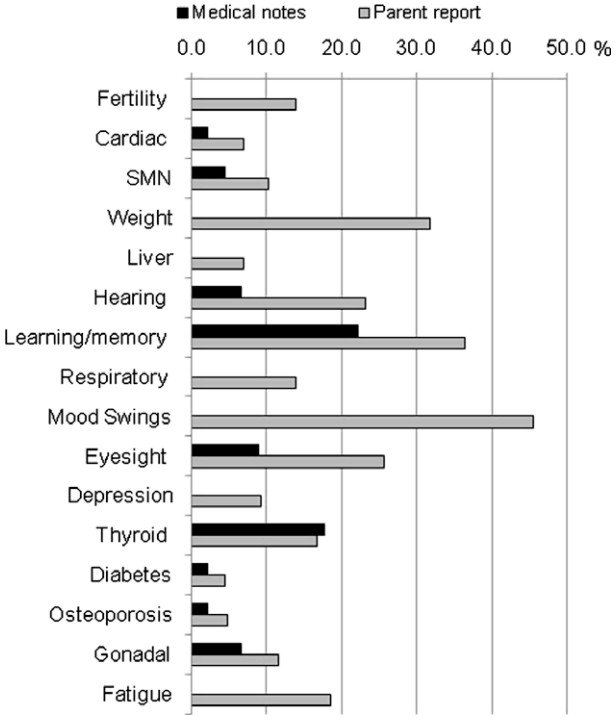

Fig. 3 – Comparison of late effects reported by parents (for under-16s) and that documented in medical notes ($n = 45$).

Level 3 ($n = 99$) survivors had significantly more late effects recorded in medical notes (mean = 3.1; CI: 2.6–3.6) than level 1

Table 3 – Late effects experienced by survivors as documented in medical notes: *n* = 290 (no information for 47 survivors).

Late effect	Level 1 (*n* = 38)	Level 2 (*n* = 160)	Level 3 (*n* = 92)	Total sample (*n* = 290)
No late effects	73.7%	60.0%	6.5%	130 (44.8%)
Endocrine				
Thyroid problems	0	1.3%	43.5%	42 (14.5%)
Growth hormone deficiency	0	0.6%	33.7%	32 (11.0%)
Gonadal dysfunction	0	3.8%	27.2%	31 (10.7%)
Adrenal insufficiency	0	0	19.6%	18 (6.2%)
Diabetes/insulin resistance	0	0.6%	8.7%	9 (3.1%)
Other endocrine problems	0	1.9%	9.8%	12 (4.1%)
Growth problems	0	2.5%	2.2%	6 (2.1%)
Weight gain	0	1.9%	4.3%	7 (2.4%)
Fertility problems	0	1.3%	1.1%	3 (1.0%)
Neuropsychological				
Learning or memory problems	2.6%	5.0%	22.8%	30 (10.3%)
Epilepsy	7.9%	0.6%	6.5%	10 (3.4%)
Other neurological problems	7.9%	5.0%	25.0%	34 (11.7%)
Psychosocial				
Depression	0	3.8%	0	6 (2.1%)
Other psychosocial problems	2.6%	4.4%	6.5%	14 (4.8%)
Fatigue	2.6%	0	2.2%	3 (1.0%)
Sensory				
Poor eyesight/visual deficits	0	2.5%	16.3%	19 (6.6%)
Hearing problems	2.6%	0	5.4%	6 (2.1%)
Organ toxicity				
Cardiac dysfunction	0	6.3%	4.3%	14 (4.8%)
Respiratory dysfunction	2.6%	0.6%	5.4%	7 (2.4%)
GI problems	0	3.1%	8.7%	13 (4.5%)
Kidney dysfunction	2.6%	2.5%	7.6%	12 (4.1%)
Miscellaneous				
Osteoporosis	0	1.9%	9.8%	12 (4.1%)
Urological problems	0	3.1%	3.3%	8 (2.8%)
Musculoskeletal problems	0	5.6%	18.5%	26 (9.0%)
SMNs	0	0	3.3%	3 (1.0%)
Other late effects	0	6.3%	12.0%	21 (7.2%)

(*n* = 55) (mean = 0.3; CI: 0.1–0.5) and level 2 (*n* = 181) (mean = 0.6; CI: 0.5–0.8; $F = 76.03$; $p < 0.001$) survivors (Table 3). They were also prescribed more medications (mean = 2.3; CI: 1.8–2.8) than level 1 (mean = 0.2; CI: 0.0–0.3) and level 2 survivors (mean = 0.4; CI: 0.2–0.6; $F = 46.38$; $p < 0.001$).

