

QUALITY OF LIFE ISSUES AND CANCER SURVIVORSHIP

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Prior to the 1970s and the advent and use of multi-modal chemotherapy, survival rates for children diagnosed with leukemia and other forms of cancer were dismal. Today, advances in treatment and the coordination of pediatric treatment through clinical trials have greatly increased the long-term life chances of these young people. Indeed, recent reports indicate that 75% of children diagnosed with various forms of cancer in the United States are expected to survive their disease and treatment.¹ Furthermore, young people under the age of 40 with a cancer history comprise 7% of the 7.1 million cancer survivors diagnosed with cancer in the last 20 years.² Many of these survivors were diagnosed as children or adolescents.

These statistics indicate increasing lengths of survival for individuals diagnosed with cancer as children and a growing number of long-term survivors. However, these numbers give no indication of their quality of life expected, enjoyed, or endured. In 1998, the American Cancer Society Task Force on Children and Cancer reported that “(T)he progress achieved in attaining 80% survival among children and adolescents and young adults with cancer can be justified only if their physical, emotional, and social quality of life also are protected” (p.822).³ Thus, success in pediatric oncology requires researchers and health care professionals to attend to the psychosocial and behavioral consequences of treatment and to the quality of life of these survivors.

Cancer Survivorship and Quality of Life

“Cancer survivorship” is a term that has come to represent the state or process of living following a diagnosis of cancer, regardless of how long a person lives. It is a concept used by many health care professionals, researchers, cancer patients, and survivors to understand not only the physical but also the social, psychological, and spiritual/existential impact of cancer on one’s life and for the remainder of one’s life. When viewed as a continual, dynamic, and ever-changing process that begins at the moment of diagnosis and continues throughout the lifespan, cancer survivorship can be defined as the experience of “living with, through, or beyond cancer.”⁴

Measuring “quality of life”

There has been substantial debate about both meaning and measurement approaches in psychosocial and quality of life studies of childhood cancer patients and survivors.^{5,6} Even when meaning has been clear, measurement and sample decisions have varied from study to study. Questions about validity and reliability abound. Sample size has varied considerably. Some investigators have used psychometric instruments standardized on “physically normal” populations, while others have normed instruments on the populations directly under inquiry. Other investigators have used approaches that are more responsive to respondent narratives than to investigators’ *a priori* orientations and have included uniquely designed questionnaires, open-ended questions, and intensive personal and small group (focus group) interviews.

To examine “quality of life” as a specified construct in childhood cancer survivors, some investigators have administered instruments designed specifically to assess multiple and varied aspects, or qualities, of cancer survivors’ lives.⁷⁻¹¹ Some of these instruments, such as the

European Organization for the Research and Treatment of Cancer (EORTC) – C30 Questionnaire,¹² the Quality of Life – Cancer Survivors¹³ and the Quality of Life Index – Cancer¹⁴ are widely-used in quality of life research and have well-established norms derived from adult cancer populations. These instruments typically assess physical, psychological, social and spiritual/existential domains, and address concerns regarding health status and physical function, sexuality and fertility, emotional distress, future outlook, school and work performance, social and family relationships, and spirituality, as well as other key medical, demographic and psychosocial elements. However, the validity, reliability, and utility of these instruments in childhood cancer *survivor* populations have yet to be established, and no gold standard for assessing “quality of life” in *survivors* of childhood cancer exists.ⁱ

Although reports of childhood cancer survivors’ “quality of life” are few, long-term physical, psychosocial and behavioral outcomes associated with cancer survivorship have been well reported. Yet, the overall portrait of childhood cancer survivors is as varied as the systematic approaches used to portray it.

