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LONGITUDINAL CANCER-RELATED HEALTH CARE
FOR ADULT SURVIVORS OF CHILDHOOD CANCER

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1.0   INTRODUCTION

Long-term survivors of childhood cancer represent a growing, at-risk and vulnerable

population with health care needs that are not being met through our current medical system.

Childhood cancer survivors, though being "cured", often experience late effects, both physical

and psychological, secondary to their cancer treatment. Because of this potential for late

occurring health problems, longitudinal, and preventive-focused health care that includes risk

assessment based upon previous cancer treatment, screening of asymptomatic individuals, and

secondary cancer surveillance is recommended for all long-term childhood cancer survivors. As

stated in the second report of the National Cancer Policy Board, *Ensuring Quality Cancer Care*

(1999), a key element of the cancer care "system" is life-long follow-up of cancer survivors.

Despite this recommendation, most adult survivors of childhood cancer do not seek/receive

periodic, cancer-related and preventive health care. This paper discusses the rationale for

longitudinal health care for this vulnerable population, describes the current status of such health

care in the U.S., and provides a theoretical framework to determine barriers and enablers that

must be addressed to ameliorate the inadequacies of the current health care system.

Because there is no published literature regarding the health care access and utilization

and barriers to long-term follow-up of childhood cancer survivors, preliminary results from two

studies are provided. The first is a recently completed analysis of the Childhood Cancer Survivor

Study (CCSS) regarding medical follow-up of 9434 adult survivors, age 18 and older (Oeffinger,

2002a). The CCSS is a 25-institution, NIH-funded retrospective cohort study that is following

over 14,000 long-term survivors of childhood cancer who were diagnosed between 1970-1986

(Robison, 2001). Baseline data were collected for participants of the study cohort using a 24-

page questionnaire. The baseline questionnaire was designed to capture a wide range of

information including demographic characteristics, education, income, employment, insurance coverage, marital status, health habits, family history, access and utilization of medical care, medication use, frequency of diagnosed medical conditions, surgical procedures, recurrent cancer, subsequent new neoplasms, and offspring/pregnancy history.

The second study, funded through the Robert Wood Johnson Foundation, is ongoing and is assessing barriers to long-term follow-up from the perspective of adult survivors of childhood cancer. As part of this study, hereafter referred to as the "RWJ Barriers" study, a subset of 1600 adult survivors were randomly selected from the CCSS cohort and mailed an 88-item questionnaire to determine factors associated with general and cancer-related health care utilization. Questions were grouped into four domains: core health beliefs, internal modifying factors, external modifying factors, and health locus of control. These domains are further described in section 5. The response rate of completed questionnaires is currently 70%, with additional mailings in process. For the purpose of this National Cancer Policy Board report, preliminary descriptive results from the first 441 respondents are provided. Salient quotes from survivors participating in the RWJ Barriers study or from a cancer survivor list-serve are used to illustrate key issues.

2.0 RATIONALE FOR LONGITUDINAL CANCER-RELATED HEALTH CARE FOR ADULT SURVIVORS OF CHILDHOOD CANCER

2.1 Growing, At-Risk Population

Advances in diagnosis and treatment have contributed to the current "cure" rates for pediatric malignancies. In the 1990's, over 70% of children who were diagnosed with a pediatric cancer survived (Ries, 1999), creating what has been referred to as an "epidemic of survival"

(van Eys, 1991). Currently 1:900 young adults, between the age of 20 – 45 years, is a childhood cancer survivor, with an increase to about 1:250 predicted within the next ten years (Meadows, 1980; Donaldson, 1993).

Sequelae of chemotherapy and radiation are common and may be asymptomatic for extended periods. As many as two-thirds of survivors will experience a late effect of chemotherapy or radiation, defined as any chronic or late occurring outcome, physical or psychosocial, that persists or develops beyond five years from the diagnosis of the cancer (Garré, 1994; Vonderweid, 1996; Stevens, 1998; Oeffinger, 2000a). Virtually all organ systems can be affected, with late effects including cognitive impairment, fertility problems, alterations in growth and development, organ system damage, chronic hepatitis, second malignant neoplasms, and quality of life issues (DeLaat, 1992; Neglia, 1993; Donaldson, 1993; Meister, 1993; Schwartz, 1995). Commonly, survivors have more than one late effect, with perhaps as many as a quarter of survivors experiencing one that is severe or life-threatening (Garré, 1994; Stevens, 1998; Oeffinger, 2000a).

These late effects, including second malignant neoplasms, are discussed in detail in other reports within the National Cancer Policy Board effort. To describe the rationale for longitudinal cancer-related health care for adult survivors of childhood cancer, a brief discussion follows regarding the role of prevention, surveillance, and management of several illustrative late effects.