More level 1 (*n* = 11) survivors compared with level 2 (*n* = 0) and level 3 (*n* = 1) survivors had been formally discharged from secondary care. Most level one survivors receiving follow-up were seen by a neurosurgeon (15/43; 34.9%) in neuro-oncology clinic (*n* = 6; 14.0%) or by an oncologist alone (*n* = 5; 11.6%). Most level 2 (125/157; 79.6%) and 3 survivors (70/88; 79.5%) were followed-up in an oncology-led late effects clinic (Table 4). Level 3 survivors were seeing more specialties (mean = 1.9; CI: 1.7–2.1) than level 1 (mean = 1.1; CI: 0.8–1.5) and level 2 survivors (mean = 1.4; CI: 1.2–1.5; $F = 12.07$; $p < 0.001$).

Survivors (>16s) in higher risk stratification groups also reported significantly more late effects themselves than those in lower groups (level 1 mean = 2.3, CI: 0.4–4.2; range 0–5; level 2 mean = 3.0, CI: 2.3–3.6, range 0–16; level 3 mean = 5.1, CI: 4.0–6.1, range 0–13; $F(2, 105) = 7.28$, $p = 0.001$). Similar results were obtained for under-16 survivors based on parent-reported late effects (level 1 mean = 1.2, CI: 0.0–2.6; range 0–3; level 2 mean = 2.1, CI: 1.0–3.2, range 0–8; level 3 mean = 3.6, CI: 2.5–4.6, range 0–73; $F(2, 43) = 3.25$, $p = 0.048$).

4. Discussion

In order to inform provision of services, we conducted a case-note analysis and follow-up of a cohort of childhood cancer survivors diagnosed between 1990 and 2005, supplemented by information from survivors and parents of younger children.

Based on the available medical notes, at least one late effect was recorded in notes for 54%; somewhat lower (58–74.5%) than previous work where data were also taken from medical notes.[22,4] Survivors (84.3%) themselves reported at least one late effect, higher than other reports of survivor-reported data (62.3%).[5] Relatively few patients had been discharged. Nearly 60% were followed-up in paediatric or adult late effects clinics and a further 14% by an oncologist or haematologist. Over 75% were followed-up annually or more frequently. Considerably more specialties were involved in patient care, compared with previous reports.[22] This range re-

Table 4 – Percentage of survivors seen by different specialties: *n* = 288 (no information for 49 survivors).

