

Models of Care for Follow up of Childhood Cancer Survivors: A Systematic Review

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LIST OF ABBREVIATIONS

CCLG	Children's Cancer & Leukaemia Group
CDSR	Cochrane Database of Systematic Reviews
CENTRAL	Cochrane Central Register of Controlled Trials
CINAHL	Cumulative Index to Nursing and Allied Health Literature
CYP	Children and Young People
CRD	Centre for Reviews and Dissemination
DARE	Database of Abstracts of Reviews of Effects
FU	Follow up
GP	General practitioner (UK)
HMIC	Health Management Information Consortium
HRQOL	Health-related quality of life
HTA	Health Technology Assessment Database
ICRP	International Cancer Research Portfolio
LTFU	Long-term follow-up
MASCC	Multinational Association of Supportive Care in Cancer
NCSI	National Cancer Survivorship Initiative
NHS EED	NHS Economic Evaluation Database
NICE	National Institute for Health and Clinical Excellence
NIHR SDO	National Institute for Health Research Service Delivery and Organisation programme
PONF	Paediatric Oncology Nurses Forum
SIGN	Scottish Intercollegiate Guidelines Network
SIOP	The International Society of Paediatric Oncology
UKCCSG	United Kingdom Children's Cancer Study Group

GLOSSARY OF TERMS

Adverse event	Any untoward medical occurrence in a patient administered a treatment which does not necessarily have a causal relationship with the treatment
Alternative communication modalities	Telephone, postal, email or SMS/text-based methods of communication
Chemotherapy	The use of cytotoxic agents to treat cancer
Central nervous system	The portion of the nervous system comprising the brain and spinal cord
Childhood cancer	Cancer diagnosed in a person younger than 18 years of age
Intention-to-treat analysis	An analysis based on the initial treatment intent, not on the treatment actually administered
Late effects	Side effects that may potentially arise after a period of time as a result of therapeutic exposures used during treatment for malignancies
Low risk chemotherapy	Chemotherapy that does not include the use of alkylating agents or anthracyclines
Megatherapy	High dose chemotherapy that requires stem cell rescue following treatment
Meta-analysis	A method of combining the treatment effects in studies to produce an overall summary of the treatment effect across studies
Quality of life (Health-related quality of life)	A concept incorporating all the factors that might impact on an individual's life, including factors such as the absence of disease or infirmity as well as other factors which might affect their physical, mental and social well-being
Randomised controlled trials	A type of experiment that is used to compare the effectiveness of different treatments by assigning patients at random to either the intervention of interest or to a comparison treatment
Survivor/survivorship	Someone who is living with or beyond cancer

1. Executive Summary

Background

Childhood cancer is very rare; in developed countries approximately 0.5% of all cancers occur in children aged 15 or under. Nevertheless, in the UK cancer accounts for approximately 20% of all deaths in children up to 14 years of age and each year approximately 1,400 new cases of childhood cancer are diagnosed. Following childhood cancer 60% of people who are more than 5 years from completion of therapy will experience at least one or more treatment- or disease-related late effects; over 30% of these problems are moderate or severe.

A wide range of models of care for survivors of cancer have been developed and previous reviews have focussed primarily upon the effectiveness of alternative approaches in the adult cancer population.

Objectives

It remains a matter of current debate as to the most effective mode of follow-up; this review aimed to examine the following:

- a comparison of alternative communication modalities to face-to-face clinic visits (for example telephone, postal, email or SMS/text-based)
- the use of physician- vs. nurse-led follow-up
- the value of hospital staff vs. primary care staff to provide clinical contacts

Methods

A systematic review was conducted. The following databases were searched from 1980 to February 2010: MEDLINE, Cochrane databases of reviews and trials (CDSR and CENTRAL), DARE, NHS EED, Health Technology Assessment (HTA) Database, PsycINFO, Health Management Information Consortium (HMIC), CINAHL, Current Controlled Trials, American Society of Clinical Oncology, National Cancer Institute Clinical Trials and International Cancer Research Portfolio. Supplementary internet and hand searches were also performed and experts were contacted.

To be included the studies had to be of survivors of cancers diagnosed by 18 years of age receiving follow-up or aftercare commencing after primary treatment had ceased. The interventions were as listed above: communication modalities, health professionals delivering the care or healthcare setting. Eligible outcomes comprised patient experience, percentage response to the contact and patient satisfaction, as were comparative rates of detection of morbidity (for example, cardiac dysfunction), secondary malignant neoplasm and mortality rates. Comparative data from retrospective or prospective groups were the focus of the review, but uncontrolled studies which included practice audit/evaluations were also documented.

Results

Our literature search yielded 4,010 studies, of which 266 references were considered potentially relevant to our research question and the full papers were sought for scrutiny. Of

these, six papers were ordered, but were not acquired, and of five foreign-language papers only one (in Japanese) could not be assessed.

We were unable to identify any controlled studies which evaluated the methods of interest of providing follow-up care for survivors of childhood cancer.

Eight observational, single arm or audit-style studies were identified that would otherwise have met our inclusion criteria and were assessed as part of this review. These included studies were broadly grouped according to the model of follow-up being evaluated.

Risk-based follow-up or problem oriented follow-up appears to be a common strategy. The observational studies identified broadly suggest that patients who are not routinely followed-up may in fact benefit from problem-oriented or informal follow-up programmes. Even where patients feel they are not showing late-effects signs there may be relevant complications which will benefit from medical attention.

A study of a shared care model combining hospital clinic-based with family doctor provision was found to be both feasible and acceptable to the majority of both patients and family doctors. The paper represents an important step in prospective evaluation of service provision, and highlights the need for comparative studies in this area. The multidisciplinary clinic model appears to overcome the gap for patients with multiple late-effects where an annual visit or 'traditional late effects clinic' is not sufficient. An audit of patient satisfaction showed families were unanimously satisfied and would use the clinic again; responders also identified benefits around scheduling appointments.

In three studies of hospital-based late-effects clinics it was apparent that the clinics varied in their aims and the services provided. All appeared to offer access to more than one health care professional (usually a specialist nurse plus a physician or consultant), and seem to be a reduced version of the newer multidisciplinary clinic models.

One study that compared predictors of patient satisfaction in attendees of a traditional paediatric late-effects clinic and a multidisciplinary adult setting clinic found that survivors were satisfied with the care they were receiving; there was no evidence that either group was more or less informed or felt at-risk of future problems. Survivors who understood the purpose of follow-up care was for clinical support were more satisfied than those expecting psychological support. It was aspects of clinic organisation rather than setting or clinic type which seemed to influence patient satisfaction.

Given the heterogeneity of the evaluation tools and follow-up programmes, it was difficult to draw any overall conclusions as to benefits or perceived patient needs. A variety of models of care have been explored and evaluated; to date these have been largely observational in nature. These studies reported that clinical care was valued highly by the majority of follow-up clinic attendees, whilst supportive care was perceived as more important by patients who required more interventions and were experiencing more late-effects symptoms. There was a contrast between a report showing patients who were not followed-up may have been receiving inadequate care both in terms of their perceived satisfaction and detection of late-effects which require treatment, and further reports demonstrating efficacy of stratified follow-up, where for a sub-group of patients, long-term follow-up is not an essential part of care.

Conclusions

Despite a rigorous search for studies of relevant designs we were unable to identify any controlled studies that evaluated methods of providing follow-up care for survivors of childhood cancer. From the small number of studies that would otherwise have met our inclusion criteria it was difficult to draw any overall conclusions as to benefits or perceived patient needs. However, it appeared that clinical care was valued highly by the majority of

follow-up clinic attendees; supportive care was perceived as more important by patients who required more interventions and were experiencing more late-effects symptoms. There were contrasting findings between a report showing 'missed' diagnoses when non-attenders were recalled and assessed, and further reports demonstrating efficacy of stratified low intensity follow-up. These studies were not formally quality assessed therefore caution is advised when considering these findings.

Implications for Research

Whilst there has been a prevailing view that survivors of childhood cancers should be followed-up for life it is unclear whether this is necessary or beneficial. The literature to date does not appear to provide answers for the follow-up of people diagnosed with cancer during childhood.

Ideally, suitably powered, well-conducted, controlled trials of adequate duration that directly compare the interventions and comparators specified within this review would be required to provide robust evidence on the optimal follow-up or aftercare for these patients. These trials should be conducted in appropriate settings and should focus upon deriving meaningful outcomes. Most studies within this review appear to only report satisfaction with service, whereas relevant outcomes should also focus upon patient experience, detection of morbidities and mortality rates. The economic implications of these interventions should also be assessed given the resource implications of providing care and services over a protracted timeframe.

This review has highlighted that there may be opportunities to undertake research in the following areas:

Primary research:

- There is a clear need for follow-up programmes to be evaluated using comparative study designs.
- Risk stratification may be particularly relevant, published guidelines advocate a stratified follow-up programme although there has been no evaluation of these recommendations to date.

Secondary research:

- Based on the screening and sifting stages, it appears that there may be sufficient research to warrant systematic reviews on the effectiveness of interventions aimed at preventing or reducing harmful behaviours in survivors of childhood cancers. Such areas could include:
 - Health promotion
 - Smoking prevention/cessation
 - Alcohol/substance abuse
 - Diet
 - Sexual health

An appropriate priority-setting exercise should be conducted to assess which, if any, aspect of these health promotion strategies could be subject to systematic review. Such a review should explicitly draw on evidence from other chronic diseases to maximise the value of the information collected.

2. BACKGROUND

2.1 Childhood cancer and survival

Childhood cancer is very rare; in developed countries approximately 0.5% of all cancers occur in children aged 15 years or under. In the UK, cancer accounts for approximately 20% of all deaths between the ages of 1 and 14 years and each year approximately 1,400 new cases of childhood cancer are diagnosed.^{1,2}

Cancers diagnosed during childhood differ in distribution according to age at diagnosis. The most common is acute lymphoblastic leukaemia which accounts for a quarter of all childhood cancers. Lymphomas, brain and spinal tumours, embryonal tumours, bone tumours, soft tissue sarcomas, germ cell and gonadal tumours and carcinoma and melanoma are also seen in children. The occurrence of childhood cancer also varies according to gender and is approximately 20% higher in boys than in girls.¹

There is no evidence that the incidence of childhood cancer has changed substantially in recent years, however improvements in the precision of diagnosis, therapy and supportive care has led to increasing survival rates since the 1960's (Figure 1). Around 75% of all childhood cancer patients diagnosed between 1992 and 1996 in the UK survived for at least five years after diagnosis, compared with just 25% of children diagnosed between 1962 and 1971.^{2,3} This has resulted in greatly increased numbers of adult survivors of childhood cancer; in 2000 there were almost 15,000 adult survivors, 45% of whom were aged 30 years or more.^{1,2} Little is known about the long-term consequences of therapy and the need for long-term surveillance has been identified in order to better characterise late-effects specific to this group of people.³

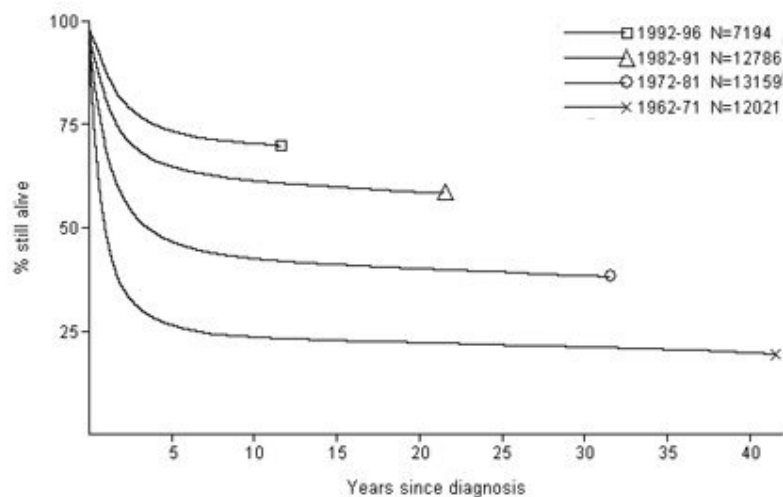


Figure 1: Five-year survival rates for childhood cancers, showing cumulative improvements for patients diagnosed in successive periods, Great Britain 1962-96²

2.2 Late effects of childhood cancer

Children who survive childhood cancer may be more likely to experience late-effects as a result of intensive multi-modality therapeutic strategies, e.g. surgery, radiotherapy, chemotherapy and combinations of these. These multi-treatment strategies often result in physical and psychosocial effects that have the potential to increase morbidity and mortality

amongst this group compared with the overall population.⁴ For the exponentially increasing cohort of cancer survivors the potential cost of cure needs to be addressed alongside actuarial survival. Equally, as overall survival increases, subsequent modifications in therapies are likely to result in smaller improvements in survival. Consequently, the need to balance the risk of late adverse effects against potential gains in duration of survival will become increasingly important.