2.2   Late Effects Diagnosed during Childhood or Adolescence

Some late effects of therapy are identified early in follow-up, during the childhood or adolescent years, and resolve without consequence. Others may persist and become chronic problems and influence the progression of other diseases associated with aging. Illustrating this process, survivors who develop chronic tubular or glomerular dysfunction secondary to

ifosfamide (Prasad, 1996; Skinner, 2000) and later develop hypertension or diabetes mellitus, two common adult health problems that often lead to secondary renal disease, may experience an acceleration of renal dysfunction. Will survivors who experience cognitive dysfunction and neuropathologic changes from cranial irradiation (CRT), such as leukoencephalopathy or mineralizing microangiopathy (Peylan-Ramu, 1978; Hertzberg, 1997) experience premature dementia-type illnesses? As a third example, soft tissue sarcoma survivors often experience skeletal delay and asymmetric growth secondary to radiation, often compounded by surgical excision of the tumor, leading to considerable cosmetic and musculoskeletal problems (Raney, 1999; Womer, 2000). Though improvements in radiotherapy and surgical approaches have resulted in improved cosmetic and musculoskeletal outcomes, by the location and nature of the tumors there are limitations to tissue sparing. These late effects often result in chronic pain. How will the chronic adaptive distribution of structural stresses affect the function and aging of weight bearing joints and muscle groups? Will these survivors be at risk for premature joint deterioration and chronic muscle spasm/pain? Because the population of adult survivors of childhood cancer is still relatively young, with a small percentage over the age of forty, there is no data available to answer these questions. Only through long-term follow-up of adult survivors will the impact of these types of late effects on the aging process become evident.

2.3   Silent and 'Late Occurring' Late Effects of Adulthood

Some late effects occur many years after treatment, have an asymptomatic interval, and then become symptomatic only with end-stage or progressive disease, often with devastating consequences. Though there have been many studies determining risk factors for such late effects, there have been few that assess the impact of risk modification or early intervention on health outcomes and quality of life. However, these principles have been well validated in a

number of diseases in the general population and form the cornerstone of preventive medicine and may be generalizable to survivors. To illustrate these principles, as they pertain to adult survivors, six different late effects or diseases are discussed. It should be emphasized that although it is appropriate to adopt screening practices developed in other populations, it does not obviate the need for further study of survivors.

2.3.1 Hepatitis C

Because most ALL patients receive blood products during therapy, patients treated before adequate blood donor screening for hepatitis C was initiated in the early 1990's are at risk for chronic liver disease. Prevalence of circulating HCV-RNA in ALL patients treated before 1990 ranges from 6.6 – 49%, with an unknown, and likely sizeable, percentage of survivors never having been tested or aware of their risk (Dibenedetto, 1994; Locasciulli, 1997; Paul, 1999; Strickland, 2000). The natural history of ALL survivors with hepatitis C is not well understood. In an Italian study, only 4% of the 56 HCV-RNA seropositive patients had persistently elevated alanine aminotransferase (ALT) over the course of a mean follow-up of 17 years (Locasciulli, 1995). In contrast, Paul et al reported that 12% of 75 leukemia survivors were anti-HCV positive and that 6/9 had liver biopsies that showed at least moderate portal inflammation and half had bridging fibrosis (Paul, 1999).

In the general population, chronic HCV infection develops in 75 – 85% of persons infected with hepatitis C (Alter, 1992; Shakil, 1995). About 30 – 40% of chronically infected persons have persistently normal ALT levels and tend to have indolent disease. The course of progressive liver dysfunction is usually insidious, progressing at a slow rate without symptoms or physical signs in the majority of patients during the first two or more decades after infection. Over a twenty to thirty year period, 20 – 30% of patients with untreated HCV will develop

cirrhosis or an extrahepatic sequelae, such as cryoglobulinemia, porphyria cutanea tarda, or membranoproliferative glomerulonephritis (Tong, 1995; Fattovich, 1997; Poynard, 1997). Alcohol consumption, even in moderate amounts, increases the risk of progression to cirrhosis (Wiley, 1998; Pianko, 2000).

Successful long-term treatment prior to liver decompensation has rapidly improved in the past decade. A sustained virologic response rate of 43% has been reported in patients with chronic hepatitis secondary to HCV who were treated with 48 weeks of interferon alpha2b and ribarvirin (Poynard, 1998). Use of pegylated interferon alpha 2b with ribavirin appears to confer an even higher response rate (Lindsay, 2001). Thus, identification of survivors who were treated with blood products prior to 1992, determination of their HCV-RNA status, assessment of the liver function of those infected, counseling regarding alcohol consumption, and appropriate treatment and follow-up is essential to reduce the risk for potentially life-threatening sequelae.

2.3.2 Anthracycline-Induced, Late-Onset Cardiomyopathy

Anthracyclines, notably daunorubicin and doxorubicin, have been used in the treatment of several childhood cancers, including Hodgkin's and non-Hodgkin's lymphomas, soft tissue sarcoma, ALL, and Wilms' tumor. In the past 10 years, it has become apparent that childhood cancer patients treated with an anthracycline are at risk for developing late onset cardiomyopathy (Lipshultz, 1991; Shan, 1996).

Anthracycline-induced cardiomyopathy is characterized by elevated afterload followed by the development of a dilated thin-walled left ventricle. Over time, this can lead to a stiff and poorly compliant left ventricle. Lipshultz et al (1991) noted that cumulative doses of doxorubicin as low as 228 mg/m^2 body surface area increased afterload or decreased contractility or both in 65% of childhood leukemia survivors up to 15 years after treatment with anthracyclines. Female

sex, younger age at treatment, higher rate of administration of doxorubicin, cumulative dose of doxorubicin, and concurrent treatment with chest/mantle radiation are independent risk factors for the development of altered left ventricular function. The use of cardioprotectants in children, such as dexrazoxane, are under investigation and appear to decrease acute toxicity secondary to anthracyclines (Wexler, 1998), but further longitudinal studies will be needed to ascertain the long-term protective action.

