Objective To describe the emergence of pediatric psycho-oncology and to summarize research on psychosocial aspects of childhood cancer and survivorship. Methods To review research into illness communication and informed consent, procedural pain, late effects, psychological distress, coping and adjustment, and special risk populations. Methodological challenges, appropriate methodology, and directions for future research are discussed. Results The past 30 years have seen change from avoidance of communication about cancer to an emphasis on straightforward discussion of diagnosis and prognosis. Behavioral research has led to interventions to reduce procedural distress. Late effects have been observed in social functioning. Although average levels of distress in survivors of pediatric cancer are typical, subsets of more vulnerable patients and family members exist. Factors predicting positive and negative coping have been identified. Conclusions As the numbers of pediatric cancer survivors increase, psychosocial researchers will be better able to conduct longitudinal studies not only of adjustment and its predictors but also of the impact of the emerging medical treatments and interventions to ameliorate late effects of treatment. Additional funding, improving methodology, and multi-institutional cooperation will aid future pediatric psycho-oncology investigators.
the focus of pediatric psycho-oncology research. Psychosocial research has in turn influenced the emotional environment in which hospitalized and home-based children with cancer experience their disease. Presently, 1 in 900 people in the United States between the ages of 15 and 45 is a survivor of pediatric cancer (Robison, 2003). With increasing survival has come increased focus on the quality of life of children who survive cancer. As we go forward, this emphasis will only become more important.

Science proceeds from observation to experimentation and theory (Berkson, 1987; Putnam, 1973). Psychosocial research in pediatric psycho-oncology, a relatively recent term, began in the 1960s and continued into the early 1970s with studies that were predominately observational of parents’ mourning and their psychological reactions to the death of the child (e.g., Binger et al., 1969; Chodoff, Friedman, & Hamburg, 1964; Futterman & Hoffman, 1973; Natterson & Knudson, 1960). The research subjects were mainly parents since children were not routinely informed about the name or nature of the diseases they suffered. It is probably not accidental that our attitudes toward open communication about diagnosis and prognosis with pediatric cancer patients changed markedly at the same time as survival rates were beginning to improve, especially for acute lymphoblastic leukemia (the survival of which had risen to 50–60% by the mid-1970s; Smith & Ries 2002). It is certainly more difficult to openly discuss a condition that is rapidly fatal than it is to discuss a cancer for which treatments exist, offering at least some hope of long-term survival.

Changes in attitude regarding hospital practice and communication with children were influenced by studies whose innovative research designs were based on astute observation of the behavior of children on cancer wards. These studies showed that children were not deceived by the avoidance of discussion of their diseases or by false reassurance about their prognosis. We learned that children understood much more than was originally thought and that they usually knew the seriousness of their condition as well as its name (Spinetta, 1974; Waechter, 1968). The adults’ silence about the central topic—the child’s imminent death—left the children to cope with their fears alone. The ultimate outcome of dissemination of findings from these studies was that open communication about cancer began to be emphasized by pediatric oncology health care professionals who talked directly to children about their illnesses and who strongly encouraged parents to talk more openly with their children.

The change toward open communication also helped fuel the inclusion of mental health professionals on treatment teams for children with cancer. If there was to be open communication about the difficult emotions of life-threatening illness or imminent death, then it was advisable to have psychological experts close at hand to help families explore and cope with these intimate and challenging issues. The presence of psychologists, social workers, and psychiatrists on pediatric cancer services in turn fostered an awareness of the behavioral challenges faced by children with cancer—notably, how to deal with the isolation of hospitalization and the pain and suffering associated with treatment procedures. The presence of mental health staff also fostered an awareness of cancer’s impact on the whole family, including parents and siblings as well as the child with cancer.

Over the past 30 years, it was the courage of many parents and physicians in pursuing new treatments that led to the resounding improvements in survival for children with cancer. Because most children with cancer are placed on a clinical trials protocol (Gurney et al., 1996; Ross, Severson, Pollock, & Robison, 1996), parents and, more recently, pediatric oncology patients have been asked to make difficult decisions between a treatment with known effects but not completely satisfactory outcomes and an experimental treatment with possibly improved potential for cure or survival but with less certain or potentially more ominous side effects. It is in the tension between the known and the unknown, between progress and safety, that advances occur in pediatric oncology or with any disease. How parents understand and make these decisions has itself become the focus of research. Parents tend to focus more than professionals do on the nature of the treatment offered and what it will entail for their child and less on the fact that the treatment is a research effort (Kupst, Patenaude, Walco, & Sterling, 2003; Levi, Marsick, Drotar, & Kodish, 2000; Ruccione, Kramer, Moore, & Perrin, 1991). Parents’ lack of awareness that their child’s treatment is under a research protocol could cause difficulties in later discussions with physicians, as the parents may not understand limits to the flexibility of treatment options by which the physician researcher is bound.

From continued research on the informed consent process, improvements in provider–parent and provider–patient communication are likely to be forthcoming. The goal of interventions in this area is reduced distress for parents and patients and a greater understanding by medical personnel and parents of the likely areas of misunderstandings and differential emphasis that could leave significant gaps in communication. Particularly important is the discussion of recent findings regarding late effects, as parents and patients must
weigh the risks and benefits of treatment in light of future functioning. Rich areas for future research include assessment of the value of tailoring informed consent discussions according to patient–parent characteristics and of providing revisitable materials using computer technologies that review choices offered and the rights of parents in making treatment decisions for their child. Future research may also include further investigation of the ethical quandaries that arise in trying to maximize autonomy and involvement of young patients while recognizing the legal rights of parents. Psycho-logists are in a good position to educate physicians and others about the developmental and emotional factors that may in some cases complicate informed consent decision making. We also need a better understanding of proxy decision making, and we need improvements in our understanding the impact of socioeconomic status and cultural and ethnic background on the ways dyadic couples and single parents make such decisions. Other areas for further inquiry include research on preferred methods of involving older children in treatment and in end-of-treatment decisions. The involvement of children in assent and consent discussions marks clearly how far we have advanced from the silent days of the 1950s and 1960s in pediatric psycho-oncology.