There are a number of possible late effects of treatment that can have a large impact on long-term survival and quality of life. These can vary from physical health effects, such as second primary tumours (present in around 4% of survivors), secondary leukaemia (around 0.2% of survivors), cardiovascular disease as an effect of radiation and chemotherapeutic agents (or as an indirect effect) and effects on fertility and growth, educational, behavioural and social problems.⁵ Survivors may also lack knowledge of their diagnosis, treatment and potential late-effects.⁶ Unhealthy lifestyle behaviours may further increase the risk of organ dysfunction and malignancy.⁷

Following childhood cancer 60% of people who are more than 5 years from completion of therapy will experience at least one or more treatment- or disease-related late effect of therapy; over 30% of these problems are moderate or severe.⁸ Physical, mental or social aspects of health may be affected which could interfere with survivors' autonomy.⁹ These late-occurring effects may not become apparent until many years after cancer therapy has ceased.¹⁰

2.3 Follow-up

The late-effects of cancer treatment in childhood have the potential to be of substantial cost to the healthcare system. Timely and appropriate management of such individuals may be facilitated by effective surveillance, though the benefit and cost of this is still uncertain.^{11, 12} The need for a successful transition from paediatric to adult healthcare providers with appropriate expertise has also been identified in several studies.^{13, 14}

There is a growing recognition of the need for lifelong follow-up in order to improve detection of the late-effects of treatment and to provide information and advice to childhood cancer survivors.^{13, 15} The National Institute for Health and Clinical Excellence (NICE) has made a number of recommendations which include the following:

- each children's cancer treatment centre should have at least one clinician with expertise in management of late-sequelae in childhood cancer survivors
- patient care and review should be provided by a multidisciplinary team with good communication between paediatric and adult and age-transitional services
- there should be robust and appropriate surveillance of survivors; an appropriate key worker should be assigned to each survivor and care plans should be devised for them.¹⁶

These messages are supported by recommendations by the Scottish Intercollegiate Guidelines Network (SIGN) and the Children's Oncology Group, which both provide guidance for follow-up^{17, 18} and concord with professional guidance from the Children's Cancer & Leukaemia Group (CCLG, formerly UKCCSG) that all survivors of childhood cancer should receive lifelong follow-up.⁵

Nonetheless, there remains a lack of consensus regarding the optimal setting and strategy for follow-up for survivors of childhood cancer.¹⁷

The most common method of follow-up in the UK is a cancer centre-based approach with a strong emphasis on paediatric oncology.¹¹ Some centres have developed age-stratified clinics (though many are situated in paediatric units). As the development and nature of late

effects depend on the type of treatment previously received, the needs of the childhood cancer survivor can vary greatly between individuals and the type of expertise needed can also differ. Additionally, in clinical practice, not all childhood cancer survivors are currently undergoing long-term follow-up as many were discharged based on clinician experience.¹¹ There are guidelines regarding the frequency and possible modes of follow-up according to predicted long-term follow-up needs for different patient groups and treatments, though there is little available evidence to support these recommendations (Table 1).^{5,17}

Level	Treatment	Method of follow-up	Frequency	Examples of tumours
1	Surgery alone Low risk chemotherapy	Post or telephone	1-2 years	Wilms' tumour stage I or II Langerhans cell histiocytosis (single system disease) Germ cell tumours (surgery only)
2	Chemotherapy Low dose cranial irradiation (<24Gy)	Led by nurse or primary care doctor	1-2 years	Most patients (e.g. acute lymphoblastic leukaemia in first remission)
3	Radiotherapy, except low dose cranial irradiation Megatherapy	Medically supervised late effects clinic	Annual	Brain tumours After bone marrow transplant Patients with stage IV tumours (any tumour type)

Table 1: Proposed levels of follow-up ^{5,17}

In recent years, particularly in the USA, nurses have conducted long-term follow-up after specific training and experience. This approach is less common in the UK but recognised to be an area where nurses will have a significant role to play in the future.^{19, 20} Transition models have also been implemented in some paediatric oncology centres (mainly in the USA). These are intended to enable survivors to maintain optimal physical health and achieve their full psychosocial, educational and vocational potential and involve the transition of care to a more age-appropriate provider at a defined age, commonly after a period of joint care.^{11, 14} Community care based in primary care settings (usually with a focus on adult care), oncology care for adults in hospital-based clinics or a combination of these models are also possible. Patient-driven follow-up (whereby the survivor is responsible for seeking medical care when particular symptoms are present) is another possible model for follow-up suggested, although this has major implications for patient education.¹¹

2.4 Previous systematic reviews

A recent systematic review by Aslett *et al.*¹⁵ investigated current long-term follow-up practices for survivors of childhood cancer. This review found that there were variety of models of care utilised. There was also a lack of consistency in practice and variation in the level and degree to which long-term survivors were followed up.

Two reviews have compared different follow-up strategies in cancer survivors of any age; one review examined differences between primary and secondary care and the other examined patients' and healthcare professionals' views about cancer follow-up.^{21, 22} These reviews concentrated on adult cancers, while they did not explicitly exclude children the searches were not targeted to this population. No reviews have been located which compare the effectiveness of different modes of follow-up specifically in survivors of childhood cancer.

2.5 Aims

The current review sought to identify the evidence on the effectiveness of: alternative approaches to communication for follow-up; healthcare professionals delivery of follow-up care and the setting of follow-up care. The review aimed to influence clinical practice and identify key areas and approaches for future research.

2.6 Objectives

The key questions which this review aimed to answer in relation to survivors of childhood cancer were as follows:

- 1) Are alternative communication modalities of follow-up more effective than face-to-face clinic visits (for example telephone, postal, email or SMS/text-based)?
- 2) Which is more useful: physician- vs. nurse-led follow-up?
- 3) Are there differences between hospital staff vs. primary care staff providing clinical contacts at follow-up?

3. REVIEW METHODS

3.1 Searching for the evidence

A detailed search strategy was developed to ensure that as many relevant sources of data as possible are located. The search strategy comprised the following main elements:

- Searching of electronic databases and appropriate electronic resources
- Contact with experts in the field
- Scrutiny of bibliographies of included studies and existing reviews

3.1.1 Search strategy

Searches to identify relevant studies were undertaken during January and February 2010 on the following databases. No language limits were applied. Since follow-up studies first appeared in the mid 1980's, a date limit was used to retrieve studies published between 1980 and the current day in order to minimise the presence of irrelevant papers. Full details of the search strategies are reported in Appendix 1.

The following databases were searched:

- Ovid MEDLINE and Ovid MEDLINE In Process And Other Non-Indexed Citations (Ovid Online – www.ovid.com)
- Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effects (DARE), Cochrane Central Register of Controlled Trials (CENTRAL), NHS Economic Evaluation Database (NHS EED), Health Technology Assessment Database (HTA) (The Cochrane Library - www.thecochranelibrary.com/)
- PsycINFO (Ovid Online – www.ovid.com)
- HMIC Health Management Information Consortium (Ovid Online – www.ovid.com)
- CINAHL (EBSCO www.ebscohost.com/)
- Current Controlled Trials (MRCT Register) (Internet – www.controlled-trials.com/)

Searches were also undertaken on the following Internet resources.

- American Society of Clinical Oncology - www.asco.org
- National Cancer Institute Clinical Trials PDQ - www.cancer.gov/Search/
- International Cancer Research Portfolio (ICRP) - www.cancerportfolio.org/

3.1.2 Terminology

The search terms were identified through discussion between the Information Specialist and the rest of the research team (which included a paediatric oncologist). Relevant papers on the subject were also utilised as potential sources for search terms (in particular, some of the papers on the follow-up of cancer survivors written by Ruth Lewis *et al*²¹⁻²³).

To retrieve a focussed set of records we were careful to avoid the use of terminology that is generally associated in the literature with survivors of adult cancers. For this reason terms such as “check-up” and “carcinoma” were avoided.

3.1.3 Choice of databases

As is common in reviews that cover a range of disciplines, there were a large number of potentially relevant databases that could have been searched but it was considered more efficient to search a limited number of databases effectively. For instance, it was decided not to search EMBASE as well as MEDLINE due to the substantial overlap in material and potential for increasing the number of irrelevant records.

The final database selection was made to include representatives from general medicine, psychology, and nursing as well as ongoing trials and other “grey” literature.

3.1.4 Choice of Internet resources

There are many web sites that would seem to be candidates for inclusion based on their subject matter but that did not contain information of the type we required (for instance The International Society of Paediatric Oncology, SIOP; www.siop.nl/ and the Multinational Association of Supportive Care in Cancer, MASCC; www.mascc.org/). Therefore the final selection of Internet resources for formal searching was made on content and searchability, rather than for their relation to the subject alone.

3.1.5 Contacts

Along with extensive database and hand searching, we also contacted known experts in the area of follow-up in paediatric cancer who have published papers, position pieces and descriptions of service provision. Members of the advisory group for this review (see Section 7) were asked for any relevant references which might be eligible for inclusion, and appeals for relevant papers were made at earlier NCSI workshops.

3.3.1 Population

Survivors of cancers diagnosed by 18 years of age were eligible. Previous reviews by Lewis *et al.* included patients of any age but the main cancers investigated were specific to adults (for example, breast cancer).^{24, 25} The present review aimed to focus on issues specific to cancers diagnosed in childhood. Any type of cancer was eligible for inclusion.

3.3.2 Intervention and comparators

Studies of follow-up or aftercare commencing after primary treatment has ceased were of interest. The interventions were considered as three questions:

- 1) a comparison of alternative communication modalities to face-to-face clinic visits (for example telephone, postal, email or SMS/text-based)
- 2) the use of physician- vs. nurse-led follow-up
- 3) the value of hospital staff vs. primary care staff to provide clinical contacts

3.3.3 Outcomes

Patient experience, percentage response to the contact and patient satisfaction were eligible for inclusion, as were comparative rates of detection of morbidity (for example, cardiac dysfunction), secondary malignant neoplasm and mortality rates. Any economic outcomes reported would have been extracted but an economic analysis was not planned.