Most survivors who develop echocardiographic evidence of left ventricular dysfunction after treatment with an anthracycline will likely remain asymptomatic, but longitudinal studies suggest that a significant proportion will experience progressive changes and may develop congestive heart failure (Lipshultz, 1995; Grenier, 1998). Within the first 10 years after treatment, about 4-5% of survivors will have overt congestive heart failure (Lipshultz, 1991; Steinherz, 1991). However, the incidence of echocardiographically demonstrated severe left ventricular dysfunction increases with the duration of follow-up, and thus, the long-term incidence of survivors who will become symptomatic is likely considerably higher. Importantly, in female survivors, the initial presentation of congestive heart failure may be abruptly precipitated by pregnancy or delivery (Shan, 1996; Grenier, 1998).

In the general population, the onset of symptomatic congestive heart failure is associated with a marked increase in morbidity and mortality. Early identification and aggressive management of left ventricular dysfunction and co-morbid diseases is associated with a reduction in morbidity and mortality and improved quality of life. The 5-year mortality rate for the unselected Framingham population was 75% in men and 62% in women (Ho, 1993). In an unselected Scottish population, the crude 1-year mortality rate was 24.2% for those who were less than 55 years of age (MacIntyre, 2000). Treatment of congestive heart failure with either an

angiotensin-converting enzyme inhibitor or a beta-adrenergic blocking agent results in improved quality of life and reduced mortality rates. Perhaps more importantly, treatment of asymptomatic patients is associated with later onset of symptomatic disease, improvement in ejection fractions, and lower rates of risk of death or hospitalization for heart failure (Exner, 1999). Treatment of co-morbid conditions, such as hypertension, diabetes mellitus, dyslipidemia, and smoking, has been shown to reduce the risk for developing heart failure (McKelvie, 1999).

Based on the benefits of early identification, risk modification, and aggressive management of adults with cardiomyopathy in the general population, there is general consensus that periodic monitoring of left ventricular function of asymptomatic survivors who were treated with moderate to high doses of anthracyclines, especially females and those treated at a younger age or with chest radiation, is important (Lipshultz, 1991; Grenier, 1998).

2.3.3   *Breast Cancer*

Women treated with mantle irradiation for childhood Hodgkin's disease face a significant increase in risk for development of breast cancer, with a cumulative incidence of about 35% at 20 to 25 years post therapy (Bhatia, 1996; Aisenberg, 1997). In a retrospective review of 885 female Hodgkin survivors, Hancock and colleagues reported a relative risk of 136 for those treated with mantle radiation prior to the age of 15 years (Hancock, 1993). In the Childhood Cancer Survivor Study (CCSS), Neglia and colleagues (2001) reported an excess standardized incidence ratio (SIR) for breast cancer of 16.2 in a retrospective analysis of 13,581 long-term survivors. Onset of breast cancer has been noted as early as eight years post radiation, with a median age at diagnosis of 31.5 years (Bhatia, 1996) and a median interval from radiation of 15.7 years (Neglia, 2001). It appears that pathologic features and prognosis for Hodgkin

survivors with breast cancer is similar to the general population (Wolden, 2000). Likewise, 5-year survival is strongly associated with stage of disease at time of diagnosis (Cutuli, 2001).

There is universal agreement that early diagnosis and treatment of breast cancer in the general population is associated with improved outcomes and reduced mortality. Screening mammography is considered a cost-effective method of early detection in women at increased risk (U.S. Preventive Services Task Force, 1996; Rosenquist, 1998; Overmoyer, 1999). Because breast cancer is common in female survivors of childhood cancer who were treated with mantle or chest/lung radiation and early diagnosis and treatment is associated with improved outcomes in the general population, there is general consensus that periodic screening mammography be started 8-10 years after completion of therapy or around age 25 (Hancock, 1993; Bhatia, 1996; Aisenberg, 1996).

2.3.4   Skin Cancer

Skin cancer is the most common group of cancers diagnosed in adults in the general population, accounting for nearly one-third of all cancers, with about 500,000 new non-melanoma skin cancers (NMSC) and 32,000 new melanomas diagnosed per year (Marks, 1995). Early diagnosis and treatment, particularly with melanoma, is associated with improved outcomes (Rhodes, 1995). More than 90% of NMSCs can be attributed to sun exposure and involve the face, ears, neck and upper extremities (American Academy of Pediatrics, 1999). Regular use of SPF-15 sunscreen to these sun exposed areas during the first 18 years of life could lead to a 78% reduction in the lifetime incidence of basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) (Stern, 1986). Public education regarding sun protection and self-examination has been associated with earlier stage of disease at diagnosis (Rhodes, 1995).

The epidermis, particularly the basal layer, is sensitive to radiation carcinogenesis, especially at a young age. In a study of the atomic bomb survivors of Japan (Ron, 1998), the excess relative risk for BCC for children exposed prior to the age of ten was 21 (95% CI, 4.1, 73). Moderate doses of therapeutic radiation for tinea capitis in childhood resulted in an excess relative risk of 1.7 at 1 Gy of radiation, with an absolute excess incidence of 0.31 per 1000 person-years (Ron, 1991).

