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Follow-up after childhood cancer: Evaluation of a three-level model

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ABSTRACT

Introduction: Follow-up for cancer survivors is recommended to detect recurrence; monitor late-effects; record toxicity and provide care and education. We describe our experience with a three-level model developed to guide decisions about intensity and frequency of follow-up [Wallace WHB, Blacklay A, Eiser C, et al. Developing strategies for the long term follow-up of survivors of childhood cancer. *BMJ* 2001;**323**:271–274].

Procedure: One hundred and ninety eight survivors (52% male) recruited over 12-months: (mean age = 23.8 years, range = 16–39 years; mean time since diagnosis = 16.2 years, range 2.4–32.7 years) reported their number of symptoms and late-effects. Information was taken from the medical records to assign each survivor to the appropriate levels by six clinic staff independently.

Results: The survivors were assigned to level 1 ($n = 8$), level 2 ($n = 97$) and level 3 ($n = 93$). There were seven cases of disagreement. Level 3 survivors self-reported more symptoms and late-effects than level 2 survivors.

Conclusions: Coding was relatively simple for experienced clinic staff, although there were some disagreements for the survivors of ALL. The relationship between assigned level and self-reported symptoms and late-effects provides some evidence for validity of the model. We conclude that it is important to maintain flexibility to allow movement between levels for individual patients and that the default should always be to the higher level.

1. Introduction

Survival rates in childhood cancer have increased in recent years, so that approximately 75% of children can expect 5-year event free survival.[2] However, typically two-thirds of survivors experience one or more late-effect, varying from the relatively benign through to severe and debilitating.[3,4]

The prevalence and range of late-effects means that regular follow-up of this population has often been recommended. Detailed recommendations regarding surveillance and treatment of late-effects have been reported by working

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groups in the US[5] and UK.[6] As the number of survivors increases, it is impossible to offer follow-up in Paediatrics indefinitely. New models of care are needed to guide decisions about the frequency and intensity of follow-up for individual survivors based on current knowledge of late-effects.

A number of models have been proposed to meet these needs. These include the late-effects normal tissue (LENT) system, which was designed to grade radiation-induced late-effects but does not include those secondary to surgery or chemotherapy.[7] A simple 4-point scale (surgery with or without short chemotherapy protocols); brain tumour surgery and low or standard risk protocols; multiple treatment modalities and high-risk disease; metastatic disease or stem cell transplantation has also been proposed.[8] The Common Toxicity Criteria, Version 2 (CTCv) was developed to compare acute toxicities, but has been successfully modified to grade late-effects.[9]

A relatively simple three-level model, shown in Table 1 and based on expert opinion, has been proposed specifically to guide intensity and frequency of follow-up in childhood cancer.[1] Where initial treatment is limited to surgery or low risk chemotherapy, postal or telephone follow-up is recommended (level 1). Nurse or GP-led follow-up is considered appropriate for those treated with chemotherapy and/or low-dose radiation (level 2), and medically supervised follow-up for those treated with radiotherapy (>24 Gy) or megatherapy (high dose therapy with progenitor stem cell rescue; level 3).

Although the model offers the potential to guide the care of the increasing numbers of survivors, there are a number of questions to be answered before routine use in a clinic setting. These include questions about the ease with which survivors can be graded into one of the three levels, whether the necessary information is readily available and the length of time needed for coding. There is also a question about whether the survivors themselves would agree to changes in the frequency or organisation of their follow-up, or indeed how far the proposed levels reflect differences in symptoms or late-effects as experienced by the survivors themselves.

We therefore describe our preliminary experience with the model. Our aims were to determine the following:

(i) practical value of the model, i.e. to be useful it is essential that appropriate information is easily available in medical records and that coders can use the information in the model to assign survivors to a single level.
(ii) the extent of agreement between different coders.
(iii) the characteristics of any cases that were more difficult to assign to levels.
(iv) the relationship between assigned levels and survivors' own reports about the number of symptoms and late-effects experienced.