Psychosocial outcomes and “quality of life”

Historically, a number of studies have suggested that a sizable proportion of childhood cancer survivors is seriously troubled psychologically, perhaps even exhibiting psychopathologic symptoms.¹⁵⁻¹⁸ In contrast, other studies indicate that childhood cancer survivors score in the normal range on standardized psychometric measures, thereby demonstrating few significant differences in psychosocial adjustment when compared to young people without a history of cancer.¹⁹⁻²¹ Kazak and Meadows²² summarize these findings, stating that “most (survivors) score

ⁱ Some “Quality of Life” instruments have been developed specifically for children and adolescents in active treatment but have yet to be reported in off-treatment survivor populations.⁷⁷⁻⁷⁹

near normal in terms of psychological and social functioning” (p. 187). Kupst et al.²³ argue that “despite periods of intense stress, most children and families adapt well,” although “a significant minority” of survivors has problems (p. 602). Perhaps most provocatively, a few investigators^{24;25} draw attention to anecdotal reports that suggest psychological growth in this population, and several studies have demonstrated the population of childhood cancer survivors to be significantly healthier (in psychosocial terms) or more appreciative of life than population norms or healthy controls.²⁶⁻²⁹

A recently emerging literature on stress, threat, and trauma provides a new and different paradigm for examining and understanding responses to life-threatening events like cancer. For instance, several studies identify upwards of 20% of long-term survivors of childhood cancer reporting symptoms of post-traumatic stress.^{15;30;31} However, this new paradigm, in the context of childhood cancer survivorship research, also evokes the notion of resilience and raises the possibility that some people not only survive stress and trauma, but “thrive”^{25;32} -- they may experience enhanced quality of life as a result of the stress. As Folkman and Greer³³ argue, a focus on “psychiatric symptoms, such as anxiety and depression...obscures the struggle for psychological well-being and the coping processes that support it” (p. 11), and Paterson et al.³⁴ discuss how some people can transform their lives by responding to an illness in ways that enhance the quality and meaning of their lives. Indeed, preliminary work by Stuber has demonstrated a positive correlation between reporting post-traumatic stress symptoms and post-traumatic growth among survivors of childhood cancer (personal communication).

Health Behaviors

A research topic yet to be fully explored is the extent to which childhood cancer survivors engage in behaviors that are likely to compromise or promote their future health and well-being. Although studies are few, there is some evidence that health risk-taking behaviors may exist at problematic levels among childhood cancer survivors. Compared to national norms, survivors have demonstrated higher rates of alcoholism and equivalent smoking rates³⁵ despite their increased risks for second cancers, and some have reported substantial habits (greater than 1/2 pack per day).³⁶ One study shows survivors are less likely to quit smoking as compared to sibling controls,³⁷ although an analysis of smoking outcomes in a large multi-institutional study (the Childhood Cancer Survivors Study) demonstrated no significant differences in quit rates among survivors and sibling controls.³⁸ Other data suggest that while survivors may be significantly less likely than controls to initiate smoking, once having started smoking they are as likely as controls to become regular smokers.³⁶

Given long-term survivors' increased risks for second cancers and mortality,³⁹⁻⁴² cigarette smoking and alcohol or drug abuse are particularly dangerous for this population. These behaviors have the potential to contribute to relapse or onset of second cancers, either directly (as in the case of smoking) or indirectly (e.g., alcohol and drug use impacts proper nutrition, sleep, exercise, etc.). Therefore, it is imperative to promote long-term health in childhood cancer survivors and to develop interventions that support health promotion and disease prevention in this population.

As for other health-risk and health-promoting behaviors like dieting practices, cancer prevention screening (i.e., mammography, pap test, colon and prostate screening), exercise, use of sunscreen, or safe sex practices, these issues have yet to be addressed in the childhood cancer survivor literature.

How does age relate to psychosocial and behavioral outcomes?