Physical Symptoms and Distress During and After Treatment

Treatment Effects

In the late 1970s and early 1980s, there was increased research interest in helping the child with cancer who was undergoing treatment involving painful procedures and side effects (see reviews by Peterson, Harbeck, Chaney, Farmer, & Thomas, 1990; Zeltzer, 1994). Well-designed behavioral observation studies increased our understanding of children's distress (Blount, Davis, Powers, & Roberts, 1991; Dahlquist, Gil, Armstrong, Ginsberg, & Jones, 1985; Jay, Ozolins, Elliott, & Caldwell, 1983; Katz, Kellerman, & Siegel, 1980; Manne et al., 1990). From these studies, we learned that children do not necessarily habituate to the stressors and that coping does not always improve with time (Dahlquist et al., 1985; Jay et al., 1983). Previous experiences, age and developmental level, level of parental anxiety or distress, level of social support, current coping skills, and perceived control were all found to be related to the child's pain and distress (Zeltzer, 1994). The need to help children deal with anticipatory anxiety, pain, and nausea and vomiting (Morrow, Hoagland, & Morse, 1982; Redd & Andrykowksi, 1982) triggered the development of effective interventions that became common practice in pediatric oncology clinics (Dahlquist et al., 1985; Jay & Elliott, 1990; Redd, 1989; Zeltzer, 1994). As noted by Kazak (2005), subsequent improvements in pharmacologic aids for reducing distress and the integration of psychological and pharmacologic interventions have reduced the burden of pain and suffering for children undergoing cancer treatment.

Late Effects

With markedly increased numbers of pediatric cancer survivors, increased funding opportunities, and improving methodologies, we have learned more about the physical and psychosocial functioning of survivors. The field of late effects has burgeoned, and there is now a formidable late-effects literature (see review by Friedman & Meadows, 2002). Long-term effects of treatment vary and can include neurocognitive deficits (see Butler and Mulhern, 2005), organ damage, decreased growth, and infertility (Oberfield & Sklar, 2002). Not surprising, these physical sequelae can affect social functioning and relationships (Boman & Bodegard, 2004; Byrne et al., 1989); academic success (Hays et al., 1992; Katz, Rubinstein, Hubert, & Blew, 1988); employment (Hays et al., 1997; Mackie, Hill, Kiomdryn, & McNally, 2000; Zeltzer et al., 1997), personal functioning (Greenberg, Kazak, & Meadows, 1989; Madan-Swain et al., 2000; Mulhern, Wasserman, Friedman, & Fairclough, 1989; Smith, Ostroff, Tan, & Lesko, 1991), and family functioning (Kazak et al., 2001; Kupst & Schulman, 1988). Recent attention to the genetic transmission of some cancers likely confounds concern among survivors about cancer risk for their children, even though hereditary etiology for childhood cancers is rare (Ganjavi & Malkin, 2002; Patenaude, 2003). From these studies emerging over the past two decades, we have learned with increasing specificity that no child with cancer remains unchanged by the experience.

Psychological Adjustment

Early behavioral studies paved the way for more intensive investigation of psychological responses to the diagnosis, treatment, and late effects of pediatric cancer. In the mid-1970s and 1980s, the National Cancer Institute increased the level of funding to address these questions in adult and pediatric cancer patients. In addition to studies examining treatment-related stressors—such as procedural distress, pain, nausea and vomiting, and anticipatory anxiety—researchers began examining the intra-personal effects of the disease and treatment on the patient's
Until the early 1980s little was known about the psychological status and functioning of childhood cancer survivors. Most studies have found little evidence of serious psychological adjustment or maladjustment in pediatric cancer patients. A review of chronic illness studies (Lavigne & Schullman, 1989) found that children with cancer were at lower risk for problems than were children with other chronic illnesses. Many studies have found that most survivors show good adjustment on psychological self-report measures and that their scores are not significantly different from those of norms, controls, or other chronic illness children.

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in other domains. As Simms et al. (2002) have noted, “clinically relevant distress (not necessarily psychopathology) and adaptive functioning may be interrelated concurrent outcomes” in long-term survivors.

Positive Outcomes
Some studies have found not only a lack of problems but also a set of positive outcomes. It is a fairly common finding that survivors recount problems associated with their having had cancer as well as some associated positive outcomes, including positively perceived changes in focus, a reordering of life priorities, an increased resilience, and a greater appreciation of life and relationships (Eiser et al., 2000; Zebrack & Chesler, 2002). In a study of 161 young adult survivors of pediatric cancer, Elkin, Phipps, Mulhern, and Fairclough (1997) found low levels of psychological distress and significantly better psychological health than would be expected given normative comparisons. Similarly, and in a departure from the usual focus on internalizing problems, Verill, Schafer, Vannatta, and Noll (2000) found that pediatric cancer survivors reported lower levels of aggressiveness, antisocial behavior, and substance abuse outcomes than did case controls.