Specialty	Level 1 (*n* = 43)	Level 2 (*n* = 157)	Level 3 (*n* = 88)	Total (*n* = 288)
Formally discharged	25.6%	0	1.1%	12 (4.7%)
Oncology				
Adult late effects clinic	7.0%	65.0%	61.4%	159 (55.2%)
Paediatric late effects	2.3%	14.6%	18.2%	40 (13.9%)
Oncology	11.6%	9.6%	8.0%	27 (9.4%)
Neuro-oncology	14.0%	1.3%	8.0%	15 (5.2%)
Orthopaedic oncology	0	2.5%	0	4 (1.4%)
Neurosurgery	34.9%	1.9%	9.0%	26 (9.0%)
Ophthalmology	7.0%	2.5%	21.6%	26 (9.0%)
Haematology	0	8.3%	1.1%	14 (4.9%)
Orthopaedics	2.3%	4.5%	6.8%	14 (4.9%)
Neurology	4.7%	1.3%	8.0%	11 (3.8%)
Dermatology	2.3%	1.3%	6.8%	9 (3.1%)
Plastic Surgery	2.3%	2.5%	2.3%	7 (2.4%)
Cardiology	0	3.8%	1.1%	7 (2.4%)
Mental health professional	0	2.5%	2.3%	6 (2.1%)
Endocrinology	0	0.6%	6.8%	7 (2.4%)
Urology	2.3%	1.9%	1.1%	5 (1.7%)
Gynaecology	4.7%	1.3%	1.1%	5 (1.7%)
Paediatric surgery	0	2.5%	1.1%	5 (1.7%)
Respiratory medicine	2.3%	0	5.7%	6 (2.1%)
Nephrology	2.3%	0.6%	3.4%	5 (1.7%)
Dietician	0	1.9%	1.1%	4 (1.4%)
Dentistry	2.3%	1.3%	1.1%	4 (1.4%)
ENT	2.3%	1.3%	1.1%	4 (1.4%)
Gastroenterology	0	1.3%	1.1%	3 (1.0%)
Metabolic bone	0	0.6%	2.3%	3 (1.0%)
General surgery	2.3%	(0.6%	1.1%	3 (1.0%)
Audiology	0	0	3.4%	3 (1.0%)
General paediatrics	2.3%	0	1.1%	2 (0.7%)
Physiotherapy	0	1.3%	0	2 (0.7%)
Community paediatrics	0	0	1.1%	1 (0.4%)
Endocrine surgery	0	0	1.1%	1 (0.4%)
General medicine	2.3%	0	0	1 (0.4%)
Speech and language therapy	2.3%	0	0	1 (0.4%)
Immunology	0	0	1.1%	1 (0.4%)
Rheumatology	0	0	1.1%	1 (0.4%)

Table 5 – Association between risk stratification and frequency of follow-up: *n* = 272 (no information for 65 survivors).

Frequency	Level 1 (*n* = 39)	Level 2 (*n* = 151)	Level 3 (*n* = 82)	Total (*n* = 272)
3–6 Monthly	1 (2.6%)	5 (3.3%)	16 (19.5%)	22 (8.1%)
6–12 Monthly	2 (5.1%)	28 (18.5%)	28 (34.1%)	58 (21.3%)
Yearly	24 (61.5%)	74 (49.0%)	33 (40.2%)	131 (48.2%)
2-Yearly	1 (2.6%)	39 (25.8%)	4 (4.9%)	44 (16.2%)
5-Yearly		1 (0.7%)		1 (0.4%)
Open		4 (2.7%)		4 (1.5%)
Discharged	11 (28.2%)		1 (1.2%)	12 (4.4%)

flects the diverse late effects experienced by survivors and the need for multi-disciplinary care.

We found a significant discrepancy between late effects recorded in medical notes and those reported by survivors or parents, especially for those involving very general problems such as mood swings, weight gain and learning problems. There are a number of possible explanations for these discrepancies. Some problems reported by survivors may be managed in primary care and consequently not documented in hospital notes. Psychological problems may simply not be recorded in notes, perhaps because survivors assume it is not appropriate to burden a busy oncologist with such information. It is possible that survivors and parents of younger children misinterpreted the task, and recorded late effects they understood might be a problem in the future. This may explain the relatively high incidence of second cancers

reported by survivors; they reflect concerns about possible future problems. In addition, recurrent disease may be mistaken for second cancer and reported as such by parents and survivors. Our data suggest that reliance on either case-notes or patient report alone is insufficient. Some problems (e.g. learning/memory problems, depression) may be more reliably reported by survivors and are unlikely to be recorded in case-notes.

Discrepancies between survivor-reported late effects and those recorded in medical notes demonstrate the need to routinely consult with survivors and their families. Differences between survivors' reports of late effects and those documented in notes may potentially cause problems if stratified follow-up is routinely adopted. This applies especially to patients who feel that their current or future health is poorer than that might be anticipated by medical staff whose knowledge is based on late effects typical of the specific cancer.