3.3.4 Study Designs

This review intended to include studies which presented comparative data from retrospective or prospective groups. Due to the paucity of research in this area uncontrolled studies which included practice audit/evaluations were also documented.

3.4 Data extraction strategy

Data were to be extracted independently by one reviewer, using a standardised data extraction form, and checked by another. Discrepancies would have been resolved by discussion, with the involvement of a third reviewer when necessary. Attempts would have been made to contact authors for missing data. Data from multiple publications of the same study would be extracted and reported as a single study.

Extraction was intended to include data on: study details (e.g. study identifier, author, year, country, setting, number of participants) patient characteristics (e.g. age, gender, cancer site and stage), intervention (full details of the follow-up package and delivery, duration and points of initiated contact if relevant), comparison (type of comparison with full details of follow-up strategy), study quality, study design, and relevant outcomes (morbidity detection rates, response rates, measures of patient satisfaction, relevant costs). A sample data extraction proforma is shown in Appendix 2.

Uncontrolled single-arm observational studies were documented by one reviewer and checked by a second using broadly similar headings to those listed for data extraction.

3.5 Quality assessment strategy

Study quality was not used as a criterion for the inclusion or exclusion of studies from the review; quality assessment of studies was to be conducted as part of the data extraction process. The quality of the individual studies was to be assessed by one reviewer, and independently checked for agreement by a second. Any disagreements were to be resolved by consensus and if necessary a third reviewer would have been consulted.

Criteria for quality assessment were derived from CRD's guidance on undertaking reviews of effectiveness and NICE public health guidance.^{26, 27} A 14 item checklist was constructed to assess the quality of randomised controlled trials, an 8-item checklist for non-randomised studies and a 6-item checklist for qualitative studies. Criteria for the controlled trials comprised some elements specific to childhood cancer.²⁸ The proposed quality assessment criteria are reported in Appendix 4.

3.6 Methods of analysis/synthesis

Due to the lack of eligible primary studies a full analysis was not possible. Data extracted from the included studies would have been tabulated and discussed in a narrative review. The results of the quality assessment would have been tabulated, and where possible, the effect of study quality on effectiveness data and the findings of the review were to be discussed. Where appropriate, meta-analysis was to be employed to estimate a summary measure of effect on relevant outcomes based on intention to treat analyses. Meta-analysis would have been carried out using fixed and random effects models as appropriate using suitable software. Heterogeneity would have been explored through consideration of the study populations, methods and interventions, by visualisation of results and, in statistical terms, by the I^2 statistic. If the evidence allowed, meta-analysis may have been carried out comparing follow-up strategies.

Data extracted from the studies retained despite not meeting study design criteria were tabulated and discussed in a narrative review. No quality assessment was carried out for these studies. The narrative summary covers the nature of the follow-up care offered, how it was evaluated and the resultant outcomes. Studies were grouped according to the type of FU care and setting offered. Comparisons were drawn between and within categories where possible. Recommendations for further research have been made as a result of gaps in the evidence base and the existing observational data.

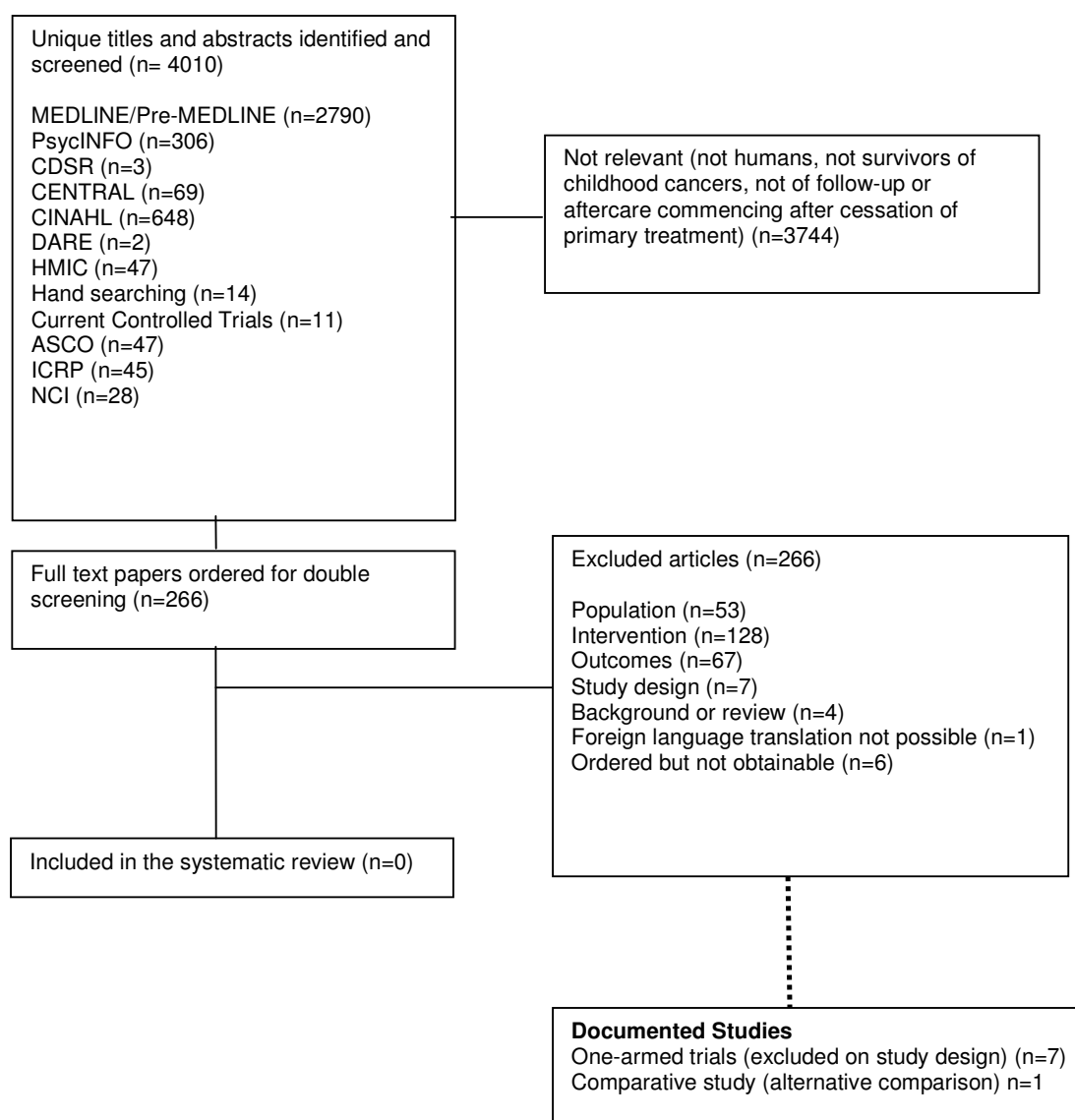
3.7 Advisory Group

An advisory group comprised four clinical and methodological advisors (see Section 7 for details). We also included patient representatives by contacting survivors via Faith Gibson and the Children and Young People (CYP) Survivor Group. Two individuals expressed interest and were sent an article on how to read a systematic review, copies of the protocol and final report for their comments. Both representatives provided feedback verbally and one also contributed written comments.

4. Studies included in the review

Our literature search yielded 4,010 studies, of which 266 references were considered potentially relevant to our research question and full papers were scrutinised. Of these six papers were ordered, but were not acquired (Appendix 4), and of five foreign-language papers only one (in Japanese) could not be assessed.

Figure 3: Flowchart of study inclusion



5. RESULTS

We were unable to identify any comparative studies which evaluated methods of providing follow-up care for survivors of childhood cancer. Where observational, single arm or audit-style studies were identified that would otherwise have met our inclusion criteria, these references were retained and are described below. These studies do not directly answer the review questions but they do illustrate the nature of the research currently available and highlight areas for future development.

5.1 Description of Studies

A total of eight papers were retained despite not meeting the study design inclusion criteria with the intention of reflecting the evidence base as it currently stands.²⁹⁻³⁵ All but one of these papers were available as full publications, the final study was published only as an abstract reporting provisional results.²⁹ In the main, these studies were feasibility or audit type studies which aimed to clarify whether a particular service design was feasible, and if patients found it useful. There was also one study which compared predictors of satisfaction in two clinics, one in an adult setting versus one in a traditional paediatric late effects clinic.³⁶ Fuller details of these studies are given in Tables 2 and 3.

Participants were largely convenience samples of patients already attending/recently referred to the clinics under evaluation,³¹⁻³⁵ or in two cases patients who were not currently being followed up for various reasons.^{29, 30} All were survivors of cancer diagnosed in childhood; where this definition was explicit, the diagnosis had to have been made before the age of 16 or 17 years in most cases. In general all childhood cancers were included in the samples with only one study excluding central nervous system tumours.³¹ Sample sizes of survivors were small to moderate (42 to 245 patients) and response rates to both invitations to attend and return of questionnaires varied considerably. The low response rate in Chan *et al.* has not been considered here as the only data available is from a preliminary abstract.²⁹

The follow-up models under evaluation varied from risk or problem-based care,^{29, 30} new multidisciplinary clinics,³² shared care between hospital and family doctors³¹ and late-effects hospital based clinics.³³⁻³⁵

The single comparative study compared follow-up settings where care was delivered in either a traditional paediatric late effects clinic or a multi-disciplinary adult clinic, both of which were hospital based.³⁶ This study was included to provide as comprehensive a picture of the evidence base in this area as possible, although we acknowledge it does not directly answer our research question.

The outcomes measured included knowledge about the purpose of follow-up, late-effects symptoms, satisfaction with the service (views of patients, families and doctors) and preferences for future follow-up care. Where details of the evaluation methods were reported these appeared to be internally compiled questionnaires which used a combination of symptom or side-effect lists and Likert rating scales. Only one of these measures was reported as having been validated or piloted,³³ making it difficult to assess the reliability or accuracy of the findings.

Table 2: Table of documented studies

Focus	Studies	N of participants
Problem-oriented and informal follow-up ^{30 29}	2 audits of patients not attending FU or discharged	428 patients
Shared-care model ³¹	1 observational study of randomly selected patients	121 patients 115 doctors
Multidisciplinary clinic ³²	1 observational study of patients offered appointments at new clinic	130 patients
Late effects hospital based clinic ^{33 34 5}	3 studies; one cohort, one observational, one audit	274 patients
Adult versus paediatric hospital clinic ³⁶	1 comparative study looking at predictors of satisfaction	198 patients

5.2 Summary of findings

The included studies have been broadly grouped according to the model of follow-up being evaluated.

5.2.1 Problem-oriented and informal follow-up

As outlined in the introduction, risk-based follow-up or problem oriented follow-up appears to be a common strategy. One observational study from Sweden evaluated their unstructured, problem oriented follow-up programme and concluded that this was not a successful model on the basis of 38% of patients reporting some level of dissatisfaction with their follow-up care to date.³⁰ These patients evaluated the follow-up care they had received to date, although it was not clear what this comprised. A second observational study from Canada has reported preliminary results of inviting patients at high risk for late-effects based on previous treatments to attend a follow-up clinic.²⁹ The visits reported had increased knowledge, and in particular for 50% of patients new problems were diagnosed, of which 70% required some kind of intervention.

These studies broadly suggest that patients who are not routinely followed-up may in fact benefit from such programmes, and even where patients feel they are not showing late-effects signs there may be relevant complications which will benefit from medical attention.