Higher doses of radiation used in the treatment of childhood cancers, such as Hodgkin's and non-Hodgkin's lymphomas, soft tissue sarcoma, and Wilms' tumor, are associated with an increased risk for melanoma, BCC, and SCC (Meadows, 1985; Olsen, 1993; Swerdlow, 1997). The SIR of all skin cancers following treatment for childhood cancer was 4.1 in a cohort of 8602 survivors from Denmark (Olsen, 1993). In an analysis of 1039 patients treated for Hodgkin's disease, Swerdlow and coworkers (1997) reported an SIR of 4.0 and 3.9 for malignant melanoma and NMSC, respectively. NMSC secondary to ionizing radiation occur in skin fields exposed to the radiation, which may be in an unusual or non-sun exposed part of the body. Whether or not sun protection will confer a reduced risk in those exposed to ionizing radiation of a sun-exposed part of the body is not known (Ron, 1991; Ron, 1998; Lichter, 2000). Again, recognizing the increased risk for skin cancer after radiation and the benefits of early diagnosis and treatment, it is important that health care providers counsel survivors regarding methods of sun protection, the ABCs of skin cancer, and the importance of periodic examination of the skin in and around the radiation field.

2.3.5   *Obesity*

A recent analysis of a large retrospective cohort of 2298 adult survivors of childhood acute leukemia (mean age, 24.4 years) and two comparison groups found that previous treatment

with CRT $\geq$ 20 Gy was associated with an increased risk for obesity, particularly for females treated at a younger age (Oeffinger, 2002b). The age- and race-adjusted odds ratio (OR) for obesity in survivors treated with CRT $\geq$ 20 Gy in comparison with siblings of childhood cancer survivors was 2.72 for females (95% CI; 2.01, 3.78) and 1.66 for males (95% CI; 1.20, 2.26). Risk was modified by age at diagnosis, with females treated at a younger age at highest risk. The age- and race-adjusted OR for obesity in females diagnosed 0-4 years of age and treated with CRT $\geq$ 20 Gy was 4.26 (95% CI 2.60, 6.78).

Further increasing this risk, it appears that leukemia survivors are more likely to be physically inactive and have reduced exercise capacity. In a cross-sectional study of 34 long-term survivors of ALL, 21 survivors of other malignancies, and 32 healthy sibling controls, ALL survivors had a decreased activity level and total daily energy expenditure that correlated with percentage of body fat (Warner, 1998). Similarly, in a cross-sectional analysis of 26 young adult survivors of childhood ALL with a median age of 20.9 years, the median physical activity index score was 1,328 kcal/week (inactive range), with 35% of the participants falling in the sedentary range of less than 1,000 kcal/week (Oeffinger, 2001). Maximal and submaximal exercise capacity were reduced in 70 ALL survivors who were 4.2 years post therapy in an age- and sex-matched cross-sectional study (Jenney, 1995). In a study of 53 ALL survivors with a longer interval from diagnosis (mean 10.5 years), 25% and 31% of survivors were unable to reach normal maximal oxygen uptake and normal oxygen uptake at the anaerobic threshold, respectively (Black, 1998).

Obesity in childhood, adolescence, and young adulthood is an important predictor of eventual development of adult-onset diabetes mellitus, hypertension, dyslipidemia, and ultimately cardiovascular disease (Sinaiko, 1999). Even modest weight gain from age 20 is

strongly associated with an increased risk of coronary heart disease (Rosengren, 1999). Population-based studies suggest that over 75% of hypertension is directly attributable to obesity (Krauss, 1998). Over half of the variance in insulin sensitivity in the general population is accounted for by obesity (Krauss, 1998). The risk of death from all causes, cardiovascular disease, cancer, and other diseases increases throughout the ranges of overweight and obesity in males and females (Calle, 1999; National Task Force on the Prevention and Treatment of Obesity, 2000). Physical inactivity is associated with an increased risk of cardiovascular disease (Krauss, 1998; Lee, 1998). A relative risk of 1.31 (95% CI, 1.15-1.49) for all-cause mortality was seen in men with a physical activity index < 2,000 kcal/week in the Harvard Alumni Study (Paffenbarger, 1986).

Primary and secondary prevention of obesity and physical inactivity have been shown to reduce the cardiovascular morbidity and mortality and improve quality of life in the general population, and likewise should lower risk in adult survivors. Periodic follow-up to assess weight, physical activity levels, and screen for potential obesity-related diseases is important for adult survivors of childhood cancer, especially those who were treated with cranial irradiation.

2.3.6 *Impairment of Peak Bone Mass and Dysfunction of Bone Metabolism*

It appears that a large percentage of survivors of childhood cancer, including males, are at risk for a prevalent disease of middle to later life, osteoporosis. Several well-designed, small to medium sized cross-sectional studies of childhood cancer survivors, with median ages at evaluation ranging from 12 – 25 years, consistently showed reduction in bone mineral density (BMD), bone mass content (BMC), and/or age-adjusted bone mass (Hesseling, 1998; Aisenberg, 1998; Arikoski, 1998; Nysom, 1998; Hoorweg-Nijman, 1999; Vassilopoulou-Sellin, 1999; Warner, 1999). In an ongoing prospective cohort study, Atkinson et al (1998) reported that by 6

months of therapy for ALL, 64% of children had a reduction from baseline measures of BMC, and by the end of 2 years of therapy, 83% were osteopenic.

