*Journal of Pediatric Psychology,* Vol. 25, No. 6, 2000, pp. 449–460

# Examining the Psychological Consequences of Surviving Childhood Cancer: Systematic Review as a Research Method in Pediatric Psychology

*Christine Eiser,* BSc, PhD, *Jacqueline J. Hill,* BSc, MSc, and *Yvonne H. Vance,* BSc, MSc
*University of Sheffield*

***Objective:*** **To report the results of a systematic review to determine the psychological consequences of surviving childhood cancer.**

***Methods:*** **Searches were conducted using Psyclit, Medline, Cinahl, and Bids and articles selected on the basis of predefined criteria. Key information was extracted to data sheets and these were rated by two coders.**

***Results:*** **Twenty studies were identified, seventeen from the United States. Survivors did not show deficits in measures of anxiety, depression, or self-esteem when compared with population norms or matched controls. Survivors of some cancers (bone tumors) have poorer outcomes.**

***Conclusions:*** **The results of this review support findings of previous descriptive reviews. Methodological problems include poorly reported medical information (for example, time since diagnosis), heterogeneous samples, self-selection of participants, poorly chosen/lack of suitable measures, and a lack of longitudinal work. Findings are discussed in terms of the need for cross-cultural work on adjustment to childhood cancer, the need for studies to take on a more developmental approach, and for greater national and international collaboration.**

***Key words:*** *childhood cancer; pediatric psychology; systematic review; psychological consequences of cancer.*

Improvements in treatment and coordination of care have contributed to increased survival following diagnosis of childhood cancers so that now almost 70% of children may expect to survive at least 5 years following diagnosis (Stiller, Allen, & Eatock, 1995). However, because many survivors experience residual physical, behavioral, or social sequelae associated with the disease or its treatment, considerable implications remain both for individuals and health services (Hawkins & Stevens, 1996). Given the low incidence of cancer in children, greater national and international collaboration might lead to a clearer understanding the psychological sequelae. This review attempts to synthesize current work in the area, to stimulate more thorough and defensible methodologies in the future.

Due to the number of sequelae associated with different therapies, interest in the long-term *physical* outcome of cancer treatment has grown steadily in recent years (Hawkins & Stevens, 1996). However, the long-term *psychological* and *behavioral* consequences of cancer also merit study. In attempts to summarize these findings, at least five reviews of

*All correspondence should be sent to Christine Eiser, Department of Psychology, University of Sheffield, Western Bank, Sheffield, S10 2TP, England. E-mail: C.Eiser@sheffield.ac.uk.*

this literature have been published (Chang, 1991; Eiser, 1998; Eiser & Havermans, 1994; Kazak, 1994; Zeltzer, 1993). All identify methodological problems in empirical work, particularly the focus on measures of maladjustment and depression rather than coping. All also conclude that there is no evidence to suggest that survivors inevitably fare badly, but at the same time they point to subgroups who show more serious adjustment and emotional problems. The more recent reviews (Eiser, 1998; Kazak, 1994) emphasize that most empirical work has failed to distinguish between survivors of different cancers; consequently, more is known about some cancers than others (e.g., Hodgkin's disease or acute lymphoblastic leukemia [ALL]). Methodological limitations are widely noted in this field, especially the reliance on cross-sectional work rather than longitudinal research. Longitudinal studies demand both time and money but are unique in their ability to determine causal relations and trace characteristics that identify at-risk groups over time.

Given the low incidence of childhood cancer, progress in treatment has been achieved in large part through national and international collaboration which has resulted in more rapid understanding of the etiology of cancer and in advances in medical care. It is disappointing that such collaboration has not been evident for more psychosocial issues. Differences in perception of cancer and in attitudes toward individuals with cancer are likely to enhance understanding of adaptation and coping. As survival increases, issues of coping become paramount.

These reviews have raised awareness about the range of outcomes for survivors of childhood cancer but, like all narrative reviews, are themselves the source of bias. For example, investigators may fail to search the complete spectrum of journals relevant to the issue; they may fail to include all studies without specifying the criteria on which exclusions are made; and they may interpret the literature according to a predefined hypothesis. Failure to specify the specific purpose of the review may limit the extent to which the work has any impact on clinical practice and patient management.

For these reasons, systematic reviews are increasingly recommended, especially in health sciences work, where reviews of research evidence are considered important to allow for planning services and allocating resources. Systematic reviews are organized round a specific topic and should yield information of direct relevance to health planners. Systematic reviews "differ from other types of review in that they adhere to strict scientific design in order to make them more comprehensive, minimise the chance of bias, and so ensure their reliability. Rather than reflecting the bias of the authors or being based only on a selection of the published literature, they contain a comprehensive summary of the evidence" (Cook, Sackett, & Spitzer, 1995).

A number of guidelines for conducting systematic reviews have been described (Oxman, 1994). It is recommended that the work is conducted in eleven phases. Phase 0 includes an assessment of the need for the specific review and must involve reference to potential sources including computer databases and the Cochrane Collaboration to determine that no comparable review has been, or is being, undertaken. Phases 1 and 2 involve planning the review. A preliminary assessment of the potential scope of the review needs to be undertaken and a decision made as to whether answering the specified research question is possible. A protocol needs to be written in which questions are defined and methods determined. The protocol should state the databases to be searched and the criteria for inclusion of a study into the review. A data extraction sheet must be described that summarizes the main information to be extracted from each individual article in the review.

