

Quality of Life in Adult Survivors of Childhood Cancer

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ABSTRACT. Sixty-four adult survivors of childhood cancer, recruited via Israel's largest pediatric cancer treatment center, participated in a multi-dimensional assessment of long-term adjustment and quality of life in the domains of educational achievement, employment status, military service, family status, health, and psychological well-being. Subjects had been diagnosed with cancer prior to age 18, were three years or more off therapy with no evidence of disease, and over 18 years old at the time of the study. Data from structured interviews were compared to responses on similar items from a control group with no history of serious illness during childhood, matched for age, sex, and parental education levels. Results indicated an overall pattern of integration into the social mainstream, with similar objective levels of achievement for survivors and controls for most measures of education, employment, significant relationships, and psychological well-being. Results also indicated certain areas of disadvantage, such as military recruitment difficulties, lower income levels, and higher rates of workplace rejection. Significantly, almost half of the survivor sample reported subjective feelings that their illness experience had impaired their achievement in several domains. Quality of life is considered an important outcome parameter in terms of clinical decision making as well as in guiding preventive and supportive

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Advances in biomedical science and technology have resulted in dramatic improvements in the prognosis of children and adolescents diagnosed with cancer. While only a few decades ago past survival was measured in months, today approximately 60% of children with cancer are achieving criteria for "cure," i.e., disease-free survival of five years or more (Sposto & Hammond, 1985). Thus, childhood cancer has evolved from an invariably fatal illness to a life-threatening chronic disease. The annual incidence of childhood cancer in the U.S. is approximately 12 per 100,000 children, or an estimated 8,800 newly diagnosed cases in 1997 (American Cancer Society, 1997). Available data suggest that the epidemiology of childhood cancer in Israel is comparable to that of the U.S., with 300 to 400 newly diagnosed cases per year (Zaizov, 1984). Although relatively rare, cancer in children and adolescents remains the leading disease-related cause of death in this age group (American Cancer Society, 1997). Given current overall survival rates of 60%, it is projected that by the year 2000 one in 1,000 young adults between the ages of 20 and 29 will be survivors of childhood cancer (Meadows & Hobbie, 1986).

Concern for the late effects of treatment has grown with this increased survival. Late effects on the cardiovascular, endocrine, gastrointestinal, musculoskeletal, nervous, pulmonary, and genitourinary systems have become evident (Byrd, 1985). In addition, the aggressive treatment regimens responsible for the improved survival rates are characterized by a host of accompanying stressors and coping challenges (Dolgin & Jay, 1989). Thus, with extended survival, issues pertaining to long-term psychological adjustment and quality of life have assumed an increasingly prominent role in pediatric oncologic care, as well as in the development and evaluation of treatment protocols (Boggs, Graham-Pole, & Miller, 1990). A growing literature has begun to document the psychosocial, intellectual, and academic late-effects associated with treatment (Dolgin & Jay, 1989; Fletcher & Copeland, 1988; Koocher & O'Malley, 1981). In line with the evolution of comprehensive oncologic care for adult patients, pediatric oncologists, social workers, psychologists, nurses, and other health care professionals have become increasingly concerned with the cumulative impact of these various treatment effects on patient quality of life.

With regard to general psychosocial adjustment, a somewhat equivocal picture emerges. Holmes and Holmes (1975), in an early study of 124 long-term survivors, found generally adequate functioning: Educational and occupational achievements were not impaired, although illness was cited as the most common reason for remaining unmarried. Still, the majority of survivors reported little impact of the illness on their lives. In contrast, Koocher and O'Malley (1981) reported mild to severe adjustment problems in approximately half of their sample of 118 childhood cancer survivors. These included increased psychological symptomatology, manifest anxiety, dissatisfaction with self, and ambiguity with regard to the future. Factors correlated with better psychological adjustment included earlier illness onset, shorter treatment course, longer time since diagnosis, and fewer long-term physical sequelae. Teta, Del Po, Kasl, Myers, and Mulvihill (1986) found comparable rates of lifetime major depression in 450 childhood cancer survivors compared to their siblings, although problems in the areas of education, employment, military service, and insurability were more prevalent among the survivors. Lansky et al. (1986) found their sample of survivors to have an increased incidence of depression, alcoholism, and suicide attempts compared to population statistics, with the majority of survivors recalling disruption of school functioning, career plans, and peer relations as a result of cancer treatment. Mulhern, Wasserman, Friedman, and Fairclough (1989) reported a three-to four-fold higher incidence of behavior problems and social competence deficits in survivors, with functional impairment, physical disability, CNS treatment, and single parent families serving as risk factors. CNS radiation and chemotherapy has been documented to have damaging neuropsychological effects in some children with leukemia, and the incidence of mental retardation in children with leukemia who experience CNS relapse is 10 times that of the general population (Fletcher & Copeland, 1988; Mulhern, Friedman, & Stone, 1989).