A variety of treatments used for childhood cancer can reduce peak bone mass and/or interfere with bone metabolism. Some chemotherapeutic agents, such as corticosteroids and methotrexate, appear to directly alter bone metabolism during treatment, thus reducing peak bone mass (Nysom, 1998; Hoorweg-Nijman, 1999). Alkylating agents, notably cyclophosphamide and ifosfamide, appear to alter gonadal endocrine function leading to subclinical or premature ovarian failure or Leydig cell dysfunction (Byrne, 1999; Kenney, 2001). Cranial irradiation for CNS-tumors, ALL, T-cell lymphoma, and soft tissue sarcomas can cause subclinical hypothalamic/pituitary dysfunction resulting in inadequate growth hormone secretion and/or hypogonadotropic hypogonadism (Gilsanz, 1990; Hoorweg-Nijman, 1999). Older methods of pelvic irradiation for Wilms' tumors and genitourinary soft tissue sarcomas that did not adequately protect the gonads resulted in primary gonadal dysfunction and ovarian/testicular failure. Hence, cancer treatment predisposes many survivors to bone mineral deficiency and osteopenia/osteoporosis by a direct effect on bone accretion or secondarily through pituitary-hypothalamic or gonadal dysfunction.

Reduction in peak bone mass in young adults is a significant risk factor for developing osteoporosis and subsequent fracture, and measures to prevent or reverse bone loss are important. Exercise increases bone density in obese children (Gutin, 1999) and young adults (Valdimarsson, 1999) and has recently been shown by meta-analysis (Wolff, 1999) to prevent or reverse almost 1% of bone loss per year in pre- and postmenopausal females. Long-term survivors of childhood cancer should be periodically assessed to determine risk for osteoporosis

and counseled regarding adequate calcium intake and the benefits of exercise and avoidance of smoking.

2.3.7   Risky Behaviors

The risk for each of the above diseases can be increased by risky behaviors. Alcohol intake increases the likelihood of liver decompensation in individuals with chronic HCV. Physical inactivity and obesity may increase risk for breast cancer and progression of left ventricular dysfunction and definitely increase risk for osteoporosis. Increased intensity or duration of sun exposure increases risk for melanoma and NMSC.

Despite these risks, some adult survivors practice risky behaviors. Mulhern and Tyc (1995) surveyed 110 parents of long-term survivors and 40 young adult survivors and found that both groups perceived a greater need to protect a survivor's health than what they perceived was the need for most other healthy people. Nevertheless, 47.5% of the young adults reported trying tobacco, 17.5% continued to smoke and 12.5% reported binge drinking. In an analysis of 9709 adult survivors in the Childhood Cancer Survivor Study, Emmons and colleagues reported that though survivors were less likely to smoke than the general population, 17% were still current smokers (Emmons, 2001). Survivors who had received chest radiation or anthracyclines were no less likely to smoke than other survivors. These studies underscore the need for risk counseling in survivors.

Longitudinal care that includes counseling about risky behaviors, particularly smoking, has been associated with changes of lifestyles in the general population. Risky behaviors increase frequency and severity of risk for late effects in adult survivors and, thus, periodic assessment and counseling regarding health behaviors is important.

2.4 **Concept of Longitudinal Cancer-Related Health Care**

The intent of describing these six late effects is to emphasize the potential benefits of proactive and anticipatory periodic evaluation and counseling to reduce risk and minimize progression of disease, rather than reacting to disease at it occurs. Optimum care of childhood cancer survivors should include the following key components:

- longitudinal care that is considered a continuum from cancer diagnosis to eventual death, regardless of age;

- continuity of care consisting of a partnership between the survivor and a single health care provider who can coordinate necessary services;

- comprehensive, anticipatory, proactive care that includes a systematic plan of prevention and surveillance;

- multi-disciplinary team approach with communication between the primary health care provider, specialists of pediatric and adult medicine, and allied/ancillary service providers;

- health care of the whole person, not a specific disease or organ system, that includes the individual's family and his cultural and spiritual values;

- sensitivity to the issues of the cancer experience, including expressed and unexpressed fears of the survivor and his family/spouse.

Thus, the ideal plan to optimize the health and quality of life of a childhood cancer survivor should be longitudinal, comprehensive, and preventive in its approach, based on continuous and coordinated cancer-related care by a single health care provider who uses a multi-disciplinary team to address the needs of the person within the context of the family.

3.0   CURRENT STATUS OF LONGITUDINAL CANCER-RELATED HEALTH

CARE OF ADULT SURVIVORS IN THE UNITED STATES

To understand the need for longitudinal cancer-related health care of adult survivors of childhood cancer, it is important to assess the current status of follow-up of this vulnerable population.

3.1   Current Estimates of Cancer-Related Care of Adult Survivors

It is likely that only a minority of adult survivors seek and receive cancer-related health care. In the CCSS analysis of 9434 adult ($\geq$ 18 years of age) survivors of childhood cancer, only 42% reported a health care visit in the previous two years that was related to their previous cancer treatment (Oeffinger, 2002a). This percent decreased with age, from 48.6% in 18-19 years olds to 37.8% in those 35 years or older ($p < 0.01$). In multivariate modeling, factors associated with lack of cancer-related follow-up, in addition to increasing age, included male gender (OR 1.18; 95% CI 1.06-1.30), college education (OR, 1.19; 95% CI 1.06, 1.34), lack of medical insurance (OR 1.72; 95% CI 1.47, 2.00), and lack of concern about future health (OR 1.45; 95% CI 1.29, 1.64). Race and ethnicity were not associated with lack of cancer-related follow-up.