5.2.2 Shared-care model

The study by Blauwbroek *et al.* outlines a shared care model combining hospital clinic-based with family doctor (primary care) provision in the Netherlands. The results suggest this is both feasible and acceptable to the majority of both patients and family doctors.³¹ As the commentary and editorials around the paper have emphasised, this study represents an important step in prospective evaluation of service provision, and highlights the need for comparative studies in this area.

5.2.3 Multidisciplinary clinic

The 'CHIP' multidisciplinary clinic appears to have been established to meet an informally acknowledged need to better fulfil the medical requirements of patients with multiple late-effects where an annual visit or 'traditional late effects clinic' was not sufficient.³² Indicative of this was said to be the number of patients who previously failed to follow through on referrals (20%). This new clinic model involved same-day, same-clinic access to psychological support, tests, information and medical information. It was felt to overcome these difficulties, families were unanimously satisfied and would use the clinic again and benefits around scheduling appointments were identified.³² This survivorship clinic was described in some detail and appears to provide a comprehensive integrated service. The authors report that it enhanced clinical efficiency, however no economic data were presented in terms of cost of the service.

5.2.4 Late effects hospital based clinics

The paper by Eiser *et al.* described a long-term follow-up hospital-based clinic which aimed to encourage the 'handover' of care from the parent to the young adult, and generally provide information on long term prognosis to survivors who had been off treatment for at least five years.³³ The majority of patients were classed as satisfied with the care overall and in particular 41% of patients felt they had no health related problems and were more likely to prefer being seen by their GP for future follow-up. Unfortunately this study did not report any data around late-effects symptoms or new diagnoses, but relied entirely on patient and family self-reports making it difficult to compare the results with other studies. The authors concluded that there may be a sub-group of patients for whom follow-up is not in fact a desirable outcome based on the proportion of patients who preferred seeing their GP for future follow-up.

Kinahan *et al.* reported on the perspectives of survivors and their parents who had participated in a survivorship clinic which was hospital-based and included nurse and physician specialists.³⁴ All survivors were invited to take part and 53% were interviewed. Of most relevance to this review were the results around perceived benefits of follow-up care. Almost all of the survivors reported at least one benefit, and the top three benefits were considered to be late-effects care, personal relationship with the nurse and health maintenance. These results only apply to survivors who have opted to attend the clinic, and you might expect these to be fairly committed attendees as the mean time since diagnosis was 18 years.

Finally a late-effects hospital clinic offering consultant led support with input from a paediatric oncologist, endocrinologist and late effects special nurse was evaluated.³⁵ Clinical care was rated more important than supportive care generally. Patients with more late-effect symptoms, higher future vulnerability and lower mental health related quality of life rated supportive care more highly. It was not possible to interpret the satisfaction results due to poor reporting. When asked to rate follow-up care options, survivors preferred consultant-led care over nurse, GP or telephone/postal based follow-up.

These hospital-based late-effects clinics clearly varied in their aim and the services provided. All appeared to offer access to more than one healthcare professional (usually a specialist nurse plus a physician or consultant), and seem to be a reduced version of the multidisciplinary clinic models.

5.2.5 Paediatric versus adult clinic (hospital based)

This study compared predictors of patient satisfaction in attendees of a traditional paediatric late-effects clinic and a multi-disciplinary adult setting clinic.³⁶ Appointments were longer in

the paediatric clinic (30 minutes versus 10 minutes) and the clinic was staffed by paediatric specialist oncologists among other professionals.

Overall, survivors were satisfied with the care they were receiving, there was no evidence that either group was more or less informed or felt at-risk to future problems. Survivors who understood that the purpose of follow-up care was for clinical support were more satisfied than those expecting psychological support. It was aspects of clinic organisation (e.g. waiting time, length of consultation) rather than setting or clinic type which seemed to influence patient satisfaction.

5.3 Overall findings

Given the heterogeneity of the evaluation tools and follow-up programmes, it was difficult to draw any overall conclusions as to benefits or perceived patient needs. However it appeared that clinical care was valued highly by the majority of follow-up clinic attendees as might be expected for this self-selected sample. Supportive care was perceived as more important by patients who required more interventions and were experiencing more late-effects symptoms. There was a contrast between findings that patients who were not followed-up may have been receiving inadequate care both in terms of their perceived satisfaction and detection of late-effects which require treatment, and the idea that there may be a sub-group of patients for whom long-term follow-up is not an essential part of care. These findings may represent different sub-groups of patients (potentially relating to risk stratification models), or they may be conflicting results from similar patient groups.

A variety of models have been explored and evaluated; to date these have been largely observational in nature. The evaluation tools may not have been reliably developed and validated, and lack of comparability makes it more difficult to draw together the available evidence. The studies discussed in this section were not formally quality assessed therefore caution is advised when considering these findings.

Table 3: Table of study characteristics

Reference Data collection	Setting	Patients	Follow-up details and evaluation method	Findings
<p>Absolom <i>et al.</i> (2006)³⁶</p> <p>Comparison of satisfaction predictors between an adult and a paediatric clinic</p>	<p>Hospital based clinics: traditional late effects paediatric clinic versus multi-disciplinary clinic in adult setting UK</p>	<p>All eligible survivors attending either clinic over 12 months were invited to take part (treated for cancer before 16yrs, aged between 16 and 40yrs). N=198 attendees (n=93 adults clinic, n=105 paediatric clinic). Response rate to the post-visit questionnaire was 78% from the adult clinic and 71% in the paediatric. No significant differences between clinic groups on age at diagnosis, age, sex or treatment severity. More CNS tumours in adult clinic group. Mean age = 23-24 years, time since diagnosis = 16 years, males = 51-53%. Diagnoses listed as leukaemia/lymphoma: 50-60%, solid tumours: 37-38% and CNS tumours as 4 – 12%.</p>	<p>Paediatric clinic: based in an outpatients department within a children’s day hospital, staffed by a paediatric oncologist, staff grade clinician and late-effects nurse. 30 minute consultations.</p> <p>Adult setting clinic: based in an outpatients department in a teaching hospital. Consultations last 10 minutes with referrals to appropriate specialists.</p> <p>Data were collected at two time points (pre and post visit) using a questionnaire. This included late-effects and perceived vulnerability, perceived purpose of follow-up, satisfaction, waiting time and preferences for future follow-up methods.</p> <p>Likert rating scales were used extensively, no information on the development of validation of the questionnaire or its’ components were reported.</p>	<p>Comparison of paediatric and adult clinic patients: there were no significant differences between the two groups in terms of: number of symptoms or late effects; vulnerability score; perceived purpose of follow-up (psychological or clinical). They were equally likely to be accompanied by a parent and the majority wanted to continue with care at their current clinic. Overall satisfaction was not significantly different and ranged from a mean of 64/80 for adult clinic and 67/80 for paediatric clinic patients.</p> <p>Predictors of satisfaction: path analysis was used to explore variables associated with satisfaction. Direct effects ($p < 0.01$) were found for number of topics discussed (which was affected by type of clinic); length of consultation; time waiting; clinical support and sex (women gave lower satisfaction scores).</p> <p>Conclusions: overall survivors were satisfied with the care they were receiving, there was no evidence that either group was more or less informed or felt at-risk to future problems. Survivors who understood the purpose of follow-up care was for clinical support were more satisfied than those expecting psychological support. Overall it was aspects of clinic organisation rather than setting or clinic type which seemed to influence patient satisfaction.</p>

<p>Arvidson <i>et al.</i> (2006)³⁰</p> <p>Audit using postal/telephone questionnaires</p>	<p>Tertiary referral paediatric oncology centres Sweden</p>	<p>Adult survivors (>18yrs) of childhood cancer diagnosed since 1975 with a follow-up time of more than 5 years as of 2000. N=335 contacted N=245 responders: mean age 25 years, mean follow-up since diagnosis 17 years. More females than males responded (81% vs. 67%, p=0.003), otherwise no significant differences.</p>	<p>The two hospitals do not currently have structured follow-up programmes for patients who have been discharged from the paediatric outpatient clinics. The discharged patients were contacted via postal or telephone questionnaire to evaluate the problem-based follow-up care which they had received to date.</p>	<p>Follow-up visits: 40% had or were scheduled for a visit. Of these, 50% with adult specialist; 36% with paediatric specialist; 9% with community care and 4% with private practitioner. 87% of responders felt these visits were 'necessary', 3% said they were 'unnecessary', remainder 'didn't know'</p> <p>Satisfaction: 38% of responders were in some way dissatisfied with the follow-up programme, and those with no planned visits were statistically significantly more dissatisfied than those with planned follow-up visits, p<0.001.</p> <p>Perceived complications: 47% of respondents reported at least one symptom they felt was a late effect. Of those who answered 'no' but detailed other complaints, 17% were likely to be late effects though the patient was unaware. Of those with a perceived complication, 51% were dissatisfied versus 25% without, p<0.001.</p> <p>Need for follow-up: of the 60% who did not have any regular follow-up, there were clear medical or personal reasons for follow-up to be obtained in 80% of these cases.</p> <p>Conclusion: the problem-oriented approach used in these centres has failed and a national health programme along with education of health professionals and patients is needed.</p>
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<p>Blauwbroek <i>et al.</i> (2008)³¹</p> <p>Observational feasibility study using a single group of randomly selected patients</p>	<p>Hospital-based FU clinic followed by local family doctor assessment Netherlands</p>	<p>Adult survivors of childhood cancer (>18yrs at diagnosis) diagnosed between 1968 and 1997 treated at least 5 years previously. CNS tumours were excluded. Patients were randomly selected from hospital list of 210 eligible survivors. N= 133 invited to participate, 121 took part plus 115 family doctors.</p>	<p>Visit 1: Patients were recalled by letter to the LTFU hospital based clinic and underwent full assessment including late effects, quality of life. Visit 2: one year later survivors invited to attend (letter) local family doctor – information forwarded from LTFU clinic. Visit 3: a further year later, repeat appointment at the LTFU clinic advising on future FU based on individual risk. Three categories: 1) postal FU, 2) family doctors plus access to LTFU clinic, 3) shared care intensive model</p> <p>Patients and doctors were asked to complete short questionnaires at each visit rating their views on follow-up and the information available.</p>	<p>Data were reported for visit 2 assessments. Patient satisfaction: 88% of survivors were satisfied with the family doctor care at visit 2. 14% felt the family doctors knowledge of their medical history was inadequate. Doctor satisfaction: 82% of the family doctors were satisfied with the shared care collaboration and felt the information from the LTFU clinic was sufficient, 16% had no opinion and 3% were dissatisfied. Conclusion: Shared care by paediatric oncologists and family doctors is feasible for long term follow-up of adult survivors of childhood cancers.</p>
<p>Carlson <i>et al.</i> (2008)³²</p> <p>Detailed description of FU clinic and audit of patient satisfaction</p>	<p>Hospital based multidisciplinary cancer survivorship clinic USA</p>	<p>Existing patients attending other services or from new referrals were offered appointments at the new clinic. 130 patients used the clinic during the first 18 months of operation for 556 speciality appointments and 403 ancillaries.</p> <p>25% brain tumours 24% neuroblastoma 22% leukaemia</p>	<p>Multidisciplinary clinic model providing same-day, same-clinic access to psychological support, tests, information and medical information. Held once a month with various experts available throughout the day. Appointments coordinated by a nurse and an oncologist who reviews history and risk and schedules the relevant experts and tests. Treatment plan is reviewed by multidisciplinary team on the morning of the clinic and post-clinic considering the problem list, recommended interventions and necessary follow-up. Summary letter/report is created and shared with all care providers, primary physician and the patient.</p>	<p>Previous referral failures: 20% of the patients attending the new clinic had previously failed to follow-up on a referral to a specialist. Identification of new problems: between 16 and 40 patients were identified as having new medical problems within one of four categories. Patient/family satisfaction: 100% would use the clinic again about their child's health, 86% indicated new health issues had been indentified, and patients generally felt that treatment plans were better coordinated. Benefits identified included fewer missed days of school/work and less time needed to schedule appointments. Conclusion: This multidisciplinary approach supports clinical efficiency and</p>