More recent studies of adult survivors of childhood cancer confirm that while major psychiatric disorders are not characteristic, some adjustment difficulties are common. These include increased health concerns and somatic complaints, academic problems, delayed marriage, and worry regarding fertility (Zeltzer, 1993). In one large scale study, Hays, Dolgin, Lansverk et al. (in press) reported that cancer survivors had completed fewer years of education, had higher rates of unemployment and generally lower occupational status and income

levels as compared to matched controls. Survivors of CNS tumors had lower educational and occupational achievement levels than non-CNS tumor survivors. Discrimination toward survivors in employment settings and in the armed services was reported.

These and other studies of long-term adjustment tap specific domains of functioning which, taken together, bear on what has come to be termed "quality of life." This concept has received growing attention in the adult cancer literature, and efforts to quantify and measure quality of life have gained momentum. These have ranged from early, unidimensional ratings such as that designed by Karnofsky and Burchenal (1949), to more contemporary multidimensional measures that assess a range of domains, such as vocation/activity, affect, psychological state, somatic sensation, sociability, and family situation (e.g., Schipper, Clinch, McMurray, & Levitt, 1984).

Most recent quality of life studies of adult cancer patients incorporate the three dimensions of health outlined in the World Health Organization (WHO) definition: "Health is not only the absence of infirmity and disease but also a state of physical, mental, and social well-being." Thus, quality of life should be conceptualized as a composite of multidimensional factors measuring the patient's physical, psychological, and social functioning (Schipper & Levitt, 1985).

The purpose of the current study was to assess the quality of life of adults who, as children, had been successfully treated for cancer in Israel. As such, it represents the first study of its kind conducted on an Israeli sample and, to the authors' knowledge, the first to target this population outside the United States. The multidimensional assessment of quality of life included the following domains: educational achievement, employment experience, military experience, family status, health status and attitudes, and psychological well-being.

METHOD

Subjects

Subjects were drawn from a larger pool of potential participants appearing in the registry of the Long-term Follow-up Clinic of the Department of Hematology-Oncology of the Schneider Childrens Medical Center in Israel. Letters of invitation to take part in the study were sent to 132 former patients who met the following criteria for

inclusion: (1) age 18 or above at the time of the study; (2) three years or more after cessation of cancer treatment with no evidence of further disease; (3) under the age of 18 at diagnosis. Of these letters of invitation, 42 were returned as the addressee was not locatable. An additional four potential subjects was excluded due to varying reasons (e.g., death, travel abroad). In nine cases, follow-up telephone calls revealed that the subjects' parents had intercepted the letters and had chosen not to pass them on to their (adult) children. Among the reasons these parents resisted their children participating in the study was the concern that the study might revive dormant memories and anxieties, and the fact that, in a few cases, parents were convinced that their children were still unaware of their original diagnosis, and did not want that fact upset by exposure to the study.

Of the 77 potential subjects contacted, six (8%) refused participation—an acceptably low refusal rate for a survey such as this. Of the 71 subjects who agreed to participate, seven data sets were incomplete and therefore not included in the statistical analyses. Thus, 64 of the 77 potential subjects contacted, representing an overall consent and completion rate of 83%, were included in the current analyses.