In the preliminary results of the RWJ Barriers study, only 26% (114/441) adult survivors reported a health care visit in the previous two years that they thought was related to their previous cancer treatment. Multivariate analysis will be performed when the dataset is completed. It should be noted that both of these studies used self-report of the survivors and that some cancer-related health care may have been provided without the knowledge or understanding of the survivor. Also, some may have sought such care but could not find a provider.

3.2   Childhood Cancer Centers and Long-Term Follow-up Programs

In the 1970-80s, survival rates increased, the survivor population grew, and the potential for late effects were recognized, leading to a gradual shift that includes not only the paradigm of cancer-free survival but also the long-term health and quality of life of survivors. As a result of this paradigm shift, many cancer centers have developed "long-term follow-up" programs to educate survivors and their families about treatment-related risks and to identify late effects. In 1997, 53% of the institutions of Children's Cancer Group (CCG) and the Pediatric Oncology Group (POG) institutions had some type of long-term follow-up program for childhood cancer survivors under the age of 18 (Oeffinger, 1998). However, most of these programs focused on acute problems and recurrence of disease. In 1999, each of the CCG and POG institutions were contacted to determine the type of services available for survivors (personal communication, Nancy Keene). The coordinator of all long-term follow-up programs were identified and asked if the program included: (1) at least a single physician interested in late effects; (2) a nurse or nurse practitioner coordinator; (3) a dedicated time and place; (4) at least 2 follow-up clinics a month; (5) comprehensive care and screening for late effects based on the survivor's treatment; (6) referral to appropriate specialists; and (7) wellness education. Only 26 programs in the U.S. fulfilled all of these criteria.

Few survivors entering young adulthood maintain contact with the treating cancer center. In the CCSS analysis, only 31% of survivors who were 18-19 years of age at time of interview had been seen by a health care provider at a childhood cancer center in the previous two years (Oeffinger, 2002a). This percent steadily decreased with age of the survivor, to 17% of those who were 35 years or older (p<0.001). Sociodemographic factors were not particularly important predictors of whether or not an adult survivor had been seen at a cancer center. In multivariate

analysis, males, white, non-Hispanic, and college educated survivors were less likely to have follow-up at a childhood cancer center. Similarly, preliminary results of the RWJ Barriers study found that although 32% (143/441) of adult survivors reported a check up at a cancer center in the previous four years, this proportion decreased with age of survivor from 61% in 18-24 year olds to 16% of survivors 35 years or older (p<0.001). Only 5% of respondents, regardless of age, had been seen in a children's cancer center in the previous two years.

These numbers are not particularly surprising. Adult survivors do not "fit" in pediatric rooms and are constantly reminded of their previous cancer when being seen in the cancer center. Most pediatricians feel uncomfortable managing health problems of young adults and most children's hospitals discourage admission of patients over the age of 21. This population is relatively mobile and often moves a significant distance from the cancer center. In response to the growing recognition that many survivors were being "lost to follow-up", multi-disciplinary transition programs, combining the expertise of pediatric oncologists with primary care providers experienced in the needs of adult patients, were recommended as a mechanism for long-term follow-up of adolescent and young adult survivors of childhood cancer (Bleyer, 1993; Rosen, 1993; Konsler, 1993; Meadows, 1993; MacLean, 1996).

Below is a brief review of the current status of transition or programs for adult survivors of childhood cancer. There are three primary models in current use: (1) continued follow-up of adult survivors at the childhood cancer center; (2) one-time evaluation of adult survivors at a childhood cancer center with a summary provided to the survivor and their primary care physician; and (3) multi-disciplinary collaborative efforts between pediatric oncologists and health care providers experienced with adult health problems.

3.2.1   Follow-up of Adult Survivors in Childhood Cancer Centers

A few long-term follow-up programs, such as Memorial Sloan Kettering, St. Jude Children's Research Hospital, Roswell Park Memorial Institute, and Los Angeles Children's Hospital, follow survivors into their young adulthood, generally to around age 25-30, but sometimes older. These programs are focused on educating survivors about long-term risks and delivering preventive health care. Though these programs are committed to communicating with other health care providers, lack of a systematic plan to transition care generally results in older survivors becoming lost to follow-up.

3.2.2   One-Time Evaluations of Adult Survivors

Several years ago, the Children's Hospital of Philadelphia (CHOP) developed a novel and successful transition program. Adult survivors, generally between the ages of 18 and 25 years, are seen for a one-time evaluation by a pediatric oncology nurse practitioner. At this visit, potential risks based on previous treatments are discussed and a medical summary with recommendations is provided to the survivor and sent to their primary care physician.

3.2.3   Multi-disciplinary Programs in Adult Settings

Duke Medical Center has a cancer center including both pediatric and adult oncologists. Childhood cancer survivors are transitioned to the adult oncologist at or around the age of 18 for long-term follow-up. University of Pennsylvania Medical Center has recently developed a similar format in conjunction with CHOP, in which young adult survivors of childhood, adolescent, and young adult cancers are followed in an adult cancer center.