Coping and Adaptation
The findings that psychopathology was not a typical outcome for children with cancer triggered an important shift in emphasis and approach to studying long-term survivors. The change in orientation came from no longer viewing cancer treatment as a necessarily pathology-inducing experience but, instead, focusing on the skills and resilience of people who were struggling with a difficult situation or a difficult set of situations. This led investigators to the next question: What do children and families do to cope effectively with a child’s cancer and cancer treatment?

Several studies of children with cancer (e.g., Bull & Drotar, 1991; Kupst & Schulman, 1988) focused on the process and situational aspects of coping with cancer in children and found that children and families showed a variety of coping strategies, each depending on the situation. Whereas many of the coping studies focused on coping during active treatment, the longitudinal studies of Kupst and colleagues (Kupst et al., 1995; Kupst & Schulman, 1988; Natta, 1995), which followed children and families from diagnosis through long-term survival, focused on coping during specific phases of treatment and beyond and assessed coping strategy (means) and adequacy of coping (outcome). These studies found a wide variety of individual differences in the use of coping strategies in children and parents and no consistently significant predictors of adaptation. A recent study (Grootenhuis & Last, 2001) asked whether coping strategies differed depending on the status of the child’s cancer (remission vs. relapse or second malignancy). Comparing 84 children with differing survival expectations, they found that disease status did not predict children’s defensiveness or use of cognitive control strategies.

A more recent trend in coping research involves less orientation toward classification of survivors’ strategies (which has not been particularly fruitful) and more interest in finding correlates or predictors of adaptation and adjustment. Several researchers have posited a repressive adaptive style to explain the common findings that children with cancer typically show lower levels of distress on self-report measures. Similar findings of low distress and indications of repressive adaptive style have been suggested in studies of long-term survivors (Elkin et al., 1997; Erickson & Steiner, 2000). Results of earlier work indicate that avoidance and even denial, for example, may be adaptive in some situations but not in others (Beisser, 1979; Compas, Worsham, & Ey, 1992; Koocher & O’Malley, 1981; Lazarus, 1981). More work needs to be done to determine the appropriateness of these coping styles and strategies under a variety of circumstances.

Although some studies have found support for one type of strategy over another, no strategy has emerged as the optimal coping mechanism (Phipps, Fairclough, Tyc, & Mulhern, 1998; Rudolph, Dennig, & Weisz, 1995). Our early optimism about finding coping styles or strategies that would predict optimal adjustment has not been well supported (Sloper, 2000). We know that the adaptiveness or maladaptiveness of a given strategy depends on characteristics of the individuals; the existing coping resources; and the characteristics of the situation, including specific demands and time (Spirito, Stark, & Knapp, 1992; Thompson & Gustafson, 1996). However, in pediatric cancer, as in adult cancer (Parle, Jones, & Maguire, 1996), there has been little attention paid to the specific demands or coping tasks involved in a given situation and how changing situational or emotional demands affect coping.

Correlates of Psychosocial Functioning
What are the factors that make a difference in the adjustment and coping of long-term survivors? With increased survival, several studies have emerged that examine the relationship of disease and treatment, personal, and family/environmental variables on adjustment or adaptation of
survivors and their families. Table I shows the variables, results, and related references.

Eiser (1998) has pointed out an important finding regarding survivors of childhood cancer compared to controls. Outcomes that are assumed to be consequences of physical deficits secondary to treatment, such as lower vocational achievement or reduced birth rates, may more accurately be seen as interactions between physical consequences of illness and treatment and the altered psychological attitudes and beliefs of survivors. For example, whereas a study showed that the number of live births to pediatric oncology survivors was 57% of that of population controls (Hawkins, Smith, & Curtis, 1988), reasons for this difference may include not only problems with impaired fertility but also psychological factors, such as reluctance to parent (based on fears for the health of potential children), reduced marriage opportunities, and fears of premature death due to cancer recurrence and about leaving young children behind. Similarly, reduced achievement and income could reflect some survivors’ altered values regarding achievement by themselves or their parents as well as cognitive problems occurring secondary to treatment. Much more attention should be paid to the developmental stage at which the child is diagnosed and to the impact of attendant interruptions in normal developmental tasks and the resulting effects on later functioning (Zebrack and Zeltzer, 2003).

### Populations at Particular Risk

Research to date has identified various subgroups of pediatric cancer survivors with more-than-average adverse psychological sequelae of their illness. Children with brain tumors and those who experience insults to their central nervous system as a result of cancer or cancer treatment have been shown to be at considerably high risk for adverse psychosocial outcomes (Boman & Bodegard, 2000; Mulhern, 1994). More specifically, survivors who have had brain or central nervous system tumors or who have had intensive central nervous system therapy appear to be most at risk for cognitive,