Information in medical notes was sufficient to assign risk stratification for over 99% of patients and inter-rater agreement (over 90%) was excellent. Survivors in higher risk stratification groups had more late effects, were taking more medications and seeing more specialties than those in lower levels. Thus, we provide further support for the comprehensiveness of this system and ease with which survivors can be stratified based on available information.[12]

Reflecting the large number of low-grade CNS tumours included, level 1 survivors had relatively few late effects, supporting the appropriateness of postal or telephone follow-up. Less than two-thirds were receiving regular follow-up in secondary care. However, there was rarely evidence of formal discharge to primary care. A formal discharge letter summarising treatment, current and potential health problems is essential to ensure appropriate follow-up in primary care.

Over 50% of level 2 survivors had no late effects recorded in medical notes. The most common problem was cardiac dysfunction, probably related to the use of anthracyclines.[4] Over 90% of level 3 survivors experienced late effects. Endocrine problems, especially thyroid dysfunction, were prevalent and one in five had learning or memory problems. These must be expected given the large number of patients who receive cranial radiotherapy/TBI following brain tumours or HSCT.

Almost all level 2 and level 3 survivors were receiving regular follow-up with an oncologist or haematologist (including almost three-quarters in late effects clinics), with just over 10% lost to follow-up and only one discharged. Although level 2 and 3 survivors received similar follow-up, level 3 survivors had more frequent appointments and were under the care of more specialties than level 2 survivors.

Study limitations include the fact that the data were collected from a single regional centre. Although a common criticism is that single centre studies are non-representative, we were able to account for all survivors who had survived over a defined period, excluding those who relapsed within the previous 2 years and those moving away and thus lost to follow-up. Inclusion of survivors in relapse would affect the results to the extent that they would be expected to show greater morbidity. Furthermore, given national protocols, there is no reason to suppose that survivors in our clinic differ significantly from the general population of cancer survivors. Thus, our conclusions regarding the needs for follow-up among survivors should be applicable to the population at large.

Response rates for self-report measures were reasonably good (54.1% for survivors over 16 and 81.4% for under-16s and parents) and comparable with previous research,[16,17,23] with male survivors having poorer response rates. The sample did not include children under 12, adults over 35 and those treated before 1990 or after 2005. Those diagnosed before 1990 would have experienced different treatment regimens and lower survival rates. Patients are more likely to become lost to follow-up as age and time since treatment completion increases[24] and so different trends would be expected for patients diagnosed before 1990. Some benign tumours, including teratomas, were excluded, as many of these survivors had never been under the care of a paediatric oncologist. Information about survivors was restricted to notes in Sheffield Children's Hospital and one adult hospital where the late effects clinic is run. Our sample was predominantly white, limiting any generalisation to other ethnic groups. The superior response rate from females is common, and may reflect their greater interest in health issues.[25]

Finally, survivors were only coded into risk stratification levels at one time point based on treatment information. If information about current problems was included, some survivors may fall into different groups. Flexibility between levels has always been considered an integral part of the risk stratification system.[11] It would be useful to compare the relationship between the stratification levels determined in this study with criteria from other schemas such as the Common Terminology Criteria for Adverse Events.[26] However, neither approach takes account of emotional distress consequent on childhood cancer. Eight-year incidence of mental disorders of 18.6% (95% CI: 12.47, 24.8) has been described by Schrag et al.,[27] with significant predictors being cancer diagnosis, age group, treatment and previous mental disorder.

4.1. *Clinical implications*

As might be expected, a significant proportion of level 1 survivors was lost to follow-up, but there was little evidence of formal discharge to primary care. Formal discharge to primary care with clear treatment summaries and guidelines about current and potential health problems is essential to ensure on-going and appropriate care. The potential value of postal or phone follow-up, for survivors or to guide future care, also needs exploration. The wide range of specialties (e.g. neurosurgery, ophthalmology, dermatology) involved in patient care emphasises the continuing burden of cancer survival for patients, costs to the health service and burden on families who must attend multiple hospital appointments.