In 1994, the Division of Pediatric Hematology Oncology and the Department of Family Practice and Community Medicine at the University of Texas Southwestern Medical Center developed a multi-disciplinary program for young adult survivors, called the After the Cancer

Experience (ACE) Young Adult Program (Oeffinger, 2000a). In mid to late adolescence, survivors are transitioned from the ACE Program at Children's Medical Center of Dallas to the Family Practice clinic. A pediatric oncology nurse practitioner coordinates both the ACE and ACE Young Adult Programs, providing a bridge of continuity between the two institutions. The author, a family physician, directs the ACE Young Adult Program. Protocols for screening and surveillance were developed by a multi-disciplinary team and are updated as needed. Adult survivors are seen on a periodic basis depending on current health problems and risks based upon treatment, lifestyle, and genetics, and a formal database with grading of late effects is maintained for all survivor visits. A medical summary of cancer diagnosis and treatment, written in lay terms, is provided to all survivors in the program. At each follow-up visit, a two-page summary of potential risks and recommendations is provided to survivors. Surveillance and screening tests are conducted at UT Southwestern or coordinated through the survivor's health management organization. A multi-disciplinary network of pediatric and adult specialists, including cardiologists, hepatologists, reproductive endocrinologists, and psychologists, has been developed for referrals.

In the past year, Children's Memorial Hospital of Chicago and the Division of General Internal Medicine at Northwestern University Medical Center adopted this model and have developed a similar program.

3.3   Follow-up of Adult Survivors by Primary Care Physicians

Many, if not most, adult survivors seek a primary care physician for some aspect of their health care. In the RWJ Barriers study, 89% of respondents (388/441) reported having a regular primary care physician or site of care. However, only 30% (130/441) had ever seen a primary care physician for a problem they thought was related to their cancer. While 36% felt that a

primary care physician could usually handle a problem related to the previous cancer treatment, 28% did not. Of the 110 survivors who felt they had a problem in the previous two years potentially related to their cancer treatment, 51% saw a primary care physician as the first point of contact while 40% saw another type of health care provider and 9% did not seek health care.

It should not be surprising that primary care physicians are not particularly aware of the risks of this population. Nationally recommended curricula for instruction of medical students and primary care residents do not include the topic of health care of childhood cancer survivors. Little has been written in U.S. or Canadian primary care-based journals (Hawkins, 1989; Grossi 1998; Oeffinger, 2000b; Oeffinger, 2000c) or general, non-cancer specific journals (Meadows, 1989; Neglia, 1991) regarding childhood cancer survivors and their long-term health care. None of the major primary care textbooks contain a section on providing health care for childhood cancer survivors. There has not been a national effort to link childhood cancer centers with primary care physicians in the transitioning process. Also, methods to assist primary care physicians navigate the complexities of the cancer center to find and communicate with the individual(s) involved in long-term care of survivors has not been addressed. Compounding these issues, a typical family physician's practice only includes about 2 to 3 adult survivors (Oeffinger, 2000b). Realizing that these survivors are heterogeneous, with a variety of different cancers diagnosed at different age periods or treatment eras, and that the recommendations for screening and surveillance are constantly evolving, it is understandable that primary care provider-initiated discussions regarding appropriate cancer follow-up may be infrequent.

3.4   Learning from Efforts with "Children with Special Health Care Needs"

Much can be learned through past and current efforts related to children with special health care needs. Optimum care of this population, which includes children with cerebral palsy,

cystic fibrosis, diabetes, and congenital heart disease, requires the same attention to coordinated and continuous health care. Needless to say, childhood cancer survivors who develop chronic health problems during treatment or later in childhood/adolescence are part of this group. The concept of a "medical home" has become the cornerstone of care for children with special health care needs and was officially adopted by the American Academy of Pediatrics in 1994. A medical home is defined as a source of ongoing, comprehensive, and family-centered care in the child's community (U.S. Department of Health and Human Services, 2001). Through collaborative efforts of the Maternal and Child Health Bureau, Family Voices, the March of Dimes, the American Academy of Pediatrics, and others, a 10-year action plan has been developed with six goals to promote the health of this population:

1. Families of children with special health care needs will partner in decision making at all levels and will be satisfied with the services they receive.

2. All children with special health care needs will receive coordinated, ongoing, comprehensive care within a medical home.

3. All families of children with special health care needs will have adequate private and/or public insurance to pay for the services they need.

4. All children will be screened early and continuously for special health care needs.

5. Community-based service systems will be organized so families can use them easily.

6. All youth with special health care needs will receive the services necessary to make transitions to all aspects of adult life, including adult health care, work, and independence.

Reflecting goal #6, a number of transition programs have been developed in the recent past for adolescents with special health care needs. The Healthy and Ready to Work (HRTW)

Transition Work Group, supported through the Health Resources and Services Administration, has developed a set of recommendations for Healthy People 2010 to address the transition of youth with special health care needs (U.S. Department of Health and Human Services, 2000) and have compiled an annotated bibliography (Reiss, 2000).

Problems of transition and subsequent adult care of children with special health care needs are similar to cancer survivors:

- There are few coordinated services available to assist in the transition process.

- Affordable and accessible health care is often problematic, with a large percentage becoming under or uninsured in their adult years.

- Adult health care providers generally lack training dealing with young adults with chronic health problems developed in childhood.