Extensive literature searching is the main task in phase 3. Both computerized and manual searches are recommended to ensure comprehensive and unbiased study identification. In phase 4, decisions are made about which studies will appear in the review. Selection criteria need to be identified and piloted to ensure they can be reliably interpreted. There are inevitable decisions to be made about how narrow inclusion criteria should be. Generalizability of the results will be affected by the strictness of the criteria adopted. Too liberal inclusion criteria can make interpretation of the results more difficult. Tables of studies included and excluded from the review should be constructed. In phase 5, the validity of studies needs to be determined. This reflects the degree to which a study is subject to bias. Decisions about validity are best made with reference to a specially developed checklist. Data extraction is carried out at phase 6. Reference should be made to the protocol to determine the information to be extracted from studies: bibliographic details, descriptions of the setting, study population, the nature

and delivery of the intervention, outcome measures used, and results. Information about sample size, attrition rates, and aspects of the methodology that might affect results also need to be recorded. Data extraction should be performed by at least two coders and disagreements discussed. Where data is missing or unclear, attempts should be made to contact the authors for further information.

The aim of phase 7 is to draw together results of the primary studies identified in phase 6 using quantitative or qualitative methods. Where appropriate, meta-analyses should be conducted. Phase 8 involves writing the report, which should include reasons for the review, methods used, tables of studies included and excluded, discussion of the strength of the evidence, practical implications, and suggestions for dissemination of the findings. In phase 9, the review is assessed by a panel of experts and meetings held to discuss the relevance of the work. The submission of the final report occurs in phase 10, which may include recommendations for further work.

The purpose of this article is to report our experience in conducting a systematic review concerned with psychological outcomes for survivors of childhood cancer. In accordance with recommendations in phase 0, we first identified the specific questions to be asked and made sure that no comparable review was being undertaken. The review was justified on the following grounds: first, current literature is published in medical, nursing, and psychology journals and it was considered useful to provide a single source; second, it is important to determine the psychological and behavioral outcomes among survivors in order to provide information for new families; third, such information is useful at a public health level in determining the extent and type of support likely to benefit families. The specific questions to be addressed were:

1. What are the main outcome measures used to assess the impact of cancer on survivors?
2. What does this literature tell us about the social and psychological outcomes for survivors of childhood cancer?
3. Do parents and teachers differ from survivors in their views of the impact of cancer?
4 Can clinical or demographic factors modify the outcomes of treatment?
5. Is there any evidence of posttraumatic stress disorder (PTSD) among survivors?
6. Are there differences in psychological outcomes dependent on the nature of the specific cancer diagnosis?

## Method

We had few difficulties in phases 0 and 1 about making a decision about the scope of the review. As argued above, the decision to conduct a systematic review of survivors of cancer was based on increased survival and recognition of late psychological and physical effects.

An initial search of the literature suggested that psychosocial effects of childhood cancer have been assessed in a number of ways: (1) learning, intelligence, and academic achievements (Mulhern, 1994); (2) lifestyles, especially health behaviors such as smoking or drinking (Haupt et al., 1992), or occupational and vocational status (Green, Zevon, & Hall, 1990); and (3) general mental health issues, including anxiety and depression. The literature on learning has been reviewed elsewhere (cf. Mulhern, 1994). The focus on health behaviors is relatively recent, and we felt there was not sufficient evidence to justify a review. This review therefore focuses *specifically* on studies involving general mental health issues.

As recommended, we followed the guidelines described above in executing the search. The review was carried out using the following databases: Psyclit, Medline, Cinahl, and Bids. Cancerlit and Pub.Med. were also accessed but revealed very few articles not covered by the preceding databases. The following key words were used as the search criteria; childhood survivors of cancer, adolescent survivors of cancer, quality of life and children with cancer, outcome measures—children—cancer. In addition, we hand-searched recent issues of key journals and identified additional references from those provided in identified papers.

### *Inclusion Criteria*

Articles were included on the basis of (1) year of publication: studies were included if published within the last decade (i.e., since 1990); (2) language: English language articles only; and (3) method: studies were included if they used standardized measures and conducted statistical tests to compare scores with population norms or matched controls. Refer-

ence Manager (Institute for Scientific Information, 1997) was used as the bibliographic software package to organize the relevant references.

## Results

Twenty studies met the inclusion criteria and are summarized in Table I. Two further articles (Boman & Bodegard, 1995; Greenberg & Meadows, 1991) were excluded on the grounds that they solely used interview methodologies and no standardized measures. Of the included articles, 17 were from the United States, 2 from the United Kingdom, and 1 from the Netherlands. Fourteen focused on general measures of adjustment and mental health, two focused specifically on social functioning, and four on posttraumatic stress disorder. There were three prospective studies (Kazak, Christakis, Alderfer, & Coiro, 1994; Kupst et al., 1995; Noll, Bukowski, Davies, Koontz, & Kulkarni, 1993), the remainder were cross-sectional.

Age of subjects ranged from 3 (Butler, Rizzi, & Handwerger, 1996) to 37 years (Gray et al., 1992a, 1992b). Sample sizes varied from 20 (Olson, Boyle, Evans, & Zug, 1993) to 309 (Barakat et al., 1997).

### *1. What Are the Main Outcome Measures Used to Assess the Impact of Cancer on Survivors?*

There has been little consensus regarding the most appropriate measures, which included assessment of self-esteem (11), anxiety (5), depression (3), social skills (2), body image (2), loneliness (2), mood (2), personality (3), coping (1), health status/quality of life (1), social desirability (2), intrusiveness (4), and symptoms (2). These are all generic measures. No studies used cancer-specific outcome measures. Three studies included specially developed interviews with standardized questionnaires. In four studies, PTSD was determined. A smaller number of measures were used for completion by parents: child behavior (4), family functioning (3), parental distress (1), parental social support (1), parent anxiety (1), and parenting stress (1). Measures used for teachers included the Child Behavior Checklist (teacher report form; Achenbach, 1991); the taxonomy of problem situations (Dodge, McClaskey, & Feldman, 1985) and the cancer-specific teacher behavior rating scale (Deasey-Spinetta & Spinetta, 1980).