Our data confirm the wide range of late effects experienced by survivors of child cancer and support arguments for stratified care. The study is unique in linking case-note analysis of late effects with survivors' own reports about experienced morbidity. We conclude that survivors' perceived needs exceed those documented in medical records especially for those that include general problems that may or may not be associated with cancer or its treatment. The patients may be reluctant to raise some of these issues with oncologists[28] and in their turn, oncologists are not always

able to identify depression in their patients.[29] It is therefore essential to consult both medical notes and survivors before instigating changes in follow-up. Discrepancies between medical notes and survivor or parent reports suggest that decisions about follow-up based on case-notes alone will result in underestimates of the extent of morbidity in the survivor population.

Sources of funding

N.T. received a bursary from Yorkshire Cancer Research, K.A. was funded by Weston Park Hospital Cancer Charity and G.M. was supported by the Swiss National Science Foundation [Grant Number PA001-117433/1].

Conflict of interest statement

None declared.

Acknowledgements

We thank Dr. Gillian Levitt for assistance with risk stratification coding, clinic clerks Joanne Smith and Linda Handley for assistance with finding medical information, the Clinical Research Facility at Sheffield Children's Hospital, in particular Wendy Swann for assistance with obtaining appropriate approvals for the study and all the staff at Sheffield Children's Hospital Department of Haematology/Oncology for help and support.

Appendix

Question about late effects

Health problems

Below is a list of common problems that can occur after a serious illness. Although many may not be relevant for you, do you now have any of these problems? Please tick one circle on each line

	Yes, a major problem	Yes, a minor problem	No problem	Not sure
a. Difficulty having children	○	○	○	○
b. Heart problems	○	○	○	○
c. Getting a second cancer	○	○	○	○
d. Putting on weight	○	○	○	○
e. Liver damage	○	○	○	○
f. Hearing problems	○	○	○	○
g. Difficulties with learning or memory	○	○	○	○
h. Lung problems/difficulty breathing	○	○	○	○
i. Mood swings	○	○	○	○
j. Poor eyesight	○	○	○	○
k. Depression	○	○	○	○
l. Thyroid problems	○	○	○	○
m. Diabetes	○	○	○	○
n. Osteoporosis (reduced bone mineral density)	○	○	○	○
o. Damage to testes or ovaries	○	○	○	○
p. Chronic fatigue	○	○	○	○

REFERENCES

1. Magnani C, Pastore G, Coebergh J, et al. Trends in survival after childhood cancer in Europe, 1978–1997: report from the Automated Childhood Cancer Information System Project (ACCIS). *Eur J Cancer* 2006;**42**:1981–2005.
2. Gatta G, Zigon G, Capocaccia R, et al. Survival of European children and young adults with cancer diagnosed 1995–2002. *Eur J Cancer* 2009;**45**:992–1005.
3. Ellison LF, Pogany L, Mery LS. Childhood and adolescent cancer survival: a period analysis of data from the Canadian Cancer Registry. *Eur J Cancer* 2007;**43**:1967–75.
4. Geenen MM, Cardous-Ubbink MC, Kremer LC, et al. Medical assessment of adverse health outcomes in long-term survivors of childhood cancer. *JAMA* 2007;**297**:2705–15.
5. Oeffinger KC, Mertens AC, Sklar CA, et al. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med* 2006;**355**:1572–82.
6. Oeffinger KC, Hudson MM. Long-term complications following childhood and adolescent cancer: foundations for providing risk-based health care for survivors. *CA: Cancer J Clin* 2004;**54**:208–36.
7. Eiser C, Hill JJ, Vance YH. Examining the psychological consequences of surviving childhood cancer: systematic review as a research method in pediatric psychology. *J Pediatr Psychol* 2000;**25**:449–60.
8. Blaauwbroek R, Groenier KH, Kamps WA, Meyboom-de Jong B, Postma A. Late effects in adult survivors of childhood cancer: the need for life-long follow-up. *Ann Oncol* 2007;**18**:1898–902.
9. NICE. Improving Outcomes in Children and Young People with Cancer; 2005. p. 77–80.
10. Skinner R, Wallace W, Levitt G, editors. *Therapy based long term follow-up: practice statement*. UK Children's Cancer Study Group. <http://www.ukccsg.org.uk/public/followup/> [cited 25.03.09].
11. Wallace WH, Blacklay A, Eiser C, et al. Developing strategies for long term follow up of survivors of childhood cancer. *Br Med J* 2001;**323**:271–4.
12. Eiser C, Absolom K, Greenfield D, et al. Follow-up after childhood cancer: evaluation of a three-level model. *Eur J Cancer* 2006;**42**(18):3186–90.
13. Kadan-Lottick NS, Robison LL, Gurney JG, et al. Childhood cancer survivors' knowledge about their past diagnosis and treatment: Childhood Cancer Survivor Study. *JAMA* 2002;**287**:1832–9.