Subjects ranged from one to 17 years of age at diagnosis, with a mean age of 11.52 years ($SD = 4.69$). Time since diagnosis ranged from four to 25 years, with a mean of 11.91 years ($SD = 5.40$). Time since treatment cessation ranged from three to 21 years, with a mean of 9.80 years ($SD = 4.59$). The distribution of cancer diagnoses in the survivor sample appears in Table 1.

As a comparison to the survivor sample, a control group was selected consisting of 51 subjects with no prior history of cancer or other serious childhood illness. Control subjects were recruited from the general population by approaching persons in public settings such as the motor vehicles department and central transportation terminals. The purpose of the study was described and consenting subjects were interviewed at a place and time of their convenience. In order to reduce any bias in terms of the quality of life outcomes, the random selection and enrollment of control subjects continued until the survivor and control groups were equal with reference to three major demographic variables: sex, age, and parents' educational level. Table 2 depicts the demographic characteristics of the survivor and control samples. Tests of differences between group means and proportions

TABLE 1. Cancer Diagnoses in the Survivor Sample (N = 64)

<u>Diagnosis</u>	<u>N</u>	<u>%</u>
Leukemia	11	17.2
Hodgkins Lymphoma	16	25.0
Non-Hodgkins Lymphoma	6	9.4
Brain Tumor	3	4.7
Wilm's Tumor	2	3.1
Neuroblastoma	3	4.7
Osteosarcoma	10	15.6
Ewing's Sarcoma	3	4.7
Rhabdosarcoma	10	15.6

TABLE 2. Demographic Characteristics of Survivor and Control Samples

	<u>Survivors (N = 64)</u>	<u>Controls (N = 51)</u>	<u>p</u>
SEX			
Male	30 (47%)	27 (53%)	N.S.
Female	34 (53%)	24 (47%)	
AGE			
Range (Years)	18-35	18-32	N.S.
Mean (SD)	23.54 (4.09)	22.94 (3.86)	
FATHER'S EDUCATION			
Elementary = 8 yrs	25%	20%	N.S.
High School 9-12 yrs	44%	41%	
Academic > 12 yrs	31%	39%	
MOTHER'S EDUCATION			
Elementary = 8 yrs	20%	14%	N.S.
High School 9-12 yrs	51%	43%	
Academic > 12 yrs	29%	43%	

(t-tests, chi square) confirmed the similarity of the two groups on these matching variables.

Procedure

Recruitment procedures included a letter explaining the purpose of the study and an invitation to participate, as well as a telephone fol-

low-up approximately one week later. Consenting subjects were given interview appointments at the Long-term Follow-up Clinic. Prior to the administration of the study measures, written informed consent was obtained from each subject. Study measures included:

1. *Structured Interview*-This 85-item survey, adapted from the work of Hays, Dolgin, Steele et al. (in press) and administered in a structured interview format, assessed subjects' levels of functioning and achievement in the domains of education, employment, military service, social/family status, and health status.
2. *Mental Health Inventory*-This 38-item instrument, originally designed by Veit and Ware (1983), has been adapted and validated for use with Israeli samples by Florian and Drori (1990). Psychological Distress (anxiety, depression, loss of control) and Psychological Well Being (general positive feeling, positive relationships) scores are combined to yield an overall mental health index score.
3. *Medical Chart Review*-Medical information including details of the survivors' illness and treatment course was obtained via systematic review of each of the subjects' relevant medical records. Data obtained or derived from the medical charts included demographic information, diagnosis, age at diagnosis, years since diagnosis, years off therapy, chemotherapy and radiation therapy protocols, surgery, and relapses. These data were collected by an oncology nurse and recorded onto structured data coding sheets.

RESULTS

Education

The objective educational achievement levels of the survivor group were not statistically different from those of the control subjects. Forty-seven percent of the subjects in each group had completed high school with matriculation diplomas. Seventeen percent of the survivors and 20% of the controls had partial academic or post high school training, while an additional 8% of survivors and 14% of controls had university degrees. On average, survivors had 12.66 (SD = 1.90) years of education, while controls had an average of 12.65 (SD = 1.65)

years. Thirty-six percent of survivors and 34% of controls were pursuing their education at the time of the study, and 74% of subjects in both groups were planning to continue their studies in the future. None of the above differences between the two groups were statistically significant. Still, forty-five percent of the subjects in the survivor group reported feeling that their illness had impacted their educational achievements “to a great extent” or “to a very great extent.”