2. Materials and methods

2.1. Procedure

We obtained ethics approval and the survivors gave permission for information to be taken from medical records. A standard *pro forma* was developed from individual treatment summaries. Over recent years, we have developed a system whereby this information is routinely available in patient notes. Where treatment summaries were not available, data were extracted from medical records and summaries written. Each *pro forma* included diagnosis, treatment history (diagnosis, age at diagnosis, chemotherapy regimens or protocols, radiotherapy dose and fractionation, relapse status, BMT details, and post treatment complications) and was anonymised. A total of six coders from two participating clinics (three paediatric oncologists and three specialist nurses) were independently asked to assign each survivor to one of the three levels. Survivors self-reported the number of symptoms and late-effects currently experienced from a standard checklist.[10]

2.2. Sample

This is an opportunistic sample including 198 survivors attending routine follow-up at two clinics in South and West Yorkshire, UK, over a 12-month period. There were no significant differences between survivors recruited from the two clinics in terms of sex (males = 52.7%, 51.4%), current age (Ms = 23.3, 23.9 years), age at diagnosis (Ms = 7.4, 7.9 years) and time since diagnosis (Ms = 16.6, 15.9 years). Significantly

Table 1 – Proposed follow-up levels for survivors more than 5 years from treatment[1]

Level	Treatment	Method of follow-up	Frequency	Examples
1	Surgery alone Low risk chemotherapy	Post or telephone	1–2 years	Wilm's tumour stage I or II Langerhans cell histiocytosis (single system disease) Germ cell tumours (surgery alone)
2	Chemotherapy Low dose cranial irradiation (<24 Gy)	Nurse or primary care-led	1–2 years	Most patients (e.g. ALL in first remission)
3	Radiotherapy, except low dose cranial irradiation Megatherapy	Medically supervised late effects clinic	Annual	Brain tumours Bone marrow transplants Patients with stage IV tumours (any tumour type)

more CNS survivors were recruited from the West Yorkshire clinic (12.9% versus 3.8%, $p < 0.05$). Details of the diagnoses are given in Table 2.

2.3. Analysis

Individuals were assigned to a single level based on the agreement between at least 4 of the 6 coders and any disagreements resolved by a seventh independent coder from another centre. Independent *t*-tests were used to compare differences in current age, age at diagnosis and time since diagnosis between survivors, where there was a good agreement between coders and for those, where there was disagreement. To assess inter-rater reliability between coders, we conducted a series of Kappa analyses. Kappa (κ) is a measure of agreement commonly used as a measure of scorer reliability. The values range from 0 to 1, with higher scores indicating greater agreement. Agreement about the Level of follow-up was compared for each pair of coders thus generating 15 kappa scores. We calculated the total number of symptoms and late effects reported by each survivor and compared these to the assigned level using *t*-tests. All analyses were conducted using SPSS, version 10.

3. Results

3.1. Availability of information

Although the amount of information in the medical records and therefore *pro formas* varied, sufficient information was available for all survivors to be assigned to one of the three levels. The task, to assign levels to all 198 survivors, took approximately 2 h for each rater.

Eight survivors were assigned to level 1, 98 to level 2 and 93 to level 3.

3.2. Inter-rater agreement

Kappa scores ranged from satisfactory (0.46) to very good (0.87) (mean = 0.64, see Table 3).

3.3. Characteristics of difficult to assign cases

On initial inspection, we identified 25 cases of disagreement. However, 12 of these were cases of ALL, assigned either to level 2 or level 3. On discussion with coders, the source of disagreement related to the fact that survivors of modern therapies would be assigned to level 2, but patients treated on older protocols who received >24 Gy CNS irradiation would be assigned to level 3. When this was resolved, there were seven remaining cases of disagreement (3.5%). These seven cases did not differ in current age, age at diagnosis or time since diagnosis from the rest of the sample and included a heterogeneous group of patients (Ewing's sarcoma, ALL, Wilm's stage II, Wilm's stage III, pontine glioma, Hodgkins stage IV, ALL t cell).

3.4. Relationship between level and survivor reported symptoms and late-effects

Given the small number of cases assigned to level 1, comparisons were made only between levels 2 and 3. Those assigned to level 3 reported more symptoms (Ms = 1.56; 0.89; $p < 001$) and late-effects (Ms = 0.87; 0.48; $p < .002$) than those assigned to level 2.