### *2. What Are the Social and Psychological Outcomes for Survivors of Childhood Cancer?*

*Comparisons with population norms*. Seven studies included comparisons with population norms, six included both population norms and a control group, and seven relied on a control group only. Only one study (Eiser et al., 1997) reported more symptoms in survivors when compared with norms; the majority ($n$ = 5) reported no differences. One study (Elkin, Phipps, Mulhern, & Fairclough, 1997) reported that survivors had fewer symptoms compared with norms.

Eiser et al. (1997) studied 41 patients all of whom had a lower limb tumor and had been treated by limb salvage. The group had worse scores than population norms (Jenkinson, Coulter, & Wright, 1993) and these were significant on subscales measuring physical functioning, physical role performance, pain, general health, and social functioning. This may reflect the fact that many bone tumor survivors continue to have problems with mobility and pain and need further treatment. This study also included some survivors who were considerably older than many of those in other studies. These outcomes may therefore partly depend on the fact that patients were treated before the introduction of modern protocols, or that the effects of cancer survival become cumulative over time.

The remaining studies reported no differences between survivors and population norms. In terms of self-esteem, no differences between survivors and age-appropriate norms were reported by Anholt, Fritz, and Keener, (1993). Noll et al. (1993) reported similar results for depression, and Radcliffe, Bennett, Kazak, Foley, and Phillips (1996) for self-perception. This latter study is particularly important as it focuses on survivors of CNS tumors, who might be expected to have poorer outcomes. Kupst et al. (1995) studied a group of survivors (16 males, 12 females; mean age = 19 years) for 10 years following diagnosis. These survivors represented 64 children originally recruited on diagnosis of ALL and assessed at intervals throughout treatment (Kupst & Schulman, 1988). Symptom scores (Derogatis, 1992) and 10-year follow-up assessments were within normal ranges.

Based on a standardized measure of symptom report, Elkin et al. (1997) found that survivors reported fewer symptoms (i.e., had better health) in comparison with population norms.

**Table I.** Summary of Studies Included in the Review

| Study | Sample (*n*) | Age of children (range; yrs) | Study origin | Parent sample | Time since diagnosis (mean) | Comparison group | Results |
|---|---|---|---|---|---|---|---|
| Anholt et al. (1993) | 62 | 7–18 | USA | No | 20 months[a] | 120 healthy children; norms | Self concept was similar to population norms.<br>Survivors rated their school status, behavior, overall happiness, and satisfaction more positively than controls. |
| Barakat et al. (1997) | 309 | 8–20 | USA | Yes | 5.86 years[a] | 219 healthy families; norms | No difference in PTSD from population norms.<br>Parents of survivors reported more PTSD than control parents. |
| Butler et al. (1996) | 42 | 3–16 | USA | Yes | 35 months[a] | Norms | Incidence of Posttraumatic Stress Disorder (PTSD) no different from population norms. |
| Eiser et al. (1997) | 41 | 8–28 | UK | Yes | 6.8 years | Norms | Scores below population norms especially on measures of physical functioning, physical role performance, pain, general health, and social functioning. |
| Elkin et al. (1997) | 161 | 14.5–30.9 | USA | No | 9.5 years | Norms | 75% showed some residual cosmetic impairments.<br>64% demonstrated physical impairment. |
| Gray et al. (1992a, 1992b) | 62 | 18–37 | USA | No | 14.6 years | Norms; peers (selected by survivors) | No significant differences between survivors and peers on standardized inventories, story-telling, or physical symptoms.<br>Compared with peers, survivors were less satisfied with social relationships; showed greater concern about infertility; expressed more perceived control and more satisfaction with their degree of autonomy; were more likely to prefer interacting with others. |
| Kazak et al. (1994) | 59 | 10–15 | USA | Yes | 96.20 months | Norms | No differences from population norms in levels of adjustment.<br>Few changes over 1 year testing.<br>Survivors with learning difficulties had more adjustment problems. |
| Kazak et al. (1997) | 130 | 8–19 | USA | Yes | 5.79 years[a] | 155 healthy children; norms | No differences in PTSD symptoms between survivors and controls.<br>Predictors of PTSD included family functioning and social support; no effects of demographic or clinic variables on PTSD. |
| Kupst et al. (1995) | 28 | 14–30 | USA | Yes | 10 years | Norms | Survivors and parents were generally well-adjusted.<br>Survivors' coping and perceived adjustment were positively related to SES and mother's coping and negatively related to academic problems.<br>No differences from population norms. |