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### Table I. Correlates of Psychosocial Functioning in Pediatric Cancer Survivors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Results</th>
<th>References</th>
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<tbody>
<tr>
<td><strong>Disease and Treatment</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis involving CNS</td>
<td>Lower cognitive and academic functioning</td>
<td>Armstrong &amp; Mulhern, 2000 review</td>
</tr>
<tr>
<td></td>
<td>More difficulties in psychosocial functioning</td>
<td>Boman &amp; Bodegard, 2000; Mulhern et al., 1994; Vannatta et al., 1998</td>
</tr>
<tr>
<td>Bone-tumors</td>
<td>More difficulties in adjustment</td>
<td>Eiser et al., 1998; Langeveld et al., 2002</td>
</tr>
<tr>
<td><strong>Type of treatment:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNS Irradiation</td>
<td>Lower cognitive and academic functioning</td>
<td>Armstrong &amp; Mulhern, 2000 (review)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>More intensive, lower adjustment</td>
<td>Zebrack &amp; Zeltzer, 2002 review</td>
</tr>
<tr>
<td>Physical sequelae/functional</td>
<td>More severe, lower psychological functioning</td>
<td>Elkin et al., 1997; Fritz et al, 1988; Greenberg et al., 1989;</td>
</tr>
<tr>
<td>impairment</td>
<td></td>
<td>Koocher &amp; O’Malley, 1981</td>
</tr>
<tr>
<td>Time since diagnosis</td>
<td>Longer, better adjustment</td>
<td>Cella &amp; Tross, 1986; Koocher &amp; O’Malley, 1981; Kupst &amp; Schulman, 1988</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>Shorter, better adjustment</td>
<td>Koocher &amp; O’Malley, 1981</td>
</tr>
<tr>
<td><strong>Personal</strong></td>
<td></td>
<td></td>
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<tr>
<td>Age at diagnosis</td>
<td>Older, better adjustment</td>
<td>Cella et al., 1987; Mulhern et al., 1989</td>
</tr>
<tr>
<td></td>
<td>Younger, better adjustment</td>
<td>Barakat et al., 1997; Elkin et al., 1997; Slavin et al., 1982</td>
</tr>
<tr>
<td>Previous functioning</td>
<td>Previous adjustment related to long-term</td>
<td>Kupst &amp; Schulman, 1988; Kupst et al., 1995</td>
</tr>
<tr>
<td>Degree of perceived stress</td>
<td>Lower, better adjustment</td>
<td>Last &amp; Grootenhuis, 1998; Varni et al., 1994</td>
</tr>
<tr>
<td>Level of cognitive functioning</td>
<td>Higher, better adjustment</td>
<td>Boman &amp; Bodegard, 2000; Kupst et al., 1995; Mackie et al., 2000; Levin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Newby et al., 2002</td>
</tr>
<tr>
<td><strong>Family/Environmental</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adaptability/cohesiveness</td>
<td>Higher, better adjustment</td>
<td>Kazak &amp; Meadows, 1989; Levin Newby et al., 2002; Rait et al., 1992</td>
</tr>
<tr>
<td>Open communication</td>
<td>More open, better adjustment</td>
<td>Fritz et al., 1988; Koocher &amp; O’Malley, 1981; Kupst &amp; Schulman, 1988</td>
</tr>
<tr>
<td>Family and social support</td>
<td>More support, better adjustment</td>
<td>Fritz et al., 1988; Kupst &amp; Schulman, 1988; Trask et al., 2003</td>
</tr>
<tr>
<td>Coping/adjustment/family</td>
<td>Higher level, better adjustment</td>
<td>Carlson-Greene et al., 1993; Kupst &amp; Schulman, 1988; Kupst et al., 1995;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sahler et al., 1997</td>
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<tr>
<td>Socioeconomic resources</td>
<td>Higher, better adjustment</td>
<td>Koocher &amp; O’Malley, 1981; Kupst et al., 1995</td>
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social, and adjustment difficulties (Armstrong & Mulhern, 2000; Vannatta, Gartstein, Short, & Noll, 1998; Zevon, Neubauer, & Green, 1990). Ironically, many outcome studies in pediatric psycho-oncology have excluded brain tumor patients from study participation, as their experiences were considered atypical to that of the majority of pediatric survivors. Pediatric brain tumor patients are a particularly challenging group to study because of the relatively small number of patients, the diversity of brain tumors, the varying functional impact of the tumors, and the range of surgical and treatment effects that can occur. Beyond the extensive neuropsychological studies of children with brain tumors (see Butler & Mulhern, 2005), recent work has focused on the social outcomes of brain tumor patients (Vannatta et al., 1998). Studies have noted that the social skills of brain tumor patients tend to be adversely affected by treatment and that patients with cognitive impairments tend to feel and be perceived as more isolated than peers (Vannatta et al., 1998) and to have more behavioral problems to a degree that is much higher than that of other pediatric cancer survivors (Carpentieri, Mulhern, Douglas, Hanna, & Fairclough 1993).

Pediatric bone tumor patients are another group that has been noted to have greater-than-average difficulties in adjustment following cancer treatment (Eiser et al., 1997; Langeveld, Stam, Grootenhuis, & Last, 2002). Whereas treatments have improved for these patients, some of the newer limb-sparing surgeries have involved more complicated recovery and reduced functionality so that quality of life may actually be reduced with the less-invasive surgery (Nagarajan, Neglia, Clohisy, & Robison, 2002). Such diverse outcomes pose challenging questions about how to present information about physical and psychosocial outcomes to patients in ways that aid decision making about the irreversible and difficult choices bone tumor patients and their families face.

As originally noted by Koocher and O’Malley (1981), children for whom treatment outcome involve uncertainty suffer more psychological distress than do children who receive treatment with predictable outcomes. When children undergo relatively new, complex procedures, it is likely that they experience heightened, often prolonged vulnerability with potential for negative long-term outcomes—as demonstrated by those who underwent bone marrow transplantation in the early 1970s or stem cell transplants in the 1990s. Similarly, parents may be especially stressed by the opposing desires of wanting to offer their child every possibility for cure while also wanting to protect the child to the furthest degree possible. The excellent research done by Pot-Mees (1989) and, more recently, by Phipps and colleagues (Phipps, Dunavant, Garvie, Lensing, & Rai, 2002; Phipps, Dunavant, Lensing, & Rai, 2002; Phipps, Dunavant, Srivastava, Bowman, & Mulhern, 2000) and Streisand, Rodrigue, Houck, Graham-Pole, and Berlant (2000), illustrate the novel challenges that bone marrow transplant involves and the powerful impact the treatment has on patients.