Current research suggests that current age and age at diagnosis may have something to do with psychosocial and behavioral outcomes and quality of life, but findings across studies are inconsistent and limited. For example, some research indicates that survivors diagnosed at an older age,²³ or who are older at the time of inquiry,^{27,30} show more negative psychosocial outlooks. Other studies have identified younger age at diagnosis as well as female gender as being risk factors for mood disturbance in long-term survivors.⁴³ In general, childhood cancer survivor studies have yet to adequately examine the extent to which being diagnosed at a particular developmental stage of life may be associated with psychosocial functioning, health behaviors, and quality of life later in life. We know that a cancer diagnosis in school age children often disrupts their school attendance and limits their ability to engage in social and physical activities.²⁴ However, the extent to which this disruption of normal developmental life tasks has implications for quality of life or the adoption of health-risk or health-promoting behaviors in the future has not been investigated. Studying young adults diagnosed and treated as children and teenagers is an opportunity to focus on the long-term impact of cancer at specific early developmental ages/life stages.

To date, we also lack an understanding of how childhood cancer survivors' needs may well change over time as they age, move further in time from treatment, and pass through later cognitive and developmental stages of life. The end of cancer treatment, returning to school, leaving home, marrying, starting a family and/or a career are all critical developmental stages of a survivor's life. They are times at which needs may change and when life offers new opportunities for personal growth and development. Each of these life stages also carries with it

the potential for a new understanding of cancer's impact, new worries or concerns, and new challenges to one's identity and social roles. These changes may result in changes in one's quality of life.

What do we know about other variables that affect quality of life?

In spite of the varied and somewhat contradictory nature of childhood cancer survivor studies, existing studies are in general agreement in that survivors who report substantial physical late effects, disease relapse, learning problems, or other life stressors also demonstrate less positive self-esteem or adjustment scores and report more problems or worse quality of life^{30;44-47}. Studies examining physical effects in childhood cancer survivors have drawn attention to an increased risk of death at an early age,^{40;41} compromise to vital organ systems, including reproduction⁴⁸⁻⁵⁰, neuropsychological and educational problems,⁵¹⁻⁵⁵ and visible physical impairments and disabilities.^{7;56;57} However, the psychosocial and behavioral implications of these sequelae for long-term survivors are not as well understood. For example, the relationships between physical symptoms and education and employment, and the potentials for increased behavioral risks (i.e. alcohol and substance use and depression) commonly associated with low educational attainment or employment difficulties, are not well understood. Also, given the risks for infertility in childhood cancer survivors, we still lack an understanding of how experiencing infertility affects these young people's quality of life, including their attitudes about having children, their concerns about their children's risks for cancer given their own cancer history, their knowledge about alternative modes of having children (i.e., adoption, artificial insemination), and their ability to financially or emotionally afford alternative modes of

creating a family. We also lack information regarding the extent to which young adult survivors engage in safe sex practices (or not) in light of their uncertainty of being able to bear children.

Work to date suggests that childhood cancer survivors with high rates of anxiety, depression, or self-esteem deficits, limited vocational potential, and physical health or functioning deficits may be especially likely to engage in risk-taking behaviors, particularly if they are male. In contrast, females in the general population are more likely to experience anxiety or depression, low self-esteem and low vocational potential⁵⁸ that secondarily may increase their risk-taking behaviors. In addition, female leukemia survivors may be more susceptible to neuropsychological damage associated with high doses of cranial radiation treatment received at a young age. Studies have shown that female leukemia survivors, but not males, score significantly below the mean on all subscales of IQ and achievement tests.^{59;60}

With regard to medical treatment, high dose radiation has been shown to increase survivors' risks for mood disturbance,⁴³ and a recent report from the Childhood Cancer Survivor Study indicates that exposure to intensive chemotherapy adds to childhood cancer survivors' risk for reporting psychological distress.⁶¹ Treatment variables, such as exposure to cranial irradiation and age at diagnosis, have been demonstrated to significantly and negatively affect educational attainment in long-term survivors of childhood leukemia,⁵³ and treatment intensity during childhood may serve as a risk factor for adult survivors' health-compromising behaviors through neuropsychological deficits that arise from cancer treatment.⁴⁴ Authors of a recent large epidemiological cohort study of childhood cancer survivors suggest, however, that the negative effects of treatment-related variables on psychological outcomes may be a function of limitations in education, employment, and income.⁶¹