14. Absolom K, Greenfield D, Ross R, et al. Predictors of clinic satisfaction among adult survivors of childhood cancer. *Eur J Cancer* 2006;**42**:1421–7.
15. Earle EA, Davies H, Greenfield D, Ross R, Eiser C. Follow-up care for childhood cancer survivors: a focus group analysis. *Eur J Cancer* 2005;**41**:2882–6.
16. Barakat LP, Kazak AE, Meaddows AT, et al. Families surviving childhood cancer: a comparison of posttraumatic stress symptoms with families of healthy children. *J Pediatr Psychol* 1997;**22**:843–59.
17. Stuber ML, Christakis DA, Houskamp B, Kazak AE. Posttrauma symptoms in childhood leukemia survivors and their parents. *Psychosomatics* 1996;**37**:254–61.
18. Blaauwbroek R, Tuinier W, Meyboom-de Jong B, Kamps WA, Postma A. Shared care by paediatric oncologists and family doctors for long-term follow-up of adult childhood cancer survivors: a pilot study. *Lancet Oncol* 2008;**9**:232–8.
19. Davies H, Greenfield D, Ledger W. Reproductive medicine in a late effects of cancer clinic. *Hum Fertil* 2003;**6**:9–12.
20. Greenfield D, Absolom K, Davies H, Ross R, Eiser C. Childhood cancer survivors: transition from pediatric to adult care. *Curr Med Lit GH Growth Factor* 2003;**18**:83–91.
21. SIGN. Long term follow up of survivors of childhood cancer. A national clinical guideline. In: *Scottish Intercollegiate Guidelines Network* (SIGN); 2004.
22. Stevens MC, Mahler H, Parkes S. The health status of adult survivors of cancer in childhood. *Eur J Cancer* 1998;**34**:694–8.
23. Lee Y-L, Santacroce SJ. Posttraumatic stress in long-term young adult survivors of childhood cancer: a questionnaire survey. *Int J Nurs Stud* 2007;**44**:1406–17.
24. Oeffinger KC. Longitudinal risk-based health care for adult survivors of childhood cancer. *Curr Probl Cancer* 2003;**27**:143–67.
25. Addis ME, Mahalik JR. Men, masculinity and the contexts of help seeking. *Am Psychol* 2003;**58**:5–14.
26. Oeffinger KC, Eshelman DA, Tomlinson GE, Buchanan GR, Foster BM. Grading of late effects in young adult survivors of childhood cancer followed in an ambulatory adult setting. *Cancer* 2000;**88**:1687–95.
27. Schrag NM, McKeown RE, Jackson KL, Cuffe SP, Neuberg RW. Stress-related mental disorders in childhood cancer survivors. *Pediatr Blood Cancer* 2008;**50**:98–103.
28. Detmar SB, Aaronson NK, Wever LDV, Muller M, Schornagel JH. How are you feeling? Who wants to know? Patients' and oncologists' preferences for discussing health-related quality of life issues. *J Clin Oncol* 2000;**18**:3295–301.
29. Passik SD, Dugan W, McDonald MV, Rosenfeld B, Theobald DE, Edgerton S. Oncologists' recognition of depression in their patients with cancer. *J Clin Oncol* 1998;**16**:1594–600.