				ongoing patient-centred care for patients with known late effects and at high risk for problems.
Chan <i>et al.</i> (2009) ²⁹ Abstract Audit using questionnaires and treatment data	Oncology unit within a paediatric hospital Canada	Adult survivors of childhood cancer (diagnosed <17yrs) not currently followed up in clinic and at high risk for late effects of treatment (details in paper) N=93 contacted	Patients invited by post to attend a follow-up clinic appointment. Appointment included: review and written summary of previous treatment; advice on potential late effects of treatment; organising tests; information about relevant research studies. No further details of the questionnaire were reported.	Response rate was 19% (preliminary results) New health problems diagnosed in 50% Interventional action required in 70% Knowledge All patients who responded found the visit useful and learned more about their diagnosis/effect of treatment Conclusion: Continued surveillance is necessary and should be provided by healthcare providers familiar with the specific health risks. Contacting former patients remains a challenge.
Eiser <i>et al.</i> (1996) ³³ Audit of clinic	Hospital based LTFU clinic UK	Adolescents (>12 yrs) and young adults off treatment for at least 5 years diagnosed with childhood cancer. 138 patients were offered appointments. 17% of patients did not attend. Data collected from 91 patients, 56 mothers and 16 fathers. Mean age of patients = 16 years, mean years since diagnosis = 11 years. There were no differences between attenders/attendees in age or diagnostic group.	The clinic was run by two oncologists and a GP on a monthly basis and aimed to encourage 'handover' of care from parent to young adult and provide information on long term prognosis. Each patient was expected to attend annually. Unclear how the invitation was issued. Six consecutive clinics were evaluated. A structured questionnaire was developed from pilot patient interviews and discussions with medical staff. Statements were rated using 5-point Likert scales.	Current attendance and barriers: 66% of patients attended annually, 23% at 6 monthly intervals and 3% each at 3 and 9 month intervals. Barriers to attending included taking time off, catching up with work/school, telling friends (more females than males). Perception of clinic visit: 70% were satisfied, 18% had no opinion and 12% felt there wasn't enough time to speak to the doctor. 79% were happy their concerns were treated confidentially. Patients reported differences between the information they wanted to be given, and what they remembered being offered. There was an even split between those who perceived no benefits of attending clinic and those who reported positive attitudes. Parents were more positive about continuing to attend clinic than patients. Patients' main reasons for attending were to be reassured that they were well and

				<p>receive information about the disease.</p> <p>Type of care and FU preferences: Overall continuing to attend the clinic, come less often or transfer to an adult clinic were most highly rated on Likert scales. 41% of patients felt they had no related problems and were more likely to prefer to be seen only by their GP in future ($p<0.05$).</p> <p>Conclusion: It may be possible to define a subgroup for which less frequent follow-up care is appropriate.</p>
<p>Kinahan <i>et al.</i> (2008)³⁴</p> <p>Audit</p>	<p>STAR (Survivors Taking Action and Responsibility) , a hospital based LTFU clinic USA</p>	<p>All adult survivors of childhood cancer seen at least once within the programme since inception in 2001. 102 survivors were eligible, of which 53% were interviewed. This study focuses on 42 survivor-parent dyads. No sig. differences between responders and non-responders. Mean age = 29 years, mean time since diagnosis = 18 years.</p>	<p>Survivors were contacted by letter and then by telephone to conduct the interview. The actual follow-up programme was not described in any detail but was referred to as 'comprehensive'.</p> <p>[further details gathered from web searches indicate patients have access to a specialist nurse, a physician and sometimes a social worker at the visits]³⁷</p> <p>The evaluation was carried out using a semi-structured interview schedule.</p>	<p>Results (only patient related given here): Benefits from the LTFU perceived by survivors: three most commonly reported benefits were comprehensive care/late effects care 43%, personal attention/relationship with the nurse 43% and health maintenance 33%. Most participants were active in the LTFU programme and 95% reported at least one benefit.</p> <p>Conclusions: these were varied and most did not relate to the topic of this review, overall they concluded that further research is needed to explore the needs of the adult survivor and their family.</p>
<p>Michel <i>et al.</i> (2009)³⁵</p> <p>Observational study of expectations and experiences of follow-up visits</p>	<p>Hospital follow-up UK</p>	<p>Cohort of young adults (18-45yrs) diagnosed with childhood cancer (<16yrs) and >5yrs since diagnosis, registered in the Late Effects Clinic. 141 contacted (93 with appointment, 48 without appointment).</p>	<p>Late Effects Clinic – consultant led clinic with input from a paediatric oncologist, endocrinologist and late effects special nurse. Other support available as needed. Evaluation: eligible patients attending clinic during the evaluation period were sent pre and post appointment questionnaires. Eligible patients not attending were sent an abbreviated</p>	<p>Response rate: 79% overall Expectations for FU: clinical care was rated more highly than supportive care ($p<0.001$) at FU overall. Women rated supportive care as more important than men ($p=0.014$) and survivors with more late effects ($p=0.04$), higher future vulnerability ($p<0.001$) and lower mental HrQoL($p=0.005$) rated supportive care as more important than survivors with the opposite characteristics.</p>

			<p>questionnaire. The outcome tool used combined Likert scales and other ratings, however the development and interpretation of these was poorly reported.</p>	<p>Outpatient satisfaction: mean satisfaction was given as 3.26 (although it was not clear how this number was derived) and not associated with any other factors. Preferences for future FU care: survivors rated consultant-led FU more highly than nurse-led, then GP-led, then postal/telephone. 52% rated consultant-led care highest and 29% felt all four models were equally preferable. Risk stratification: when stratified to three risk levels this was not associated with any differences in preference for FU care. Conclusions: survivors in active FU value clinical care and consultant-led FU regardless of risk stratification. Sustaining LTFU in a consultant-led model is not feasible but highly valued, alternatives must be explored.</p>
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6. DISCUSSION

6.1 Findings

The aim of this review was to identify studies that presented comparative data from retrospective or prospective groups. Despite a rigorous search for studies of this design we were unable to identify any comparative studies that evaluated methods of providing follow-up care for survivors of childhood cancer. The conclusion of a systematic review that there is too little or no evidence to answer the research question is not unusual, particularly in reviews of healthcare interventions.^{38, 39} Such findings, however can inform future research priorities.

A small number of studies that were excluded on study design (and one on intervention) were retained and documented to attempt to produce a more comprehensive evidence picture. These studies aimed to assess whether a particular approach was feasible in practice, or whether patients found the service useful or satisfactory. These studies tended to be relatively small and for the majority the main outcome measure was 'satisfaction'. Satisfaction has diverse applications in these studies, including satisfaction with care received,³⁶ both patient and doctor satisfaction³¹ and patient and family satisfaction;³² to aid comparison between studies, robust and comparable definitions of 'satisfaction' are desirable. This includes satisfaction from both health service users and providers.

6.2 Results of the literature search

This review undertook a comprehensive search without language restrictions; a range of electronic databases and appropriate electronic resources were searched. Additionally the bibliographies of relevant studies and associated reviews were also searched. Contact was made with experts in the field, both from within our steering group as well as other research groups in the UK and USA.

6.3 Strengths and weaknesses of the review

We carried out comprehensive literature searches including a thorough search of relevant electronic databases. The searches were conducted up to February 2010. Our study selection process was independently undertaken by two reviewers, with reference to a third reviewer where necessary, thus minimising the impact of error and bias.

A further strength of this review is the small number of unobtainable papers (see Appendix 4). Whilst every effort was made to retrieve each paper that was identified as being potentially relevant a very small number were unobtainable; likewise attempts were made to interpret foreign-language papers, just one of these was not translated. The coverage of the available literature achieved by the review suggests that we can be confident that important papers were not missed. It appears unlikely that the small number of missing papers would have altered the results of the review.

A crucial part of the review process was to incorporate the views of young people, two of whom were contacted as described in Section 2. The rapid nature of the

review and lack of any substantial findings meant that we were unable to involve them as much as we had hoped within the review process; however their comments have been incorporated within the discussion and suggested areas for future research.

6.4 Implications for further research

It is clear from this review that to date there do not appear to have been any published studies in long-term follow-up patients that have compared: alternative communication modalities to face-to-face clinic visits; physician- versus nurse-led follow-up; or the value of hospital staff versus primary care staff to provide clinical contacts. Few studies appear to have attempted to evaluate the effectiveness of follow-up from the perspective of a childhood cancer survivor at all.

Whilst a review of this nature could be criticised for failing to provide results for the effectiveness, or otherwise, of these interventions, this is not unusual.^{38, 39} The review has identified areas for focussing future research efforts and it is envisaged that the absence of research findings will provide impetus to the development of rigorous comparative evaluations that seek to address these comparisons in relevant settings and for relevant samples of patients.

There is a belief that life-long follow-up is necessary to improve detection of the late-effects of treatment and to provide information and advice to childhood cancer survivors, although little evidence of effectiveness has been presented.^{13, 15} NICE propose that there should be robust and appropriate surveillance of survivors of childhood cancer,¹⁶ and this is supported by the SIGN guidelines.¹⁷ Following up individuals for a lifetime has economic implications; a lifetime of follow-up will involve numerous contacts between the patient and health care services, many of which may be at inappropriate time points for the detection of subsequent disease or treatment related late-effects.

The purpose of long-term follow-up of survivors of childhood cancers has several goals, which include: the detection and treatment of late effects; support and advice; and ongoing health education.⁴⁰ The provision of follow-up in health care settings is likely to become unfeasible given increasing numbers of childhood cancer survivors increase.³⁵ To address this flexible models of risk stratification have been proposed:⁴¹ Level 1 – postal or telephone follow-up following initial treatment involving surgery or low-risk chemotherapy; Level 2 - nurse or GP-led follow-up following chemotherapy and/or low-dose radiation; and Level 3 - medically supervised follow-up following radiotherapy or megatherapy. Flexibility within these categories is necessary to take account of the diverse physical and psychological late effects that can occur as well as survivors' expectations about the kind of care they wish to receive.⁴² Ongoing evaluation of the experiences of survivors who are stratified and allocated to the relevant follow-up programme will be important to ensure that the needs of patients are being met in a non-clinical setting.

As reported elsewhere, the requirements for an effective service with respect to communication and information have been highlighted.¹⁵ It would appear that whilst follow-up is being implemented in this patient group there appears to be no audit regarding its effectiveness, either in terms of patient outcome or cost. To ensure that both issues are addressed there is a clear requirement for focussed evaluations that rigorously assess the follow-up experience.

6.5 Areas for future research

Whilst there has been a prevailing view that survivors of childhood cancers should be followed-up for life it is unclear whether this is necessary or beneficial. Despite the consistency between survivors and professionals preferences for follow-up care there is less clear evidence on how best to deliver these services.¹⁵ Ideally, adequately powered, well-conducted, controlled trials of adequate duration that directly compare the interventions and comparators specified within this review would be required to provide more robust evidence on the optimal follow-up or aftercare for childhood cancer survivors. These trials should be conducted in appropriate settings and be focussed upon deriving meaningful validated outcomes for the purposes of comparison. The economic implications of these interventions should be assessed given the resource implications of providing care and services over a protracted timeframe.