Few studies have adequately explored the relationship of demographic and socioeconomic status variables and psychosocial/quality of life outcomes.⁶¹⁻⁶³ Furthermore, limited investigations of race and ethnicity as they relate to outcomes for childhood cancer survivors have not demonstrated differences in health behaviors.⁶⁴ Yet, studies of health behaviors in the general population have found race or ethnic differences in behaviors associated with an increased risk for cancer,^{65,66} including higher prevalence of tobacco use among Hispanic males transitioning out of high school.⁶⁷ Given these findings, it behooves us to understand if and whether minority survivors of childhood cancer adopt health risk behaviors at rates higher or lower than expected when compared to other sub-groups, whether they continue these health patterns into adulthood, and why.

Implications for policy and practice

Survivors of childhood cancer pose a particular challenge to the US health care system. In terms of years of productive life saved, childhood cancer is one of the most remarkable examples of the advance of modern high-technology medicine. Despite these successes in medical treatment, we know that a full range of psychosocial services is not available to all children surviving cancer. Moreover, we also know that these successes, and the provision of a full range of services, are not being achieved equally in the United States. In an era in which good health is not just the absence of disease but also the presence of psychological and social well being, we must ask if these advances in pediatric oncology are resulting in what van Eys⁶⁸ called a “truly cured child.”

Since childhood cancer impacts families,⁶⁹ the health and well-being of the childhood cancer survivor population is inextricably linked to the health and well-being of their own

parents, siblings, and eventually spouses and significant others. Thus, support interventions that focus on families are very important. Today's long-term survivor clinics, cancer survivor day celebrations, oncology camps, family retreats, and community-based parent self-help organizations (like those affiliated with the Candlelighters Childhood Cancer Foundation) have become invaluable sources of support to pediatric oncology families throughout an entire span of survivorship – from diagnosis, through treatment, and beyond.

Attending to the special needs of childhood cancer survivors and their families requires not only management of disease and its potential late effects, but also long-term expansion and coordination of services, utilization of allied health care professionals, mobilization of community resources, and assistance in managing the emotional and financial impacts of the illness. Interventions also should be designed and then implemented in accordance with needs expressed by survivors at various stages of their lives. Few studies have focused on actual needs but suggest areas for intervention.^{70;71} These include the need and desire for information about disease and treatment, health insurance, and family planning (including information regarding the potential risk of “passing” cancer to off-spring in spite of existing data that suggests that offspring are not at an increased risk of developing cancer⁷²). Survivors also have expressed a need for educational and vocational counseling, supportive counseling, as well as a desire to meet other survivors.⁷¹

Implications for research

Knowledge about the determinants of psychosocial functioning and behavioral outcomes in this population is needed as a basis for the development of appropriate supportive and potentially preventive interventions throughout a continuum of care, from diagnosis through

treatment and over the long-term. Investigators and health care providers have yet to systematically test interventions that may promote positive psychosocial adjustment and the adoption of health promoting behaviors, and/or prevent negative outcomes and health risk behaviors at various points throughout the life span. Given studies documenting treatment-related physical effects (e.g., cardiac and pulmonary problems, hormonal problems, etc.) in a childhood cancer survivor population, we do not know how and to what extent these conditions contribute to psychological well-being, psychosocial functioning and health behaviors over the long-term. For instance, physical late effects such as fatigue or limited physical function may assumedly contribute to decreased self-worth or sadness in some childhood cancer survivors, but these same effects may also just as well increase survivors' awareness and practice of important health promoting behaviors such as proper diet and exercise. Similarly, perceived benefits from the cancer experience may enhance self-esteem, self-confidence and mastery but still not prevent the worry, self-doubt, or employment or insurance discrimination that may arise as survivors age and face new life challenges such as going to college, entering the work world, or starting a family. While empirical research has documented long-term sequelae in survivors of childhood cancer, we still lack knowledge about (1) the relationship between psychosocial functioning and behavioral outcomes for long-term survivors of childhood cancer and (2) about factors that mediate and/or moderate this relationship over time.