Methodological Difficulties in Pediatric Psycho-oncology Research

While in the past three decades psychological research on children with cancer has come of age, we continue to struggle with difficult methodological and conceptual issues. Many challenges in pediatric psycho-oncology research remain unsolved, and it is often difficult to compare studies, as they differ in patient diagnoses, time since diagnosis, sampling of participants, inclusion of controls or comparison subjects, variables studied and the measures used to study them. Unsolved methodological problems clearly retard the rate of progress toward answering questions of interest.

Sample Size

A frequent methodological problem is sample size limitation owing to the relatively small pediatric oncology patient populations in any one institution. In some cases these problems can be reduced by multi-institutional studies, but then issues regarding comparability of care (even when patients are treated on the same protocol) and increased study cost replace small numbers as potential problems. Multi-institutional studies increase personnel costs and require some duplication of efforts, such as institutional review board approval and data management. Research conducted within the Children’s Oncology Group offers large numbers of potential patients, but other problems may occur, such as long lag time for multistage research approval within such a large group (see Armstrong & Reaman, 2005). Psychological studies within the Children’s Oncology Group have usually been limited to those that address questions regarding the neurocognitive impact of a treatment protocol or other quality-of-life issues that bear directly on comparison of treatment protocols. There have been to date relatively few studies on psychosocial (i.e., nonneuropsychological) outcomes conducted within the framework of the Children's Oncology Group. As a result, it is often faster and easier to form informal, limited institutional collaborations to try to answer psychosocial questions of interest.
Large, carefully constructed cohort studies allow for broad assessment of health-related outcomes but may be limited in the depth of variables that can be assessed, an issue that may be particularly important in psychosocial studies. In recent years there has been a large collaboration that has produced research on some aspects of long-term pediatric cancer survivorship. The Childhood Cancer Survivor Study (CCSS) is a near decade-long project that approached 20,276 survivors of pediatric or adolescent cancers (or their proxies, if deceased) from 25 institutions, who were treated between 1970 and 1986 and were at least 5 years postdiagnosis (Hudson et al., 2003; Robison, 2003). Unfortunately, the CCSS included very defined subpopulations of the CCSS sample is possible, and some involving behavioral topics are underway, including smoking cessation and health care utilization and risk taking (Institute of Medicine [IOM], 2003). A major challenge for the CCSS (and for most survivor studies) was difficulty locating subjects: 39% of subjects required tracing beyond letters to last known address and attempts to locate them via telephone directory assistance (Robison, 2003). In spite of the ability to use computer databases to locate participants, the mobility of American young adults and the gaps in medical continuity that often occur during the transition from pediatric to adult providers make tracing long-term pediatric oncology survivors difficult and expensive. The problem of locating subjects adds another burden to the difficulties of doing longitudinal studies that attempt to assess patients at intervals over the course of their adolescent and young adult years.

What may be most critical with regard to sample size is not the absolute number but the ability to be able to access the most appropriate sample for the research question being asked. Robison (2003) has written, “While cohort studies represent a strong study design for many topics of late effects research, there are other designs, such as case-control, case-case, and cross-sectional studies, that can be employed to answer important questions” (p. 12).

Self-Selection

Questions about self-selection apply to most survivor studies and form an issue for the CCSS sample, in which nearly 3,000 survivors refused invitation to the study (Robison, 2003). It is legitimate to question whether this large sample represents the more compliant survivors and does not include the more disenfranchised and possibly more impaired survivors, who may be most in need of psychosocial intervention. Long-term pediatric cancer survivors vary enormously in the degree to which they wish to be identified as cancer survivors. Some survivors see their cancer status as a defining characteristic of who they are; others wish to put it behind them as they become spouses and parents. Thus, recruitment outreach, no matter how thorough, is more likely to be able to enlist the more adherent, positive, or altruistic group of survivors, whose experience and attitudes may vary significantly from those with more hesitancy to participate in research. In the future, legislation based on the Health Insurance Portability and Accountability Act (HIPAA) and restrictions on the sharing of health information may make it even more difficult to find patients a decade or more after they have been treated for cancer. Given these hurdles, it is easy to understand why prospective studies remain difficult to conduct.

Selection of subjects for participation in research studies necessitates careful attention to specification of eligibility criteria. The absence of universally accepted severity criteria in pediatric oncology and the lack of techniques to calibrate exposure to many treatment modalities make it difficult to compare patients with a variety of diagnoses, treatments, complications, and outcomes. Treatment protocols in pediatric oncology are constantly updated, so longitudinal study of patients with the same disease may involve participants with significantly different treatments. Further, abstraction of medical data from medical records is costly and imperfect, especially with pediatric patients who are likely to be seen in several medical settings over the course of their lives. These problems in turn make it difficult to adequately analyze the relationship between psychosocial outcomes and physical disease.

Controls are also difficult to select for pediatric cancer patients, as there are no clearly comparable life experiences. Even comparison with other chronic diseases is less than optimal. When the question involves comparison with healthy children, siblings have been utilized. However, the use of sibling controls is questionable, as research clearly shows that siblings are influenced by their brother’s or sister’s cancer experience (Sahler et al., 1994). Selection of classroom peer controls has been used successfully in several studies of social functioning to comparison with healthy age-compatible mates (Noll et al., 1990; Vannatta et al., 1998); however, this methodology is quite labor intensive and requires cooperation of schools and often entire school districts. Other problems to be addressed in sample selection are the bias toward including only English-speaking families, which omits many ethnic and cultural minorities, and difficulty in locating survivors of low socioeconomic
status, who are more likely to move often and are less likely to be reachable through telephone directories or on the Internet.