Employment

As with educational achievement, forty-six percent of the subjects in the survivor group reported feeling that their illness had impacted their employment histories “to a great extent” or “to a very great” extent. Of the survivors, 45% had been rejected from a workplace, compared with 19% of the controls ($p < 0.01$), and approximately half of these survivors felt that their workplace rejection was due to their cancer history. However, in terms of objective employment status, no differences were found between the two groups. Sixty-seven percent of the survivors vs. 61% of control were currently employed. Nineteen percent of the survivors vs. 22% of control were currently unemployed. Two percent of the subjects in both groups defined their occupation as “homemaker.” Thirteen percent of the survivors vs. 16% of controls defined their occupation as “student.” Mean ratings of Job Appropriateness (1-5 scale) were 3.60 (SD = 1.08) for survivors and 3.27 (SD = 1.35) for controls. Mean ratings of Job Satisfaction (1-5 scale) were 3.70 (SD = 1.06) for survivors and 3.60 (SD = 1.14) for controls. These differences were also not statistically significant. However, mean income levels of survivors and controls were marginally different. Survivors earned an average of 1984 New Israeli Shekels (NIS) per month (SD = 2226) while controls earned an average of 2879 NIS (SD = 2491) per month ($p < 0.10$).

Military Service

Ninety-one percent of the survivors and 90% of the controls reported having wanted to serve in the Israeli Defense Forces ($p = n.s.$). Still, only 49% of the survivors actually served, compared to 71% of the controls ($p < 0.05$). Predictably, 85% of the survivors who had not served reported medical history as the primary reason for non-service,

compared with only seven percent for those controls who had not served ($p < 0.001$). Sixty-four percent of the survivors who served did so voluntarily, despite an exemption for medical reasons. Indeed, 55% reported having had difficulty being accepted into the military. Survivors who served spent an average of 2.14 years ($SD = 1.09$) in the military, compared to an average of 2.74 years ($SD = 0.66$) for controls ($p < 0.01$). Seven percent of the survivors who served and 11% of the controls reached the rank of officer ($p = n.s.$). Mean ratings of Army Job Appropriateness (1-5 scale) were 3.86 ($SD = 1.09$) for survivors and 3.75 ($SD = 1.08$) for controls. Mean ratings of Army Job Satisfaction (1-5 scale) were 3.86 ($SD = 1.06$) for survivors and 3.72 ($SD = 1.00$) for controls. These differences were not statistically significant.

Family/Relationships

No differences were found between survivors and controls regarding marital status. Sixty-seven percent of survivors and 80% of controls described themselves as single ($p = n.s.$). Of these, 43% of survivors and 40% of controls reported being involved currently in a relationship ($p = n.s.$). Thirty-one percent of survivors and 20% of controls were either married or living with a significant other in a stable relationship ($p = n.s.$). However, the duration of these relationships were significantly longer for controls (Mean = 6.70 yrs; $SD = 3.68$) than for survivors (Mean = 3.56 yrs; $SD = 3.33$) ($p < 0.05$). Survivors had marginally fewer children (Mean = 0.90; $SD = 1.18$) than controls (Mean = 1.82; $SD = 1.47$) ($p < 0.10$). Here again, 46% of survivors reported feeling that their cancer had impacted the attainment of their social and family goals.

Health

Asked to rate their current health status on a five point scale, survivors rated their health as poorer (Mean = 4.02; $SD = 1.32$) than controls (Mean = 4.53; $SD = 0.61$) ($p < 0.01$). Forty-five percent of survivors reported having current health problems, compared to 18% of controls ($p < 0.01$). Forty-nine percent of survivors reported having current functional disabilities, compared to 10% of controls ($p < 0.001$). Eighty-seven percent of survivors attributed their current

health problems and functional disabilities to their cancer histories, and 30% reported feeling that their past illness made them more vulnerable to illness in the future.