Most studies within this review appear to only report satisfaction with service, whereas relevant outcomes should also focus upon patient experience, detection of morbidities and mortality rates. Adopting a 'patient experience' attitude towards future research could open up further areas of interest such as comparing the information delivered with that understood or found to be useful by the patient. A patient perspective on late-effects symptoms and preferences for follow-up care would also be of value.

Although there was a paucity of evidence upon which to answer the specific questions posed by this review, during the review process it became apparent that there was a body of literature that addressed various components of care for childhood cancer survivors. These include aspects of health promotion activities such as smoking cessation and smoking prevention, alcohol and substance abuse, health promotion, diet and sexual health. None of these areas have yet been formally scoped to assess the size and quality of the literature. An appropriate priority-setting exercise should be conducted to assess which, if any, aspect of health promotion strategies could be subject to systematic review. Such a review should explicitly draw on evidence from other chronic diseases to maximise the value of the information collected, combining the information in a network meta-analysis where the differing disease types are explored as covariates. Such methodologies have been used in analogous situations previously.⁴³

6.6 Summary of areas for further research

This review has highlighted that there may be opportunities to undertake research in the following areas:

Primary research:

- There is a clear need for follow-up programmes to be evaluated using comparative study designs.
- Risk stratification may be particularly relevant, published guidelines advocate a stratified follow-up programme although there has been no evaluation of these recommendations to date.

Secondary research:

- Based on the screening and sifting stages, it appears that there may be sufficient research to warrant systematic reviews on the effectiveness of interventions aimed at preventing or reducing harmful behaviours in survivors of childhood cancers. Such areas could include:
 - Health promotion
 - Smoking prevention/cessation
 - Alcohol/substance abuse
 - Diet
 - Sexual health

An appropriate priority-setting exercise should be conducted to assess which, if any, aspect of these health promotion strategies could be subject to systematic review. Such a review should explicitly draw on evidence from other chronic diseases to maximise the value of the information collected.

7. Expertise and author contributions

7.1 Team members

Bob Phillips took overall responsibility for management of the project. He is a Consultant Paediatric Oncologist and Research Fellow, with experience in developing and undertaking a range of systematic reviews.

Morag Heirs is a Research Fellow at CRD and took day to day responsibility for the project and was involved in all stages of the review from inclusion of studies to writing the final report. Morag has been involved with reviews for the past 5 years covering a range of topics from complementary and alternative medicine to photodynamic therapy for the treatment of cancer.

Kate Light is an Information Specialist who designed the search strategy, carried out the database searches, order papers and managed references. She has much experience of supporting health reviews, including reviews on antiemetic medication for prevention and treatment of chemotherapy induced nausea and vomiting in children (on behalf of the CCLG and the PONF Supportive Care Group) and Evaluating models of care closer to home for children and young people who are ill (funded by the NIHR SDO).

Russell Slack is a Research Fellow at CRD, has two years experience in systematic reviews as well as a background in health services research and health economics. He was involved in all stages of the review process

Sara Suekarran is a Research Fellow at CRD and has two years experience in systematic reviews and has been involved in several HTA projects. She was involved in all stages of the review process.

7.2 Clinical Advisors

The advisors provided clinical input to the project, commented on the protocol and various drafts of the final report, and contributed to the discussion section of the report.

Faith Gibson: Clinical Professor of Children and Young People's Cancer Care Great Ormond Street Hospital for Children and London South Bank University.

Adam Glaser: Consultant Paediatric and Adolescent Oncologist at Leeds Teaching Hospitals NHS Trust and Honorary Senior Lecturer, University of Leeds, since 1999. Adam co-ordinates the long term follow up programme in Leeds managing 1200 survivors of childhood and adolescent cancer. Adam was appointed Clinical Director of the National Cancer Survivor Initiative (N.C.S.I.) at the Department of Health in January 2010. Prior to this, he was National Clinical Lead for Children and Young People within the N.C.S.I.

Mike Hawkins: Mike Hawkins is Chair in Epidemiology and Director of the Centre for Childhood Cancer Survivor Studies. His core research interests relate to the health of

the national population of survivors of childhood cancer and their first degree relatives. Department of Public Health & Epidemiology, University of Birmingham

Jim Elliott: Research Adviser at Macmillan Cancer Support and Scientific Support for the National Cancer Survivorship Initiative research work stream. Commissioned and managed the comprehensive review of the evidence base for cancer survivorship in adults alongside this review to inform the development of research priorities for survivorship across the UK.

7.3 Patient Perspective

With thanks to James Ashton and Alexandra Brownsdon who read and commented on the full report.

7.4 Competing interests

None to declare for the members of the CRD team, patient representatives or clinical advisors.

APPENDIX 1: SEARCH STRATEGY

MEDLINE (OvidSP–www.ovid.com/)

1950 to December Week 8 2009

Searched on 8/1/2010

Retrieved 2736 hits

AND

MEDLINE In-process (OvidSP –www.ovid.com/)

January 08 2010

Searched on 11/1/2009

Retrieved 58 hits

Search Strategy:

1. adolescent/ or child/ or child, preschool/ or infant/ or infant, newborn/ or infant, low birth weight/ or infant, small for gestational age/ or infant, very low birth weight/ or infant, extremely low birth weight/ or infant, postmature/ or infant, premature/
2. exp neoplasms/
3. Survivors/
4. 1 and 2 and 3
5. ganglioneuroblastoma/ or hemangioblastoma/ or medulloblastoma/ or Wilms Tumor/ or hepatoblastoma/
6. 5 and 3
7. ((cancer\$ or neoplasm\$ or tumor\$ or tumour\$ or lymphoma\$ or leukemia or leukaemia or carcinoma\$ or malignan\$ or oncolog\$ or adenocarcinoma\$ or sarcoma\$ or acute lymphoblast\$ or acute myeloid or acute non lymphoid or chronic myeloid or myelodysplasia or pnet or ependymoma\$ or astrocytoma\$ or oligodendroglioma\$ or glioma\$ or meningioma\$ or schwannoma\$ or neuroma\$ or dnet or glioblastoma or pituitary adenoma\$ or choroid plexus papilloma\$ or carcinoma\$ or gangliocytoma\$ or ganglioneuroma\$ or ganglioglioma\$ or neurofibroma\$ or Hodgkin\$ disease or Hodgkin\$ lymphoma\$ or lymphogranuloma\$ or Hodgkin\$ granuloma\$ or malignant granuloma\$ or neuroblastoma\$ or osteosarcoma\$ or rhabdomyosarcoma\$ or craniopharyngioma\$ or retinoblastoma\$ or hepatoma\$ or teratoma\$ or teratocarcinoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$) adj3 (newborn\$ or new-born\$ or baby\$ or babies or neonat\$ or infan\$ or kid or kids or toddler\$ or adoles\$ or teen\$ or boy\$ or girl\$ or juvenil\$ or youth\$ or puber\$ or prepuber\$ pubescen\$ or prepubescen\$ or pediatric\$ or paediatric\$ or young person\$ or young

people or young adult\$ or child\$ or schoolchild\$ or schoolage\$ or school\$ or preschool\$)).ti,ab.

8. ((ganglioneuroblastoma\$ or haemangioblastoma\$ or hemangioblastoma\$ or medulloblastoma\$ or medullomyoblastoma\$ or wilms tum?r\$ or nephroblastoma\$ or hepatoblastoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$)).ti,ab.

9. (pediatric cancer\$ survivor\$ or paediatric cancer\$ survivor\$ or survivor\$ of childhood cancer\$ or childhood cancer\$ survivor\$ or survivor\$ of childhood leukemia\$ or survivor\$ of childhood leukaemia\$ or survivor\$ of pediatric leukemia\$ or survivor\$ of pediatric leukaemia\$ or survivor\$ of paediatric leukemia\$ or survivor\$ of paediatric leukaemia\$ or survivor\$ of paediatric cancer\$ or survivor\$ of pediatric cancer\$).ti,ab.

10. 4 or 6 or 7 or 8 or 9

11. limit 10 to yr="1980 -Current"

CDSR (Cochrane Database of Systematic Reviews)
DARE – Database of Abstracts of Reviews of Effects,
HTA (Health Technology Assessment Database)
NHS EED (NHS Economic Evaluation Database)
CENTRAL
(Via: The Cochrane Library – www.thecochranelibrary.com/)

2009:Issue 4

Searched on 13/1/2010

Retrieved 3 hits from CDSR, 4 hits from DARE, 1 hit from HTA, 3 hits from NHS EED, 141 hits from CENTRAL

Search Strategy:

- #1 MeSH descriptor Adolescent, this term only
- #2 MeSH descriptor Child explode all trees
- #3 MeSH descriptor Infant explode all trees
- #4 (#1 OR #2 OR #3)
- #5 MeSH descriptor Neoplasms explode all trees
- #6 MeSH descriptor Survivors, this term only
- #7 (#4 AND #5 AND #6)
- #8 MeSH descriptor Ganglioneuroblastoma, this term only
- #9 MeSH descriptor Hemangioblastoma, this term only
- #10 MeSH descriptor Medulloblastoma, this term only
- #11 MeSH descriptor Wilms Tumor, this term only
- #12 MeSH descriptor Hepatoblastoma, this term only
- #13 (#8 OR #9 OR #10 OR #11 OR #12)
- #14 (#6 AND #13)
- #15 (cancer* or neoplasm* or tumor* or tumour* or lymphoma* or leukemia or leukaemia or carcinoma* or malignan* or oncolog* or adenocarcinoma* or sarcoma* or acute lymphoblast* or acute myeloid or acute non lymphoid or chronic myeloid or myelodysplasia or pnet or ependymoma* or astrocytoma* or oligodendroglioma* or glioma* or meningioma* or schwannoma* or neuroma* or dnet or glioblastoma or pituitary adenoma* or choroid plexus papilloma* or carcinoma* or gangliocytoma* or

ganglioneuroma* or ganglioglioma* or neurofibroma* or Hodgkin* disease or Hodgkin* lymphoma* or lymphogranuloma* or Hodgkin* granuloma* or malignant granuloma* or neuroblastoma* or osteosarcoma* or rhabdomyosarcoma* or craniopharyngioma* or retinoblastoma* or hepatoma* or teratoma* or teratocarcinoma*) AND (survivor* or survival or follow* up* or followup* or aftercare or after care or surveillance*) AND (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or juvenil* or youth* or puber* or prepuber* pubescen* or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*):ti

#16 (ganglioneuroblastoma* or haemangioblastoma* or hemangioblastoma* or medulloblastoma* or medullomyoblastoma* or wilms tum?r* or nephroblastoma* or hepatoblastoma*) AND (survivor* or survival or follow* up* or followup* or aftercare or after care or surveillance*):ti

#17 (pediatric NEXT cancer* NEXT survivor*) or (paediatric NEXT cancer* NEXT survivor*) or (survivor* NEXT of NEXT childhood NEXT cancer*) or (childhood NEXT cancer* NEXT survivor*) or (survivor* NEXT of NEXT childhood NEXT leukemia*) or (survivor* NEXT of NEXT childhood NEXT leukaemia*) or (survivor* NEXT of NEXT pediatric NEXT leukemia*) or (survivor* NEXT of NEXT pediatric NEXT leukaemia*) or (survivor* NEXT of NEXT paediatric NEXT leukemia*) or (survivor* NEXT of NEXT paediatric NEXT leukaemia*) or (survivor* NEXT of NEXT paediatric NEXT cancer*) or (survivor* NEXT of NEXT pediatric NEXT cancer*)