Few studies have obtained or utilized prospective or longitudinal data, choosing instead single, cross-sectional assessment of long-term survivors at a point many years after diagnosis. One exception includes a 4-year longitudinal study (Sawyer, Antoniou, Toogood, Rice, & Baghurst, 2000) of 39 children aged 2–12 years and diagnosed with cancer, compared to a community cohort. The study found that right after diagnosis, children with cancer and parents had significantly more psychological problems than did the community sample. At subsequent assessments, the two groups did not differ in prevalence of psychological problems. Similarly, a study that followed children and families from diagnosis to 10 years after treatment (Kupst et al., 1995; Kupst & Schulman, 1988), found that despite periods of expected high stress, most of the long-term survivors and their parents continued to adjust well over time.

Ideally, as the value of continuing follow-up with pediatric oncology survivors is increasingly recognized, efforts to maintain contact over time with former patients will be seen as an important priority. The Children’s Oncology Group is reportedly planning a long-term follow-up center (IOM, 2003). Robison (2003) believes that continuing contact will not only have research benefits, serving as an “early warning system” for unrecognized late effects, but will also be a means of providing education to survivors about late-effect risks and intervention options. Such two-way interaction will also provide survivors with means of more effectively conveying their needs to the research community.

Measurement Challenges

Measurement in pediatric cancer progressed from clinical impressions and case studies to use of standard measures of anxiety, depression, and behavioral adjustment to determine prevalence of these outcomes. Although such measures have the advantage of being well normed and having good psychometric properties, it is frequently difficult to know how to interpret the results. For example, we have learned that the Child Behavior Checklist, one of the most commonly used measures of behavioral problems, can show higher average levels of behavioral and social competence problems in children with cancer and other serious illnesses (Perrin, Stein, & Drotar, 1991). Similarly, a significantly high-state anxiety or depression score may occur when a child or parent is facing a new diagnosis of cancer, going off treatment, or discovering late effects of treatment. What scores would be considered appropriate reactions given the situation? And what would be a cutoff score that would indicate a need for further assessment and intervention? For a long time, these standard clinical measures were the only tools that we had to describe the psychological states of pediatric cancer patients and families. If the question of interest concerns comparison to healthy peers or families, these standard measures are useful. However, if the question concerns changes over time in psychosocial functioning in a child or an adolescent with a life-threatening or chronic illness, other measures should be used that are appropriate to these situations. In many cases, it is a question not of comparing pediatric cancer with “normal” controls but of within-group assessment over time or comparison across different types of disease.

Although it is beyond the score of this article to provide a comprehensive list of potentially useful measures, it is worth mentioning some of the measures that have been used frequently in studies of coping and adaptation in children with chronic illness. As an observational measure, the Child–Adult Medical Procedure Interaction Scale–Short Form (CAMPIS–SF; Blount, Bunke, Cohen, & Forbes, 2001) has been used as an assessment of procedure-related distress and behavior and as an assessment of child and adult coping behaviors. As a self-report rating scale, the Kidcope (Spirito, Stark, & Williams, 1988) has been given to children with chronic illnesses to assess types of coping strategies as well as their perceived efficacy.

Pediatric Cancer–Specific Measures

If the question to be answered concerns description of the cancer experience per se, then pediatric cancer-specific measures are more appropriate. In recent years, several quality-of-life measures have emerged for use with pediatric cancer patients, a recent issue of the International Journal of Cancer (1999, Suppl. 12) contains a comprehensive review regarding many of the commonly used health-related quality-of-life instruments in pediatric oncology. Among the several well-designed measures, the most commonly used pediatric cancer–related measures cited in recent literature are the Pediatric Cancer Quality of Life Scale (Varni, Burwinkle, Katz, Meeske, & Dickinson, 2002), the Miami Pediatric Quality of Life Questionnaire (Armstrong et al., 1999), and the Pediatric Oncology Quality of Life Scale (Goodwin, Boggs, & Graham-Pole, 1994). In addition, new measures exist that look at specific concerns during and after treatment—for example, fatigue (Hockenberry et al., 2003;
Varni et al., 2002) and acute, somatic, behavioral, and affective experiences during intensive treatment such as bone marrow transplant (Behavioral Affective and Somatic Experiences Scale; Phipps, Dunavant, Jayawardene, & Srivastava, 1999). Promising data have emerged regarding the Pediatric Inventory for Parents (Streisand, Braniecki, Teracyak, & Kazak, 2001), a measure of stress in parents of children with cancer, and the Psychosocial Assessment Tool (Kazak et al., 2003), a measure to identify psychosocial risk in families of newly diagnosed patients. Although many of these measures have been used early or during active treatment, more work needs to be done in the assessment of long-term psychosocial functioning.

Eiser (1998) commented eloquently on the need to develop research techniques that tap the subtle but important ways in which survivors' lives are affected by their illness experience:

In reality, there are likely to be limitations to approaches that focus exclusively on either a deficit-centered or coping perspective, with many survivors showing adjustment difficulties in some areas while at the same time coping with other aspects of their lives with greater maturity than might have otherwise been the case. The experience of cancer, with all its implications of trauma, separation, pain, and uncertainty, cannot be reduced to such a simple issue as describing differences from a healthy population on some standardized measure, which is unlikely to be sensitive to the most critical issues. Survivors of childhood cancer have experienced unique disruptions in their childhood, they often continue to need regular medical surveillance and follow-up, and, increasingly, they are confronted with information regarding their vulnerability to both physical and psychological late effects.