**Table I.** *Continued*

| Study | Sample (*n*) | Age of children (range; yrs) | Study origin | Parent sample | Time since diagnosis (mean) | Comparison group | Results |
|---|---|---|---|---|---|---|---|
| Madan-Swain et al. (1994) | 25 | 12–18 | USA | Yes | 8.4 years | 16 healthy children | No major difficulties on measures of social competence, overall coping, and family communication.<br>Survivors reported body image and adjustment difficulties. |
| Noll et al. (1993) | 19 (time 1); 17 (time 2) | 11–18 | USA | Yes | 62.5 months | 17 healthy children; norms | No differences between survivors and controls in psychological functioning.<br>Depression scores were not significantly different from population norms.<br>No differences were found between the groups on teacher reports. |
| Olson et al. (1993) | 20 | 6–16 | USA | Yes | | 40 healthy children | Survivors showed poorer social competence, school performance, more behavioral and academic problems than controls.<br>No differences on self-esteem, family conflict, physical functioning, social skills, sense of control over health. |
| Pendley et al. (1997) | 21 | 11–21 | USA | Yes | 17 months[a] | Healthy children recruited from local advertisements | Healthy controls and survivors did not differ on measures of body image, attractiveness, loneliness, social anxiety, and school absenteeism. |
| Radcliffe et al. (1996) | 38 | 6–18 | USA | Yes | 2–5 years | Norms | Compared with norms, children rated themselves as less anxious, depressed, and athletically competent, but similar in terms of self-perception.<br>Mothers rated their children as less competent than children's self-report.<br>Teachers did not report differences between survivors and norms. |
| Sloper et al. (1994) | 31 | 8–18 | UK | Yes | 5 years | Healthy children | No differences in self-ratings of anxiety or self-esteem with controls.<br>Teachers rated survivors to have greater difficulties than controls with concentration, academic progress, and popularity. |
| Stern et al. (1993) | 48 | 14–23 | USA | No | 2.79 years[a] | 40 healthy adolescents | Survivors were relatively well-adjusted, but had a less positive self-image in terms of their social and sexual selves. |
| Stuber et al. (1996) | 64 | 7–19 | USA | Yes | 6.7 years | Norms | Compared with norms, 12.5% survivors showed severe PTSD symptoms. |
| van Dongen-Melman et al. (1995) | 95 | 8–12 | Netherlands | Yes | <2 yrs = 32%<br>2–5yrs = 42%<br>>5yrs = 26%[a] | 90 children from local schools | Survivors showed more social and internalizing problems than controls.<br>On most measures, female survivors did not show significantly more serious adjustment problems than healthy controls. |
| Vannatta et al. (1998) | 28 | 8–18 | USA | No | 3 years | 28 classroom years | Compared with peers, survivors received fewer friendship nominations.<br>Peers perceived survivors to be more sick, fatigued, and absent from school. |

[a]Time since treatment completed.

*Comparisons with control groups.* In addition to the comparisons made with population norms, Anholt et al. (1993) compared survivors with a normal group matched for chronological age. Survivors had more positive self-esteem, especially in terms of school status, behavior, and overall satisfaction. However, no differences between survivors and controls were reported by Gray et al. (1992a, 1992b), Stern, Norman, and Zevon (1993), Sloper, Larcombe, and Charlton (1994), Madan-Swain et al. (1994), and Pendley, Dahlquist, and Dreyer (1997). Noll et al. (1993) compared adaptation in survivors with matched controls (17 dyads) in a 2-year longitudinal study. Data were collected from teachers, peers, and patients themselves. There were no differences between children with cancer and controls on any measures of friendship or popularity. Children treated for cancer rated themselves and were more likely to be viewed by classmates as sensitive and isolated. No differences between the groups were found on teacher reports.

The findings from these studies are broadly in line with those where comparisons are made against population norms: few measurable differences on *standardized* measures between survivors and controls are noted, but some discrepancies do exist. For example, based on interview data, survivors were more likely to have repeated a school grade, less likely to be drinkers, and less likely to have experienced black-outs following a drinking episode (Gray et al., 1992a, 1992b). Again from interview data, Madan-Swain et al. (1994) found that survivors were more likely to report body image disturbance and adjustment difficulties, and Pendley et al. (1997) reported that survivors participated in fewer activities than controls.

### *3. Do Parents and Teachers Differ From Survivors in Their Views of the Impact of Cancer?*

Parents and teachers report that survivors have more problems than would be expected from population norms or in comparison with control groups (Radcliffe et al., 1996; Van Dongen-Melman, De Groot, Kahlen, & Verhulst, 1995). Teacher reports have been mixed, with most findings showing no differences between survivors and norms or controls (Noll et al., 1993; Radcliffe et al., 1996). However, no studies compared parent and child ratings on the same measures.

### *4. Can Clinical or Demographic Factors Modify the Outcomes of Treatment?*

It might be expected that outcomes would be moderated by family, clinical, or demographic factors, so that children with poorer clinical status would have poorer psychological outcomes. In addition, social and family circumstances may be expected to moderate outcomes. Consistent findings have not been reported.

Family variables were described by Sloper et al. (1994) and Kupst et al. (1995). Sloper et al. (1994) found that parents who report more psychological distress themselves also report more behavior problems in their child. Kupst et al. reported that higher social class and better maternal coping were associated with better adjustment among survivors. Those with school problems had poorer adjustment than those without. Age, gender, and previous coping were not associated with any of the outcome variables.

Other work has assessed the contribution of demographic or clinical factors. Van Dongen-Melman et al. (1995) reported worse outcome for those treated by CNS radiation and for those who are overweight. Particular problems were noted for male survivors both from parent and self-report. Elkin et al. (1997) reported that older patients had worse outcomes in terms of somatization, anxiety, hostility, phobic anxiety, and psychoticism, as well as a global index of symptomatology (Derogatis, 1977). A single relapse more than doubled the likelihood of higher scores on the obsessive-compulsive and paranoid ideation scales. There is thus a suggestion from two studies that family factors are important, and three others implicate treatment variables.