Focusing on survivors as a cohort is a relatively new research arena, and we need rigorous designs to overcome the limitations of existing studies (i.e., single institutions, small sample sizes, cross-sectional designs that do not assess changes over time). Quality of Life instruments, whether designed for the general population, adult cancer patients, or childhood patients, have yet to be applied and reported in off-treatment childhood cancer survivors who

have reached adulthood. Testing existing quality of life instruments and assessing their psychometric properties in survivor populations will provide some direction in the area of instrument development.⁷³ Furthermore, we must seek to expand the theoretical context for understanding cancer and its impact on life by acknowledging that the experience of cancer in children and adolescents occurs during important phases of psychosocial development and identity formation. The extent to which the cancer experience is or is not incorporated into a childhood cancer survivor's sense of self may affect that individual's quality of life.⁷⁴

Prospective longitudinal studies to assess psychological, social and behavioral outcomes and change over time, as these young people pass through different developmental stages, appear to be a logical next step. Also, collaborative research among investigators will increase sample sizes. Rigorous research methods that (1) control for salient variables not directly related to cancer (i.e. socioeconomic status), (2) stratify samples by developmental stage and age at diagnosis, (3) use various respondents (e.g., child, parent, teacher, doctor/nurse), and (4) apply statistical corrections for multiple analyses and multi-directional causal pathways will improve the scientific rigor and potential clinical relevance of future studies.⁵¹ Finally, qualitative approaches to research will enhance our ability to capture the subjective illness experience and meaning that survivors attribute to cancer and its treatment, including the interrelationships among various quality of life domains and other behavioral outcomes. Survivors' own self-reports are the clearest expressions of their own ways of thinking about and presenting their experience and quality of life. "The role of scholars is to listen to and reflect upon these self-reports, 'test' them for accuracy or unreliability, for defensiveness or obfuscation, and for internal contradiction" (p.6).²⁵ Combinations of research approaches, both qualitative and quantitative, can provide us with a sense of the credibility and trustworthiness of our findings.

Conclusion

Given the varied study results and experiences described by childhood cancer survivors, it is reasonable to conclude that they are all correct in certain regards. Some survivors of childhood cancer have managed to grow in positive ways as a result of their cancer experience. Most probably are relatively normal in psychosocial terms and would score such on most psychological measures. A small but significant minority undoubtedly experiences ongoing psychological and/or social adjustment problems -- how large a proportion and how substantial a set of problems appear unclear. Moreover, all survivors, even those apparently doing quite well, experience at least occasional problems in social adjustment and continue to be concerned about their medical and social futures. As Haase and Rostad⁷⁵ suggest: “The experience of completing cancer treatment has two faces -- one of celebration and hope, one of uncertainty and fear” (p. 1490). In their view, and as affirmed by other researchers, survivors continue to worry, more or less, occasionally or not, about relapses, more treatments, and potential problems with fertility.^{20;29;76}

Understanding how young people manage the impact of cancer and its influence throughout the rest of their lives is critical for health care professionals committed to assisting these childhood cancer survivors in their attempts to live vibrant and productive lives. This knowledge will guide subsequent investigations of *who* might benefit from *which* psychosocial support interventions *when*—during early diagnostic and/or treatment stages, at the end of treatment, or in the long-term. While it is important to identify long-term survivors “at-risk” for psychosocial sequelae for the purposes of developing preventive interventions and psychosocial treatment options, identification is not enough. Given the current knowledge that most long-term

survivors of childhood cancer are psychologically well-adjusted, and that some even describe their lives as enriched by the cancer experience, we need a fuller, more comprehensive understanding of what contributes to long-term survivors' positive adaptation. Equipped with this understanding, health care professionals, program planners, and policy makers can re-develop and create appropriate services and systems that facilitate and enhance quality of life.

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