**Mixed Methodologies**

Although the emphasis in our studies is typically on quantification, it may be that in some areas of psychosocial research we have jumped ahead too quickly and do not sufficiently understand many of the concepts of interest. It may be necessary to return to qualitative or mixed methodologies to provide an in-depth observation of the experience and understanding of survivors (Atkins & Patenaude, 1987; Woodgate, 2000). Haase, Heine, Ruccione, and Stutzer (1999), in their well-designed research on resiliency in pediatric cancer, have advocated for and have used meaning-based models that begin with a thorough qualitative assessment and that progress to quantitative measurement. Similarly, little attention has been paid to the role that appraisal and perception play in situations of pediatric cancer (Eiser et al., 2000; Last & Groenewuis, 1998). One criticism toward many of the research tools used in pediatric psycho-oncology studies is the emphasis on self-report. It would seem that by employing multiple methods and sources—such as behavioral observations, rating scales, and in-depth qualitative interviews of the same individual—our understanding of the survivor's coping abilities would improve; but at present, this is seldom done (Levin Newby, Brown, Pawletko, Gold, & Whitt, 2000). Hypothesis-driven research questions can be applied to both quantitative and qualitative investigation of survivors. Whereas the former may answer questions more specifically about the rate and extent of a psychological or behavioral outcome, the latter may extend our understanding of the personal meaning of the survivor's experience. Furthermore, it may elucidate new problems faced by survivors or new approaches to coping with long-term stressors related to being a survivor of childhood cancer.

**Randomized Clinical Trials**

In pediatric psycho-oncology, as in the rest of psychological and medical research, there is an increasing interest in evidence-based practice and in randomized clinical trials (Stinson, McGrath, & Yamada, 2003). As survival rates continue to improve, there will be increasing primary interest in psychosocial outcomes in studies of differential medical treatments. As more psychosocial interventions are proposed and tested for use with pediatric cancer survivors, there will be some increased opportunities for using the "gold standard" of empiric scientific research—the randomized clinical trial (RCT). Currently, however, RCTs are rare in pediatric psychology. Stinson et al. (2003) found that about 5% of articles in the Journal of Pediatric Psychology and the Journal of Consulting and Clinical Psychology were reports of pediatric RCTs. Of the 28 studies reviewed, 3 concerned pediatric oncology patients. An accompanying editorial (Brown, 2003) offered help from senior investigators in the challenge of planning of RCTs and in the priority publication for the results of studies that conform to Consolidated Standards of Reporting Trials guidelines (Altman et al., 2001; Begg et al., 1996). Recent attention toward the use of such guidelines in pediatric research suggests that additional or amended items may be needed in applying these standards to the reporting of psychosocial research (Davidson et al., in press) and that there may be special challenges in studies using pediatric populations (Drotar, 2002). Use of the guidelines in pediatric journals will, however, have a number of advantages (McGrath, Stinson, & Davidson, 2003), including facilitating the comparison of future studies. As has been pointed out (Stinson, McGrath, &
Yamada, 2003), it is important to differentiate clinical significance (i.e., whether there is value to the patient) from statistical significance in the findings from RCTs.

Discussion
Directions for Future Research
We are still at the beginning, perhaps at the end of the beginning, of our understanding of psychosocial aspects of childhood cancer. As the third generation of pediatric psycho-oncologists begins their work, survival of children with cancer is much improved but not ensured. Pediatric cancer remains a life-threatening illness. One area for abundant future work is the development of interventions to address the fear of recurrence, which lingers in many patients despite good psychological functioning. Entering the 21st century, the medical community understands a great deal more about late effects, but there is still much work to be done in understanding the interdependence of physical and psychosocial impact, especially for vulnerable subpopulations, and in developing targeted interventions (see Kazak, 2005). Zebrack and Zeltzer (2003) suggest that the current goal in pediatric psycho-oncology research is to define “who might benefit from which intervention when.” As an example, they point to infertility as an area where knowledge of late effects needs much-deeper exploration. They discuss the fact that we have known for many years about the reproductive problems associated with pediatric oncology treatment protocols. Despite this, there is a lack of research about how cancer survivors experience and deal with the resulting infertility and about possible educational interventions that might aid consideration of alternative reproductive technologies. The authors caution, however, that such research would have to include ethical and economic discussion about whether most survivors would have the resources to make use of these technologies.

We know that there are individual differences in the effectiveness of treatments and the outcomes of patients who appear medically similar. Genetic studies may ultimately help identify patients with similar illnesses who fare well physically and psychologically and who do not. We also understand some of the emotional and behavioral ways in which survivors react to their treatments and late effects. It will be as important to study adverse psychosocial reactions as it will be to understand interventions that enhance positive outcomes (Zebrack & Zeltzer, 2003). Our research efforts will be enhanced if, in at least some cases, we return to the first step in the scientific process—observation—and plan research that appropriately incorporates qualitative and quantitative measures. If we can design research that makes use of optimal samples, if we develop measures that work for patients as well as survivors, if we test interventions that come out of observed need for improvement in outcomes, then we may ultimately be able to develop workable theories for the relative success of one patient versus others that incorporates biological and psychological factors. Such research would be of tremendous benefit to patients, parents, and long-term survivors.