### *5. Is There Any Evidence of PTSD Among Survivors?*

*Incidence of PTSD.* Four studies have included assessments of the incidence of PTSD among survivors. Suggestions that survivors reported more symptoms of PTSD than would be expected from population norms were made by Stuber, Christakis, Houskamp, and Kazak (1996). They reported that more than half their sample of survivors reported specific symptoms of PTSD. These included bad dreams, feeling afraid or upset when they think about cancer, feeling alone inside, and feeling nervous. In total, 12.5% of survivors scored at a level that would

indicate a clinical diagnosis of PTSD. These findings have not been supported when comparisons are made with control groups. Butler et al. (1996) found little evidence of PTSD in a group of 42 survivors compared with children on treatment. Both Kazak et al. (1997) and Barakat et al. (1997) reported that the incidence of PTSD among survivors was similar to that for healthy controls.

*Moderators of PTSD.* A number of variables have been reported to contribute to PTSD. These include family functioning and social support (Kazak et al., 1997). In the study described above, Barakat et al. (1997) also found that perceived life threat and social and family resources moderated the incidence of PSTD symptoms.

### *6. Are There Differences in Psychological Outcomes Dependent on the Nature of the Specific Cancer Diagnosis?*

The majority ($n$ = 14) of studies involved samples including survivors of different cancers and did not attempt to distinguish between diagnostic groups in terms of outcomes. Two studies focused specifically on survivors of a CNS tumor (Radcliffe et al., 1996; Vannatta, Gartstein, Short, & Noll, 1998), and Eiser et al. (1997) included only those treated for a bone tumor. Three studies looked specifically at children with leukemia (Kazak et al., 1997; Kupst et al., 1995; Stuber et al., 1996). Although outcomes likely will depend on the specific cancer, the failure of any comparative study means that it is not currently possible to make any definitive comments about this issue.

## Discussion

One might argue that these findings reflect the conclusions of previous narrative reviews. However, the requirements for methodological rigor, which are an integral part of the systematic review process, mean that one can be more confident about the limitations of previous studies and about the requirements for greater quality in future work.

Simple comparisons of survivors against population norms on standardized measures of anxiety, depression, and self-esteem point to few differences. These conclusions are also true where comparisons are made against "matched" control groups. However, there are suggestions that groups differ when other methodologies are used; for example, interview data can highlight problems not included on questionnaire measures (Gray et al., 1992a, 1992b).

Parents and teachers rate survivors as having more problems than controls or norms, but as yet no comparisons have been made between survivors and parents or teachers on the same measure. Certain family, clinical, and demographic variables have been described as moderating outcomes, including parental distress (Sloper et al., 1994), social class and coping (Kupst et al., 1995), and incidence of recurrence (Elkin et al., 1997). Finally, reports of PTSD incidence have been mixed. When comparisons have been made against norms, PTSD in survivors has been higher (Stuber et al., 1996), whereas when control groups are used, few differences are found (Barakat et al., 1997; Butler et al., 1996; Kazak et al., 1997).

Evaluations of a systematic review should include comments about the adequacy of the literature and especially any methodology that might reduce the validity of the conclusions. First, critical clinical information such as time since completion of treatment can be poorly reported. Some authors adopted a general requirement that patients should be at least 5 years from diagnosis, although others were less specific. Thus, it is not clear how far recovery continues with increasing time from diagnosis. Second, studies routinely include survivors with different cancers, some of whom may have experienced less aggressive treatments compared with others. For example, it is inappropriate to include in the same study survivors of stage I Hodgkin's disease, who may have experienced relatively brief treatments, with those treated more aggressively, as is the case for a bone tumor or CNS tumor. Inconsistent results may therefore be partly attributable to disease or treatment effects, but have received little attention. Details of treatment protocols are rarely provided so that there is little evidence regarding the relationship between psychological outcome and treatment.

Third, problems in much of this work include the self-selection of participants. Response rates can be poor and can introduce bias into a study. The extent to which survivors who take part in research are representative of the total cohort needs to be considered. Inevitably this is a mobile population and some are lost to follow-up. Methods of recruitment of the control groups are sometimes questionable. Pendley et al. (1997) recruited volunteers from advertisements; Gray et al. (1992a, 1992b), asked

patients to recommend friends. Both approaches may introduce bias in the direction of recruiting individuals who are more willing to help. Where the control group is recruited from among survivors' friends, fewer differences between survivors and healthy peers may be expected, since friends are likely to share common interests. Survivors with any obvious handicap or visible disfigurement are routinely excluded from most published work (e.g., Pendley et al., 1997), perhaps resulting in an underestimation of psychological problems. At a minimal level, researchers should attempt to describe any differences between those who agree to participate and those who refuse or cannot be traced, to ensure that some idea about representativeness of survivors is possible.

Fourth, issues of measurement are not satisfactorily resolved. There are huge obstacles to choosing measures that are suitable across as wide age ranges as are customarily described. Many measures in common use were developed to assess symptoms generally and are not cancer-specific. Some questionnaires are potentially distressing or intrusive (Stuber et al., 1997). These methodological problems, including use of postal surveys and potentially distressing questionnaires, may contribute to poor completion rates. The solution has to be more focused and developmentally appropriate assessments. This can be achieved as the numbers of survivors grows, and if centers are prepared to collaborate. Pediatricians and child psychologists need to be prepared to draw on the expertise of adult clinicians to select measures appropriate for young adult survivors.