#18 (#7 OR #14 OR #15 OR #16 OR #17)

#19 (#18), from 1980 to 2010

PsycINFO (Ovid Online – www.ovid.com/)

1967 to January Week 2 2010

Searched on 15/01/2010

Retrieved 553 hits

Search strategy:

1. (adolescence 13 17 yrs or childhood birth 12 yrs or infancy 2 23 mo or neonatal birth 1 mo or preschool age 2 5 yrs or school age 6 12 yrs or young adulthood 18 29 yrs).ag.
2. exp Neoplasms/
3. Survivors/ or Posttreatment Followup/ or aftercare/
4. 1 and 2 and 3
5. ((cancer\$ or neoplasm\$ or tumor\$ or tumour\$ or lymphoma\$ or leukemia or leukaemia or carcinoma\$ or malignan\$ or oncolog\$ or adenocarcinoma\$ or sarcoma\$ or acute lymphoblast\$ or acute myeloid or acute non lymphoid or chronic myeloid or myelodysplasia or pnet or ependymoma\$ or astrocytoma\$ or oligodendrogloma\$ or glioma\$ or meningioma\$ or schwannoma\$ or neuroma\$ or dnet or glioblastoma or pituitary adenoma\$ or choroid plexus papilloma\$ or carcinoma\$ or gangliocytoma\$ or ganglioneuroma\$ or ganglioglioma\$ or neurofibroma\$ or Hodgkin\$ disease or Hodgkin\$ lymphoma\$ or lymphogranuloma\$ or Hodgkin\$ granuloma\$ or malignant granuloma\$ or neuroblastoma\$ or

osteosarcoma\$ or rhabdomyosarcoma\$ or craniopharyngioma\$ or retinoblastoma\$ or hepatoma\$ or teratoma\$ or teratocarcinoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$) adj3 (newborn\$ or new-born\$ or baby\$ or babies or neonat\$ or infan\$ or kid or kids or toddler\$ or adoles\$ or teen\$ or boy\$ or girl\$ or juvenil\$ or youth\$ or puber\$ or prepuber\$ pubescen\$ or prepubescen\$ or pediatric\$ or paediatric\$ or young person\$ or young people or young adult\$ or child\$ or schoolchild\$ or schoolage\$ or school\$ or preschool\$)).ti,ab.

6. ((ganglioneuroblastoma\$ or haemangioblastoma\$ or hemangioblastoma\$ or medulloblastoma\$ or medullomyoblastoma\$ or wilms tum?\$ or nephroblastoma\$ or hepatoblastoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$)).ti,ab.

7. (pediatric cancer\$ survivor\$ or paediatric cancer\$ survivor\$ or survivor\$ of childhood cancer\$ or childhood cancer\$ survivor\$ or survivor\$ of childhood leukemia\$ or survivor\$ of childhood leukaemia\$ or survivor\$ of pediatric leukemia\$ or survivor\$ of pediatric leukaemia\$ or survivor\$ of paediatric leukemia\$ or survivor\$ of paediatric leukaemia\$ or survivor\$ of paediatric cancer\$ or survivor\$ of pediatric cancer\$).ti,ab.

8. 4 or 5 or 6 or 7

9. 8

10. limit 9 to yr="1980 -Current"

HMIC (Ovid Online – www.ovid.com/)

January 2010

Searched on 15/01/2010

Retrieved 65 hits

Search Strategy:

1. exp YOUNG PEOPLE/ or children/ or children/ or exp INFANTS/ or pre school children/

2. exp neoplasms/

3. exp after care/

4. 1 and 2 and 3

5. ((cancer\$ or neoplasm\$ or tumor\$ or tumour\$ or lymphoma\$ or leukemia or leukaemia or carcinoma\$ or malignan\$ or oncolog\$ or adenocarcinoma\$ or sarcoma\$ or acute lymphoblast\$ or acute myeloid or acute non lymphoid or chronic myeloid or myelodysplasia or pnet or ependymoma\$ or astrocytoma\$ or oligodendroglioma\$ or glioma\$ or meningioma\$ or schwannoma\$ or neuroma\$ or dnet or glioblastoma or pituitary adenoma\$ or choroid plexus papilloma\$ or

carcinoma\$ or gangliocytoma\$ or ganglioneuroma\$ or ganglioglioma\$ or neurofibroma\$ or Hodgkin\$ disease or Hodgkin\$ lymphoma\$ or lymphogranuloma\$ or Hodgkin\$ granuloma\$ or malignant granuloma\$ or neuroblastoma\$ or osteosarcoma\$ or rhabdomyosarcoma\$ or craniopharyngioma\$ or retinoblastoma\$ or hepatoma\$ or teratoma\$ or teratocarcinoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$) adj3 (newborn\$ or new-born\$ or baby\$ or babies or neonat\$ or infan\$ or kid or kids or toddler\$ or adoles\$ or teen\$ or boy\$ or girl\$ or juvenil\$ or youth\$ or puber\$ or prepuber\$ pubescen\$ or prepubescen\$ or pediatric\$ or paediatric\$ or young person\$ or young people or young adult\$ or child\$ or schoolchild\$ or schoolage\$ or school\$ or preschool\$)).ti,ab.

6. ((ganglioneuroblastoma\$ or haemangioblastoma\$ or hemangioblastoma\$ or medulloblastoma\$ or medullomyoblastoma\$ or wilms tum?r\$ or nephroblastoma\$ or hepatoblastoma\$) adj3 (survivor\$ or survival or follow\$ up\$ or followup\$ or aftercare or after care or surveillance\$)).ti,ab.

7. (pediatric cancer\$ survivor\$ or paediatric cancer\$ survivor\$ or survivor\$ of childhood cancer\$ or childhood cancer\$ survivor\$ or survivor\$ of childhood leukemia\$ or survivor\$ of childhood leukaemia\$ or survivor\$ of pediatric leukemia\$ or survivor\$ of pediatric leukaemia\$ or survivor\$ of paediatric leukemia\$ or survivor\$ of paediatric leukaemia\$ or survivor\$ of paediatric cancer\$ or survivor\$ of pediatric cancer\$).ti,ab.

8. or/4-7

9. 8

10. limit 9 to yr="1980 -Current"

CINAHL - Cumulative Index to Nursing & Allied Health Literature (EBSCO – www.ebscohost.com/)

1981 - current

Searched on 18/01/2010

Retrieved 1096 hits

Search Strategy:

1. (MH "Infant, Newborn+") or (MH "Infant") or (MH "Child, Preschool") or (MH "Child") or (MH "Adolescence+")
2. (MH "Neoplasms+")
3. (MH "After Care") or (MH "Cancer Survivors")
4. S1 AND S2 AND S3
5. TI (newborn* or new-born* or baby* or babies or neonat* or infan* or kid or kids or toddler* or adoles* or teen* or boy* or girl* or juvenil* or youth* or puber* or prepuber* pubescen* or prepubescen* or pediatric* or paediatric* or young person* or young people or young adult* or child* or schoolchild* or schoolage* or school* or preschool*)

6. TI (cancer* or neoplasm* or tumor* or tumour* or lymphoma* or leukemia or leukaemia or carcinoma* or malignan* or oncolog* or adenocarcinoma* or sarcoma* or acute lymphoblast* or acute myeloid or acute non lymphoid or chronic myeloid or myelodysplasia or pnet or ependymoma* or astrocytoma* or oligodendroglioma* or glioma* or meningioma* or schwannoma* or neuroma* or dnet or glioblastoma or pituitary adenoma* or choroid plexus papilloma* or carcinoma* or gangliocytoma* or ganglioneuroma* or ganglioglioma* or neurofibroma* or Hodgkin* disease or Hodgkin* lymphoma* or lymphogranuloma* or Hodgkin* granuloma* or malignant granuloma* or neuroblastoma* or osteosarcoma* or rhabdomyosarcoma* or craniopharyngioma* or retinoblastoma* or hepatoma* or teratoma* or teratocarcinoma*)7. TI (survivor* or survival or follow* up* or followup* or aftercare or after care or surveillance*)
8. S5 AND S6 AND S7
9. (MH "Childhood Neoplasms")
10. S9 AND S3
11. TI (ganglioneuroblastoma* or haemangioblastoma* or hemangioblastoma* or medulloblastoma* or medullomyoblastoma* or wilms tum?* or nephroblastoma* or hepatoblastoma*)
12. S11 AND S7
14. S4 OR S8 OR S10 OR S12

metaRegister of Controlled Trials (mRCT) – via Current Controlled Trials – www.controlled-trials.com/

Searched on 26/01/2010

Retrieved 35 hits Including duplicates)

Search Strategy

The search interface to this resource is a very simple one and the search had to be modified accordingly.

The following phrases were searched individually and the results collated.

"childhood cancer survivor%"	11 hits
"Pediatric Cancer survivor%"	1 hit
"paediatric cancer survivor%"	0 hits
"survivor% of childhood cancer%"	11 hits
"childhood cancer survivor%"	11
"survivor% of childhood leukemia%"	1 hit
"survivor% of childhood leukaemia%"	0 hits
"survivor% of pediatric leukemia%"	0 hits
"survivor% of pediatric leukaemia%"	0 hits
"survivor% of paediatric leukemia%"	0 hits
"survivor% of paediatric leukaemia%"	0 hits

"survivor% of paediatric cancer%" 0 hits

"survivor% of pediatric cancer%" 0 hits

American Society of Clinical Oncology - www.asco.org

Searched on 27/01/2010

Retrieved 48 hits (including duplicates)

Search Strategy:

The search interface to this resource is a very simple one and the search had to be modified accordingly

A search of the abstract body generally retrieved an unmanageable number of hits so all search terms were limited to titles only.

The search engine on this site uses the Boolean AND to combine any terms entered. It was not possible to do anything more complicated than enter a string of words.

Pediatric cancer survivor 0 hits

Pediatric cancer survivors 3 hits

Pediatric cancers survivor 0 hits

Pediatric cancers survivors 0 hits

Paediatric cancer survivor 0 hits

Paediatric cancer survivors 0 hits

Paediatric cancers survivor 0 hits

Paediatric cancers survivors 0 hits

Childhood cancer survivor 14 hits

Childhood cancer survivors 25 hits

Childhood cancers survivor 0 hits

Childhood cancers survivors 1 hit

survivor childhood leukemia 1 hit

survivors childhood leukemia 4 hits

survivor childhood leukemias 0 hits

survivors childhood leukemias 0 hits

survivor pediatric leukemia 0 hits

survivor pediatric leukemias 0 hits

survivors pediatric leukemia	0 hits
survivors pediatric leukemias	0 hits
survivor paediatric leukemia	0 hits
survivor paediatric leukemias	0 hits
survivors paediatric leukemia	0 hits
survivors paediatric leukemias	0 hits

**National Cancer Institute Clinical Trials PDQ -
www.cancer.gov/search/SearchClinicalTrials.aspx**

Searched on 01/02/2010

Retrieved 28 hits (including duplicates)

Search Strategy:

The interface uses a combination of menu selections and very basic free text searching.

The following selections were made:

Cancer type – all

Location: not used

Trial/treatment type: all

Trial status (both active and closed trials were searched for)

Trial Phase: all

Trial ID/sponsor: not used

Search phrases had to be searched for separately, then the results collated.