Psychosocial research questions will change with changes in the treatment of childhood cancer and with increased understanding of the late effects of treatment and the links between biological and psychological phenomena. Research on the biological underpinnings of stress and the relationship between stress and immune function—or research on biomarkers that may predict the utility of a certain treatment or prognosis—will suggest the need for psychosocial interventions to incorporate empirical findings into the treatment of patients and survivors and to help them to understand limits to the interventions. The same is true with the increasing interest in alternative or complementary treatments. Interventions that may work to reduce distress should be tested and, if successful, integrated into the options offered to patients and survivors. However, care must be taken to avoid transferring to patients and survivors the responsibility for their own survival. Patients whose expectations for self-efficacy in affecting their own mortality are raised beyond what is proven realistic often suffer double burdens when cancer recurs, experiencing a threat to their survival and a sense of failure. This scenario can be avoided with sensitive and accurate integration of only those interventions with confirmed patient benefits.

It is likely that in the future, treatment of children with cancer with involve pharmacogenomics and gene therapy. In the latter case, genetic analysis will determine which treatments work best for which patients. This may confound psychosocial research by further dividing already small groups of patients with the same disease into many smaller groups of patients undergoing identical treatments. Gene therapy, the introduction of vectors that actually repair deleterious mutations in disease genes, has great promise but remains at present a frightening prospect for patients and parents. Research on the understanding of what gene therapy is and the acceptability of the treatments will be necessary forerunners of widespread acceptance of such treatments.
Future Opportunities

Evidence for the importance of continued work relating to psychosocial concerns of survivors of pediatric malignancy comes from the findings of two recent reports. First, the “National Action Plan for Childhood Cancer” (Arceci et al., 2002) recommends increased and improved screening, education, and treatment for children and adolescents who are at risk for late effects. One of the research priorities frequently cited by this group—one comprising over 30 medical, psychosocial, patient, and parent organizations—was additional psychosocial and quality-of-life research with pediatric cancer survivors to provide research-based evidence for the establishment of a national standard for care of survivors that takes into account physical, neurocognitive, and psychosocial functioning. Second, the recent Institute of Medicine report (August 2003) “Childhood Cancer Survivorship: Improving Care and Quality of Life” specifically mentions the “paucity of studies of survivors and their families regarding the psychosocial burden and economic costs associated with late effects.” Among the general recommendations made by the authors of this report are

to develop evidence-based clinical practice guidelines for care of survivors;
to define a minimum set of standards for comprehensive, multidisciplinary care;
to improve awareness of late effects among children and their families;
to improve education and training of professionals who work with long-term survivors; and
to increase support for research in survivorship.

The latter report stresses that only with large cohorts of survivors can the full extent of late effects be understood. Such research could measure prevalence of late effects, identify etiology of late effects, and evaluate effectiveness of interventions to ameliorate late effects. It will be essential to include psychosocial research in the assessment of late effects and in the studies documenting the efficacy of interventions to improve quality of life. Looking at the functioning of the pediatric cancer survivor in schools and jobs, in their roles as spouses and parents, and as utilizers of health care resources will help to develop a well-rounded picture of the benefits and costs of success in the medical treatment of children with cancer.

The pediatric cancer survivor is a vivid and important illustration of the power of medicine to conquer cancer. Psychosocial studies can enlarge our image of the ways in which the costs of that success are absorbed into the daily lives of those who survive. They can also help illustrate the ways in which our understanding of those costs can be used to develop interventions that reduce adverse treatment effects, minimize distress, and encourage positive outcomes for survivors of pediatric cancers.

A further encouraging step for psychosocial research in pediatric oncology is the designation of cancer survivorship as an “extraordinary opportunity for investment” in the 2004 budget requests from the National Cancer Institute. The request for $46 million dollars aims to support research that would accelerate the pace of intervention research, aid in measurement development, enhance the capacity for the institute to follow and track long-term survivors, and improve understanding of psychological and social mechanisms that affect a patient’s response to disease, treatment, and recovery. The National Cancer Institute is the home of the Office of Cancer Survivorship, which was created in 1996 to further the needs of pediatric and adult cancer survivors. Since its inception, the office has provided ongoing research funding as well as offered several requests for application on topics of particular interest to survivors.

Conclusion

The newest generation of researchers in pediatric psycho-oncology need not fear that all the interesting questions are solved. On the contrary, it seems likely that these investigators will have many interesting and important research agendas to pursue. They will be able to stand on the shoulders of the researchers who came into this field before it had a name, before there were many survivors to study, and before there were many funding sources to appeal to for support. Although still lagging behind the funding for adult survivorship, improved funding for pediatric psycho-oncology research is now available from not only federal sources but also the American Cancer Society and private foundations, including the more recently created Lance Armstrong Foundation, which has support of survivorship research as one of its specific aims. Despite the hurdles, it will become easier to create cohorts of patients who may be longitudinally followed. It will also, ideally, become easier to create alliances of researchers to develop multi-institutional studies that can answer many of the particular questions in this area. Studies of positive outcomes will be mixed with an awareness of the continuing handicap in some groups of survivors. Utilization of
Internet- and computer-based methodologies may improve researchers’ access to pediatric cancer survivors and enhance the scope of potential interventions. The work on psychosocial aspects of pediatric cancer survivorship will continue to engage and fascinate psychological researchers for many decades to come, perhaps long after pediatric cancer ceases to be a life-threatening condition.

**References**


Lavigne, J. V., & Faier-Routman, J. (1992). Psycholog-