Fifth, only Kupst and her colleagues have traced outcomes over a significant period of time (from diagnosis for more than 10 years). Longitudinal work has the important advantage over cross-sectional studies of charting changes in adjustment and functioning over time. However, using longitudinal data can also have severe shortcomings. Comparisons of group means on a variety of measures can give the impression that adjustment does not change over time, while inspection of individual scores (for example, individuals who move from scoring at a clinically elevated level to a nonclinical level on a measure) can show a completely different pattern (cf. Thompson, Gustafson, George, & Spock, 1994). Researchers should attempt more longitudinal designs, while remaining alert to individual differences within the data.

### *Implications*

*Theoretical.* Our review emphasizes how far research continues to adopt a deficit-centered theoretical perspective and to focus on maladjustment rather than coping. New theoretical frameworks are crucial. At the least, theories are needed to direct assumptions about the ways in which development might be affected by surviving a life-threatening disease and, consequently, the behaviors to be measured. At the same time, it must be recognized that the goals of the individual child also include those of "leading a normal life." For this reason, theoretical frameworks that focus on the developmental tasks to be achieved during adolescence (Havighurst, 1953) may also be important. Future work needs to address how normative developmental tasks can be attained with as little psychological distress as possible.

*Clinical.* A priority of a systematic review is to provide information relevant to hospital managers so as to influence priority setting and decisions about resources. Unfortunately, methodological limitations restrict the generalizability of findings and their use in clinical settings. Survivors with pronounced difficulties are excluded from much research with the result that perceptions of the need for services for survivors is likely to be underestimated. Survivors with obvious physical difficulties are routinely excluded, and there has been very little follow-up of survivors of CNS tumors who are more likely to need educational support.

A major issue for providers concerns the appropriateness of follow-up care. Follow-up clinics are recommended in order to gain information about the toxicity of different treatments and direct changes in subsequent protocols. For survivors themselves, the requirement for follow-up may seem to contradict their otherwise healthy status and lack of awareness of the possibility of future health complications. Thus, attendance at follow-up can be poor and confuses the issue of how it may be affected by provisions of adult- or pediatric-based services. In either case, survivors are likely to be given threatening information regarding their current and future health, and information about the best way to do this would be useful. Again this literature offers no guidance to those concerned with how to give potentially threatening information in such a way that survivors respond pragmatically rather than by denying the existence of problems.

Although the aim of a systematic review is to

increase our ability to assess research in an objective manner, the method itself is inevitably associated with problems. As with any review, a systematic review can be no better than the empirical work on which it is based. The process of conducting a systematic review in some contexts (e.g., randomized control trials; RCTs) has been well described, and guidelines are available about the most appropriate search strategies. Much less advice is available when conducting a systematic review of literature not involving RCTs. Decisions need to be made in determining the criteria for inclusion of a study into the review. No studies reported power or effect sizes, making judgments about appropriateness of sample sizes impossible. (Attempts at producing power calculations might reduce the confusion in the literature but could not be conducted here due to lack of the relevant data.) In attempting to determine the validity of studies, critical information, such as time since treatment, was often missing. Yet, clearly, if strict inclusion criteria were adopted, almost no study would be satisfactory.

A problem with defining strict inclusion criteria is that the potential exists for a single study (or group of studies) to be used in policy decision-making and resource allocation. By relaxing the criteria for inclusion in our review, there is the potential for misuse of these data in policy development. However, in Table II we define methodological criteria for inclusion that should guide future studies. With this standard established, researchers can be better aware of the public policy implications and uses of their research, and improvements in reported studies can evolve more effectively and efficiently.

Although our conclusions do not differ substantially from those made in previous narrative reviews, the attempt to conduct a systematic review focuses attention on the methodological issues involved in this work. At the least, this exercise should be used to establish a degree of quality control in the area and alert researchers to the level of sophistication that needs to be more routinely integrated in psychosocial work in pediatric oncology. This is especially pertinent considering the extremely stretched resources in medical services across most, if not all countries around the world. Research findings can potentially be used to guide allocations of resources and planning services, so that it makes sense to increase the quality of our work in order to use these resources wisely. Systematic reviews offer a methodology that emphasizes that only quality work should be used to guide these resources. Thus, Table II offers a guide for future research. These standards need to be upheld by forthcoming researchers in order to set the tone and quality for future research in this area.

**Table II.** Suggested Methodological Criteria

| Issue | Criterion |
|---|---|
| Measurements | Well-validated and reliable measures. |
| Respondents | Both parent and child (if child is age-appropriate and in good health). |
| Control/ comparison group | Well-matched control group, or compared with measurement norms (care must be made that norms are culturally appropriate). |
| Information about sample | Age; gender; ethnic composition; location of sample (e.g., rural or urban sample); SES; respondent rate; time since diagnosis (or time since treatment ended); exact cancer diagnosis. Additional information concerning the parents' age, marital status, and employment status. |
| Results | Appropriate rigorous statistical tests to be used. |

It is generally recognized that improvements in survival in childhood cancer have been achieved at least partly as a result of collaboration achieved through national and international clinical trials. This collaboration raises questions about cross-cultural implications of cancer. With respect to late consequences of surviving childhood cancer, the literature is predominantly conducted in the United States (we identified only three studies published elsewhere). No studies were included in this review from anywhere outside the United States and Europe. This may be partly due to a publication bias in American and European journals and also because of our criterion that each study be published in English. However, considering the differences in adjustment to cancer across cultures, it raises issues about the functioning of childhood cancer survivors in other countries. For instance, with regard to desired medical communication or disclosure, the traditional North American or West European response is one of full disclosure. However, the traditional Asian response is one of patient protection (Gotay, 1996). Another example of cross-cultural differences lies in attitudes toward autonomy. In North American or West European cultures, individual rights and individual independence are of great importance, whereas Asian cultures tend to stress interconnectedness and interdependence. These is-

sues are also important when considering measurement. For example, with regard to the issue of independence, it is not surprising that North American quality of life measures stress physical functioning and a person's ability to act independently (Gotay, 1996). However, in a sample of Indian patients, individual functioning was rated as the least important aspect of their quality of life, with issues such as family happiness and spiritual satisfaction rating much higher (Chaturvedi, 1991). Future work must consider the ethnic and cultural background of survivors, in helping them through the illness and to a cure.