4. Discussion

This preliminary study addresses the potential practical value of the model to guide decisions about the type and intensity of follow-up appropriate for survivors of childhood cancer. Our first concern related to availability of the required information. Although past record-keeping was variable, we were able to find the information for all survivors. Where up-to-date treatment summaries were available, coding was reported to be very easy and quick to do. However, this does not include the time previously required to search and extract the data from medical records, or create treatment summaries initially. The value of the model is therefore dependent on the quality of prior record keeping. Coding can be facilitated by the development of structured treatment summaries

Table 2 – Information about diagnosis

Cancer diagnosis	Frequency (%)	Level assigned		
		Level 1	Level 2	Level 3
ALL	58 (29.3)		42	16
AML	10 (5.1)		5	5
CNS tumours	16 (8.1)			16
Renal tumours	21 (10.6)	3	2	16
Hepatic tumours	3 (1.5)		1	2
Osteosarcomas	8 (4.0)		8	
Rhabdomyosarcomas	11 (5.6)		4	7
Gonadal and germ cell tumours	6 (3.0)	1	2	3
Carcinoma and melanoma	2 (1.0)			2
Hodgkin's disease	21 (10.6)		8	13
Non-Hodgkin's lymphoma	16 (8.1)		12	4
Neuroblastoma	6 (3.0)	1	3	2
Ewing's sarcoma	5		4	1
Other	15	3	6	6
Total	198	8	97	93

Table 3 – Inter-rater agreement for level assignment

	Paed Onc 1	Paed Onc 2	Paed Onc 3	Spec Nur 1	Spec Nur 2
Paed Onc 1	–	–	–	–	–
Paed Onc 2	.87	–	–	–	–
Paed Onc 3	.81	.80	–	–	–
Spec Nur 1	.82	.87	.83	–	–
Spec Nur 2	.54	.52	.47	.46	–
Spec Nur 3	.56	.49	.50	.45	.55

with information extracted from medical records on a regular basis. Education and training about the model may be necessary to ensure that the correct information is extracted from records. This will very much add to its value on a day-to-day level.

We achieved considerable agreement between coders who were able to assign 96.5% of the sample to a single level. This was despite the fact that previous medical information was not stored with the goal to facilitate this kind of coding, and that coders received no special training. Given the good agreement, we would recommend that coding can be successfully achieved by an experienced paediatric oncologist working alone, but training is needed for less experienced staff. Critically, some knowledge of past protocols is needed, as this was the single most common cause of disagreements among less experienced staff.

Cases of disagreement were more frequent for ALL patients than other diagnostic groups. Level 2 follow-up for ALL can be problematic. They are numerically the largest group on follow-up, and have good survival. Although these patients do not now receive CNS radiation, they can still have significant late effects. It is important to allow for movement between levels 2 and 3. For example, ALL patients may be treated at level 2 but will need to move to level 3 if a growth problem develops. Where there is disagreement (whatever the level), on designation we recommend that the default should always be to the higher level.

Largely because of the wide range of late-effects experienced by survivors of CNS tumours, they are referred to specialist tumour clinics in adult oncology in both clinics studied. Consequently, the number of survivors assigned to level 3 in our study under-estimate the numbers requiring level 3 follow-up.

We identified few cases assigned to level 1. In one of the clinics studied, many level 1 patients are on 2 or 3 yearly follow-up with questionnaire contact between visits. It may also be that level 1 survivors were already discharged, or discharged themselves, from follow-up care. This suggests that the model is formalising current practice with regard to this group. Critically, there were no cases of disagreement between coders about level one patients. This is vital for these patients if they are to be discharged with confidence.

This was an opportunistic study to the extent that we included survivors who attended clinic over a defined period of time, but past work suggests no difference in diagnostic groups between attenders and non-attenders.[11] Non-attendance rates of 18%[11] and 17%[12] have been reported. It is not known whether non-attenders include a number of level 1 patients who do not feel it necessary to attend follow-up.

There remains a need for the model to be flexible. Follow-up needs to take into account latencies between specific cancers, subsequent late-effects and interactions between treatments and between treatment and individual patient susceptibility.[13] Individuals may also experience late psychological effects at any time,[14] regardless of the initial diagnosis, and for this reason, routine psychological screening has been recommended.[15] These patients may benefit from more intensive and directed follow-up at least for a defined period.

The increasing number of survivors poses a challenge for the delivery of a paediatric-based follow-up service. We conclude that the model[1] is reliable and easy to use, with a potential to guide decisions and ensure that the survivors are managed appropriately. The system is robust, and relatively simple to use by experienced oncologists and specialist nurses. We provide the first evidence for the validity of the model by demonstrating a relationship between allocated level and survivors' own reports of their symptoms and late-effects.

Ultimately, if changes to follow-up are to be made, it is important to determine the acceptability of these recommendations to survivors, i.e. would survivors accept more or less frequent follow-up than they currently experience? Typically, survivors are satisfied with the care they are offered and are reluctant to change.[10,16] In order to implement changes to the intensity or frequency of follow-up, it will be necessary to address survivors' concerns and prepare them adequately.

Conflict of interest statement

We declare no conflicts of interest.

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