Search strategy:

Keywords/Phrases: "Pediatric cancer survivor"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Pediatric cancer survivors"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Paediatric cancer survivor"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Paediatric cancer survivors"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Childhood cancer survivor"

Trial Status: Active *5 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Childhood cancer survivors"

Trial Status: Active *16 hits*

Trial Status: Closed *2 hits*

Keywords/Phrases: "Childhood cancers survivor"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "childhood cancers survivors"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Survivor of childhood leukemia"

Trial Status: Active *1 hit*

Trial Status: Closed *0 hits*

Keywords/Phrases: "Survivors of childhood leukemia"

Trial Status: Active *2 hits*

Trial Status: Closed *2 hits*

Keywords/Phrases: "survivor of childhood leukemias"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivors of childhood leukemias"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivor of pediatric leukemia"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivor of pediatric leukemias"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivors of pediatric leukemia"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivors of pediatric leukemias"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivor of paediatric leukemia"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivor of paediatric leukemias"

Trial Status: Active *0 hits*

Trial Status: Closed *0 hits*

Keywords/Phrases: "survivors of paediatric leukemia"

Trial Status: Active 0 hits

Trial Status: Closed 0 hits

Keywords/Phrases: "survivors of paediatric leukemias"

Trial Status: Active 0 hits

Trial Status: Closed 0 hits

**International Cancer Research Portfolio (Internet –
www.cancerportfolio.com/index.jsp)**

Searched on 02/02/2010

Retrieved 45 hits

Search Strategy:

The interface uses a combination of menu selections and free text searching.

The following were set to their default of any: City, State, Country, Project Type, Type of cancer, Funding organisation

The text boxes for "Institution receiving the award" and "Principle investigator" were left blank

Year: - The Portfolio includes material from 2000 onwards. All years were selected.

Type of research:

6.1 Cancer Control, Survivorship and Outcomes Research - Patient Care and Survivorship Issues;

6.2 Cancer Control, Survivorship and Outcomes Research - Surveillance;

6.6 Cancer Control, Survivorship and Outcomes Research - End-of-Life Care;

6.8 Cancer Control, Survivorship and Outcomes Research - Complementary and Alternative

Approaches for Supportive Care of Patients and Survivors;

6.9 Cancer Control, Survivorship and Outcomes Research - Resources and Infrastructure Related to

Cancer Control, Survivorship, and Outcomes Research

Any of these words: newborn* new-born* baby* babies neonat* infan* kid kids toddler* adoles* teen* boy* girl* juvenil* youth* puber* prepuber* pubescen* prepubescen* pediatric* paediatric* child* schoolchild* school* preschool* schoolage*

APPENDIX 2: DRAFT DATA EXTRACTION

General

Author, year, ENL #
Linked papers ENL#
Data source [full paper, abstract, unpublished report, other]
Country [list of countries, not-stated, multiple – specify]
Language [list]
Study design [RCT, prospective CT, retrospective control, other]
Number participants
Number centres if relevant

Population Details

Eligibility Criteria
Patient Characteristics
 Age
 Gender
 Diagnosis
 Time since diagnosis/off treatment
 Relapsed & retreated
 BMT / radiotherapy / craniospinal radiotherapy

Follow-up Details (repeat for each comparator arm/condition)

Method [face-to-face, SMS, postal, email, telephone]
Initiated by [patient, care-giver]
Duration and Frequency
Any concurrent follow-up

Outcomes

Clinical

Morbidity detection rates
Response rates

Patient-focused

Satisfaction with follow-up method
Ease of use
Method of assessment (validated/not etc)
Proportion responding to request to participate

Economic

Costs attached to each intervention

APPENDIX 3: PROPOSED QUALITY CRITERIA

Controlled studies

1. Was the number of participants that were randomised clearly stated?
Yes/No/Unclear

Were the actual numbers allocated to each arm clearly stated in the paper.

2. Was the study randomised appropriately? Yes/ No/ Unclear

Appropriate includes random numbers generated by computer, tables of random numbers and drawing of lots or envelopes. If the description of randomisation is poor, or the process used is not truly random (e.g. using date of birth or alternating between one group and another) then the randomisation is flawed.

3. Were selection/eligibility criteria adequately reported? Yes/ No/ Unclear

Was the method of selection of participants from the eligible population well described? Were the inclusion/exclusion criteria explicit and appropriate?

4. Was allocation concealment used appropriately? Yes/ No/ Unclear

Adequate allocation concealment would include centralised allocation or computerised allocation systems.

5. Were the study arms comparable at baseline? Yes/ No/ Unclear

Assess whether there were differences between groups in important confounders (age, sex, time since active treatment etc) at baseline.

6. Were losses to follow-up reported and acceptable? Yes/ No/ Unclear

Were losses to follow-up reported – if so were losses to follow-up (that is, dropped or lost pre-/during/post- intervention) acceptably low (< 20%).

7. Were at least 90% of those included at baseline followed-up?
Yes/ No/ Unclear

8. Was an ITT analysis conducted? Yes/ No/ Unclear

Were all participants (including those that dropped out or did not fully complete the intervention course) analysed in the trial arms to which they were originally allocated.

9. Was a power calculation reported? Yes/ No/ Unclear

Is a power calculation (of adequate size) presented - power of 0.8 is the conventionally accepted standard.

10. Were primary outcomes defined? Yes/ No/ Unclear

Were all important outcomes assessed to determine the benefits or otherwise of the intervention versus the comparator.

Other factors for bias/generalisability:

11. Was the study undertaken in a community-wide setting? Yes/ No/ Unclear

Studies undertaken in a range of settings (clinic & non-clinic) would be considered appropriate (ie 'yes'), whereas those in a purely a specialist clinic setting may have more limited applicability.

12. Was the time from diagnosis, and subsequent follow-up, less than 10 years?
Yes/ No/ Unclear

Studies undertaken in a shorter duration of follow-up may fail to detect longer-term effects

13. Were comorbidities adequately reported? Yes/ No/ Unclear

Was sufficient detail regarding co-morbidities (cardiovascular, neurological, endocrine) reported ?

14. Crossover trials – was adequate follow-up of both parts reported (for analysis we may restrict to pre-crossover)

Was there adequate follow-up of the arms of the trial.

Non RCTs

1. Were selection/eligibility criteria adequately reported? Yes/ No/ Unclear

Was the method of selection of participants from the eligible population well described? Were the inclusion/exclusion criteria explicit and appropriate?

2. Was the selected population representative of that seen in normal practice?
Yes/ No/ Unclear

Was the eligible population representative? Would not be representative if important groups were underrepresented.

3. Was an appropriate measure of variability reported? Yes/ No/ Unclear

For example, SDs.

4. Were losses to follow-up reported or explained? Yes/ No/ Unclear

Were losses to follow-up reported and if so were reasons for loss adequately explained.

5. Were at least 90% of those included at baseline followed-up? Yes/ No/ Unclear

6. Were patients recruited prospectively? Yes/ No/ Unclear

7. Were patients recruited consecutively? Yes/ No/ Unclear
8. Are comorbidities adequately described. Yes/ No/ Unclear

Was sufficient detail regarding co-morbidities (cardiovascular, neurological, endocrine) reported.

Qualitative studies

1. Is the context for the study clear? Yes/No/Unclear
Is the purpose of the study discussed – aims/objectives/research question/s? Is there adequate/appropriate reference to the literature? Are underpinning values/assumptions/theory discussed?

2 Is the study design defensible/rigorous? Yes/No/Unclear
Is the design appropriate to the research question? Is a rationale given for using a qualitative approach? Are there clear accounts of the rationale/justification for the sampling, data collection and data analysis techniques used? Is the selection of cases/sampling strategy theoretically justified?

3. Are the data collection methods clearly described and systematic? Yes/No/Unclear
Are the data collection methods clearly described? Were the appropriate data collected to address the research question? Was the data collection and record keeping systematic?

4. Is the data analysis clearly described and systematic? Yes/No/Unclear
Is it clear how the data was analysed to arrive at the results? Is it clear how the themes and concepts were derived from the data?

5. Is the analysis reliable? Yes/No/Unclear
Did more than one researcher theme and code transcripts/data? If so, how were differences resolved? Did participants feedback on the transcripts/data if possible and relevant? Were negative/discrepant results addressed or ignored?

6. Were the conclusions supported by the results? Yes/No/Unclear
How clear are the links between data, interpretation and conclusions? Are the conclusions plausible and coherent? Are the implications of the research clearly defined?

APPENDIX 4: UNOBTAINABLE REFERENCES

The following references were identified but full papers were either not retrieved or we were unable to properly assess them for inclusion (due to translation difficulties). The papers we were unable to get were not available in-house, on the Internet or from the British Library, without asking for extended or world-wide searches. Extensive searches of this nature are expensive, time consuming and often not successful. Where papers were not available without taking this route, the information we had was assessed by the team to help us make a decision about whether or not to proceed

What's new in cancer research: highlights of the 44th Annual Meeting of the American Society of Clinical Oncology. *Coping Cancer* 2008;22:26-7.

Cancer survivors not following through. *ASRT Scanner* 2009;41:10.

Balling KA. *Surviving childhood cancer: The impact on transition to emerging adulthood [Thesis]*. Balling, Karla A.: U Wisconsin - Madison, US; 2003.

Dalton A. Using technology to meet long-term needs of childhood cancer survivors. *Oncol Times* 2005;27:15-6, 19.

Green D. The further survival of five year survivors of childhood and adolescent cancer. *J Insur Med* 1995;27:81-90.

Hobbie W, Jacobs LA. What happens after cancer? Nurse practitioners play important roles in survivorship programs. *Nurse Pract World News* 2006;11:17, 24.

The following reference was obtained but not used: Japanese paper – not able to translate

Kaneko M. [Late effects of cancer treatment in children--problems to be solved in adult]. *Journal of Japan Surgical Society* 2009;110:203-6.

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4. American Academy of Pediatrics Section on Hematology/Oncology. Long-term follow-up care for pediatric cancer survivors. *Pediatrics* 2009;**123**:906-15.
5. Wallace WHB, Blacklay A, Eiser C, Davies H, Hawkins M, Levitt GA, et al. Developing strategies for long term follow up of survivors of childhood cancer. *BMJ* 2001;**323**:271-4.
6. Bashore L. Childhood and adolescent cancer survivors' knowledge of their disease and effects of treatment. *J Pediatr Oncol Nurs* 2004;**21**:98-102.
7. Landier W, Wallace WHB, Hudson MM. Long-term follow-up of pediatric cancer survivors: education, surveillance, and screening. *Pediatr Blood Cancer* 2006;**46**:149-58.
8. Oeffinger KC, Mertens AC, Sklar CA, Kawashima T, Hudson MM, Meadows AT, et al. Chronic health conditions in adult survivors of childhood cancer. *N Engl J Med* 2006;**355**:1572-82.
9. Ganz PA. Monitoring the physical health of cancer survivors: a survivorship-focused medical history. *J Clin Oncol* 2006;**24**:5105-11.
10. 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.
11. Skinner R, Wallace WHB, Levitt GA. Long-term follow-up of people who have survived cancer during childhood. *Lancet Oncol* 2006;**7**:489-98.
12. Jenney M, Levitt G. Survivors of childhood cancer. *BMJ* 2009;**339**:3-4.
13. Ginsberg JP, Hobbie WL, Carlson CA, Meadows AT. Delivering long-term follow-up care to pediatric cancer survivors: transitional care issues. *Pediatr Blood Cancer* 2006;**46**:169-73.
14. Freyer DR, Kibrick-Lazear R. In sickness and in health: transition of cancer-related care for older adolescents and young adults. *Cancer* 2006;**107 (7 Suppl)**:1702-9.
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