The question of psychological outcome following the experience of a life-threatening disease and its treatment remains to be determined, but good studies are important in order to determine the scope and range of remedial resources needed by some survivors. As with clinical work, these answers are most likely to be achieved through collaboration, both between professionals and internationally.

## Acknowledgments

This research was supported by a grant from the Cancer Research Campaign, (CP 1019/0101 & CP 1019/0104). We thank Sarah Bennett for help in conducting the searches.

*Received March 5, 1999; revisions received August 14, 1999; accepted September 18, 1999*

## References

Achenbach, T. M. (1991). *Manual for the child behavior checklist/4–18 and 1991 profile*. Burlington: University of Vermont, Department of Psychiatry.

Anholt, U. V., Fritz, G. K., & Keener, M. (1993). Self-concept in survivors of childhood and adolescent cancer. *Journal of Psychosocial Oncology, 11,* 1–16.

Barakat, L. P., Kazak, A. E., Meadows, A. T., Casey, R., Meeske, K. & Stuber, M. L. (1997). Families surviving childhood cancer: A comparison of posttraumatic stress symptoms with families of healthy children. *Journal of Pediatric Psychology, 22,* 843–859.

Boman, K., & Bodegard, G. (1995). Psychological long-term coping with experiences of disease and treatment in childhood cancer survivors. *Acta Paediatrica*, *84,* 1395–1402.

Butler, R. W., Rizzi, L. P., & Handwerger, B. A. (1996). Brief report: The assessment of Posttraumatic Stress Disorder in pediatric cancer patients and survivors. *Journal of Pediatric Psychology, 21,* 499–504.

Chang, P. (1991). Psychosocial needs of long-term childhood cancer survivors: A review of literature. *Pediatrician, 18,* 20–24.

Chaturvedi, S. (1991). What's important for quality of life to Indians—in relation to cancer. *Social Science and Medicine, 33,* 91–94.

Cook, D. J., Sackett, D. L., & Spitzer, W. O. (1995). Methodological guidelines for systematic reviews of randomized controlled trials in health care from the Potsdam consultation on meta-analysis. *Journal of Clinical Epidemiology, 48,* 167–171.

Deasey-Spinetta, P., & Spinetta, J. J. (1980). The child with cancer in school: Teacher's appraisal. *American Journal of Pediatric Haematology and Oncology, 2,* 89–94.

Derogatis, L. R. (1977). *The SCL-90-R administration, scoring and procedures manual—I*. Baltimore, MD: Clinical Psychometric Research.

Derogatis, L. R. (1992). *The Brief Symptom Inventory: Administration, scoring, and procedures manual—II*. Baltimore, MD: Clinical Psychometric Research.

Dodge, K. A., McClaskey, C. L., & Feldman, E. (1985). Situational approach to the assessment of social competence in children. *Journal of Consulting and Clinical Psychology, 53,* 344–353.

Eiser, C. (1998). Practitioner review: Long term consequences of childhood cancer. *Journal of Child Psychology and Psychiatry, 39,* 621–633.

Eiser, C., Cool, P., Grimer, R., Carter, S., Ellis, A., Kopel, S., & Eiser, J. R. (1997). The role of monitoring in determining quality of life following treatment for a bone tumour. *International Journal of Behavioural Medicine, 4,* 398–415.

Eiser, C., Cool, P., Grimer, R. J., Carter, S. R., Cotter, I. M., Ellis, A. J., & Kopel, S. (1997). Quality of life following treatment for a malignant primary bone tumour around the knee. *Sarcoma, 1,* 39–45.

Eiser, C., & Havermans, T. (1994) Long term social adjustment after treatment for childhood cancer. *Archives of Disease in Childhood, 70,* 66–70.

Elkin, T. D., Phipps, S., Mulhern, R. K., & Fairclough, D. (1997). Psychological functioning of adolescent and young adult survivors of pediatric malignancy. *Medical and Pediatric Oncology, 29,* 582–588.

Gotay, C. G. (1996). Cultural variation in family adjustment to cancer. In L. Baider, C. L. Cooper, & A. Kaplan-De-Nour (Eds.), *Cancer and the family.* Chichester, England: John Wiley.

Gray, R. E., Doan, B. D., Shermer, P., Vatter-Fitzgerald, A., Berry, M. P., Jenkin, R. D. T., & Doherty, M. A. (1992a).

Psychologic adaptation of survivors of childhood cancer. *Cancer, 70,* 2713–2721.

Gray, R. E., Doan, B. D., Shermer, P., Vatter-Fitzgerald, A., Berry, M. P., Jenkin, D., & Doherty, M. A. (1992b). Surviving childhood cancer: A descriptive approach to understanding the impact of life-threatening illness. *Psycho-Oncology, 1,* 235–246.

Green, D. M., Zevon, M. A., & Hall, B. (1990). Achievement of life goals by adult survivors of modern treatment for childhood cancer. *Cancer, 67,* 206–213.