Despite these differences in physical health status, scores for the two groups on the Mental Health Inventory were virtually identical. Mean Total MHI scores for survivors was 166.48 (SD = 25.20) and 166.45 (SD = 25.66) for controls ($p = n.s.$). Both of these mean scores were similar to the mean score of 169.87 (SD = 28.32) for the Israeli normative sample (Florian & Drori, 1990) ($p = n.s.$).

DISCUSSION

Beyond its humanistic significance, data on specific late effects, as well as the more encompassing domain of quality of life, have direct practical applications in guiding clinical decision making and preventive intervention efforts, and as crucial end points in the overall evaluation of clinical trials. As stated in the *Journal of the National Cancer Institute*, "The benefit of a cancer treatment regimen should outweigh its cost in patient suffering. By adding quality of life end points to the traditional end points of overall survival, disease-free survival, and tumor response, medical researchers can make more informed decisions about risk-benefit tradeoffs; for example, two types of quality of life tradeoffs can be described. In one case, two treatments are associated with similar survival rates, but one treatment produces more severe toxic effects; in another case, one of the two treatments demonstrates a better survival rate but has more severe toxic effects. Quality of life data can add to medical knowledge obtained in the conduct of clinical trials . . ." (Moinpour et al., 1989, p. 485).

The current data represent a "good news, bad news" story. The "good news" is that adult survivors of childhood cancer, as represented in the current sample, do seem to be integrating into the societal mainstream in terms of several major quality of life dimensions. Objectively, their achievements in the domains of education, employment, and the establishment of significant relationships appear comparable to those of a control sample. In addition, no evidence of increased psychological impairment or pathology was found among survivors, as compared to controls.

The "bad news" is that certain objective indicators find the survivors at a disadvantage. These included military recruitment difficul-

ties—a factor that in Israeli culture carries with it significant social implications and possible stigma, lower earned income, and higher rates of workplace rejection, despite comparable levels of educational achievement. Current health problems, functional disabilities, and the perception of increased future vulnerability to illness were highly prevalent among survivors. The subjective reports among survivors of feeling disadvantaged are also highly meaningful. Despite generally normative achievements in the educational, employment, and social/family domains, approximately half of the survivors reported feeling that their illness had influenced their attaining of their goals in these areas. These subjective perceptions may represent an emotional burden that expresses itself in neither diminished objective achievements nor in measurable psychopathology, but which nevertheless have great ongoing meaning for the survivor in reference to his or her earlier illness experience and its impact on their identity.

This preliminary study, the first of its kind in Israel, is one of an emerging series in the literature focusing on survivors of childhood cancer into their adulthood (e.g., Hays et al., in press), and its findings must be evaluated in terms of certain limitations. The relatively small sample size is one such limitation, although as the Israeli database continues to grow, follow-up and comparative studies will be possible. The current sample also had few survivors of brain tumors, a particularly high-risk group. The sample also included survivors who had been diagnosed at widely varying ages and who had completed treatment over a broad range of time. There may be real differences in quality of life outcomes for childhood cancer survivors who are diagnosed at different ages and stages of development, and who are closer or further in time from their diagnosis and treatment. While exploratory correlational and regression analyses performed on this data set did not reveal significant associations between age at diagnosis or time since diagnosis and the outcomes reported here, the small sample size and preliminary nature of this study preclude any meaningful conclusions. Clearly, this is an important issue for future investigations.

Further studies, including ones aimed at identifying risk factors for later disadvantage, are important in light of the dual trends of increased survival on the one hand, along with increasingly aggressive treatment regimens (e.g., chemotherapy, bone marrow transplantation) on the other hand. On both of these counts, attention to the long range quality of life needs of survivors will become more urgent with time.

Further descriptive and predictive studies, as well as the tailoring of support services, social policy efforts, and legislation to the specific needs of survivors, will be needed to ensure optimal quality of life for this fast growing population.

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