Greenberg, H. S., & Meadows, A. T. (1991). Psychosocial impact of cancer survival on school-age children and their parents. *Journal of Psychosocial Oncology, 9,* 43–56.

Haupt, R., Byrne, J., Connelly, R. R., Mostow, E. N., Austin, D. F., Holmes, G. R., Holmes, F. F., Latourette, H. B., Teta, J., Strong, L. C., Myers, M. H., & Mulvihill, J. J. (1992). Smoking habits in survivors of childhood and adolescent cancer. *Medical and Pediatric Oncology, 20, 301–306*.

Havighurst, R. J. (1953) *Developmental tasks and education*. New York, Longmans, Green.

Hawkins, M. M., & Stevens, M. C. (1996). The long term survivors. *British Medical Bulletin, 52,* 898–923.

Institute for Scientific Information. (1997). Reference Manager Version 8 for Windows. Research Information Systems, US.

Jenkinson, C., Coulter, A., & Wright, L. (1993). Short Form 36 (SF 36) Health Survey Questionnaire: Normative data for adults of working age. *British Medical Journal, 306,* 1437–1440.

Kazak, A. E. (1994). Implications of survival: Pediatric oncology patients and their families. In A. Bearison & R. Mulhern (Eds.) *Pediatric psychooncology*. New York: Oxford University Press.

Kazak, A. E., Barakat, L. P., Meeske, K., Christakis, D., Meadows, A. T., Casey, R., Penati, B., & Stuber, M. L. (1997). Post traumatic stress, family functioning and social support in survivors of childhood leukemia and their mothers and fathers. *Journal of Consulting and Clinical Psychology, 65,* 120–129.

Kazak, A. E., Christakis, D., Alderfer, M., & Coiro, M. J. (1994). Young adolescent cancer survivors and their parents: Adjustment, learning problems, and gender. *Journal of Family Psychology, 8,* 74–84.

Kupst, M. J., Natta, M. B., Richardson, C. C., Schulman, J. L., Lavigne, J. V., & Das, L. (1995). Family Coping with pediatric leukemia: Ten years after treatment. *Journal of Pediatric Psychology, 20,* 601–617.

Kupst, M. J., & Schulman, J. L. (1988). Long-term coping with pediatric leukemia: A six year follow-up study. *Journal of Pediatric Psychology, 13,*7–22.

Madan-Swain, A., Brown, R. T., Sexson, S. B., Baldwin, K. et al. (1994). Adolescent cancer survivors: Psychosocial and familial adaptation. *Psychosomatics, 35,* 453–459.

Mulhern, R. K. (1994). Neuropsychological late effects. In A. Bearison & R. Mulhern (Eds.), *Pediatric psychooncology*. New York: Oxford University Press.

Noll, R. B., Bulowski, W. M., Davies, W. H., Koontz, K., & Kulkarni, R. (1993). Adjustment in the peer system of adolescents with cancer: A two-year study. *Journal of Pediatric Psychology, 18,* 351–364.

Olson, A. L., Boyle, W. E., Evans, M. W., & Zug, L. A. (1993). Overall function in rural childhood cancer survivors: the role of social competence and emotional health. *Clinical Pediatrics, 32,* 334–342.

Oxman, A. D. (Ed.). (1994). *Preparing and maintaining systematic reviews: The Cochrane collaboration handbook*. Oxford: Cochrane Collaboration.

Pendley, J. S., Dahlquist, L. M., & Dreyer, Z. A. (1997). Body image and psychosocial adjustment in adolescent cancer survivors. *Journal of Pediatric Psychology, 22,* 29–43.

Radcliffe, J., Benettt, D., Kazak, A. E., Foley, B., & Phillips, P. C. (1996). Adjustment in childhood brain tumor survival: Child, mother and teacher report. *Journal of Pediatric Psychology, 21,* 529–539.

Sloper, P., Larcombe, I., & Charlton, A. (1994). Psychosocial adjustment of five-year survivors of childhood cancer. *Journal of Cancer Education, 9,* 581–588.

Stern, M., Norman, S. L., & Zevon, M. A. (1993). Adolescents with cancer: Self-image and perceived social support as indexes of adaptation. *Journal of Adolescent Research, 8,* 124–142.

Stiller, C. A., Allen, M. B., & Eatock, E. M. (1995). Childhood cancer in Britain: The National registry of childhood tumours and incidence rates 1978–1987. *European Journal of Cancer, 31A,* 2028–2034.

Stuber, M., Christakis, D., Houskamp, B., & Kazak, A. (1996). Posttrauma symptoms in childhood leukemia survivors and their parents. *Psychosomatics, 37,* 254–261.

Thompson, R. J., Gustafson, K. E., George, L. K., & Spock, A. (1994). Change over a 12 month period in the psychological adjustment of children and adolescents with cystic fibrosis. *Journal of Pediatric Psychology, 19,* 189–203.

Van Dongen-Melman, J. E., De Groot, A., Kahlen, K., & Verhulst, F. C. (1995). Psychosocial functioning of children surviving cancer during middle childhood. In J. E. Van Dongen-Melman (Ed.), *On surviving childhood cancer.* Alblasserdam, The Netherlands: Haveka BV.

Vannatta, K., Gartstein, M. A., Short, A., & Noll, R. B. (1998). A controlled study of peer relationships of children surviving brain tumors: teacher, peer, and self ratings. *Journal of Pediatric Psychology, 23,* 279–287.

Zeltzer, L. K. (1993). Cancer in adolescents and young adults—psychosocial aspects: Long-term survivors. *Cancer, 71,* 3463–3468.