- Pediatric specialists may resist transition because of fear of loss of continuity of care of their patients.

- Patients may resist transition because of strong and trusting bonds developed with their pediatric specialist.

There are, however, some significant differences between most cancer survivors and children with special health care needs. Notably, the chronic disease causing special needs generally persists into adulthood, whereas the cancer is cured. Further, the long-term health care problems of the adolescent or young adult with a childhood chronic illness is a result of the illness. In contrast, the health care problems of cancer survivors are usually a consequence of their treatment. There is limited experience in how these "toxic" treatments will affect the aging process of normal tissue, and thus, the long-term needs are much less defined for this population. Perhaps most importantly, though, most survivors who experience health problems in adulthood

will be relatively asymptomatic during their childhood and adolescent years. The problems and issues of enhancing longitudinal health care for asymptomatic, at-risk patient populations are different than those with patients with continuing symptomatic chronic health problems.

4.0   MODELS TO PREDICT AND EXPLAIN HEALTH BEHAVIORS

Thus far, this paper has described the potential health problems of a vulnerable, at-risk, and growing population, their need for longitudinal cancer-related health care, and the current inadequate status of survivor care. Before developing interventions to improve the long-term health care of survivors, it is essential that potential barriers and enablers be assessed. Survivor, provider, and health care system-related issues are complex and interrelated. A theoretical framework is necessary to begin disentangling these complexities and to provide a foundation for developing interventions intended to enhance and facilitate optimum health care of adult survivors.

Prior to discussing a proposed framework, a brief synopsis is needed of the models that have been developed to explain and predict health behaviors, such as seeking preventive care, in the general population. In their seminal work, Kasl and Cobb (1966) defined health behavior as the following:

Preventive health behavior - any activity undertaken by an individual who believes himself to be healthy, for the purpose of preventing or detecting illness in an asymptomatic state.

Illness behavior - any activity undertaken by an individual who perceives himself to be ill, to define the state of his health, and to discover a suitable remedy.

<u>Sick-role behavior</u> - any activity undertaken by an individual who considers himself ill, for the purpose of getting well. It includes receiving treatment by medical providers, generally involves a whole range of dependent behaviors, and leads to some degree of exemption of one's usual responsibilities.

To predict and explain the likelihood that an asymptomatic individual would seek preventive health care or practice a healthy or preventive behavior, several models have been developed over the past three decades. Simplistically, these models can be grouped into several categories, including "continuum" and "stage" models. Continuum models, such as the health belief model (Rosenstock, 1974a; Rosenstock, 1974b; Becker, 1974), the behavioral model of utilization (Andersen, 1995, Phillips, 1998), the theory of reasoned action (Fishbein, 1975; Ajzen, 1980), multi-attribute utility model (Beach, 1976), the subjective expected utility theory (Edwards, 1954), the protection motivation theory (Maddux, 1983), and the theory of planned behavior (Ajzen, 1986) can be used to identify variables that influence action. Stage models, including the transtheoretical model (Prochaska, 1983) and the precaution adoption process model (Weinstein, 1988) assume that factors affecting behavioral change vary from stage to stage.

Three well-recognized and broad-based models are particularly suitable to this exploratory phase of study of the factors necessary for longitudinal cancer-related health care of survivors. The health belief model (Rosenstock, 1974a; Rosenstock, 1974b; Becker, 1974) postulates that in order for an individual to take action to avoid a disease, he would need to believe that he was personally susceptible to it, that the occurrence of the disease would have at least moderate severity on some component on his life, and that taking a preventive action would be beneficial. As the health belief model evolved, six primary domains were recognized as influential in health behavior: (1) general health motivation (threat of disease, control over health

matters, attitude towards medical authority, and general health concern); (2) perceived susceptibility or vulnerability to disease; (3) perceived severity or seriousness of disease; (4) perceived benefits of the preventive action; (5) perceived barriers to action; and (6) cues to action (advice of others, mass media).

Early in the development of the health belief model, "control of one's health measures" was considered to be a measure of self-efficacy, or a situation-specific belief about one's ability in a specific setting. As the multidimensional health locus of control model was developed and evolved, the concept of self-efficacy was replaced by locus of control (Rosenstock, 1988) and many include it as a separate domain when using the health belief model. Derived from the foundations of the social learning theories of Rotter and Bandura, multidimensional health locus of control refers to a person's beliefs regarding the source(s) of control over one's health (Wallston, 1976a; Wallston, 1976b; Wallston, 1978a; Wallston, 1978b). Health locus of control beliefs are measured along three dimensions: (1) belief in self-control (internal) over health action; (2) belief in chance health outcomes; and (3) belief in control by "powerful" others.

In addition to the concepts of the health belief and health locus of control models, the behavioral model of utilization (Andersen, 1995; Phillips, 1998) emphasizes the importance of enabling resources of the individual, the environment, and the health care provider. Enabling resources related to the individual and the family include income, health insurance, and distance to health care. Environmental variables include characteristics of the health care delivery system, external environment, and community-related enabling resources, such as availability of health personnel to deliver care. Provider-related variables include having a regular source of care and demographic characteristics of the provider as they may relate to the patient.

5.0 BARRIERS AND ENABLERS TO LONGITUDINAL CANCER-RELATED HEALTH CARE OF ADULT SURVIVORS

Adapted from these three models, a theoretical framework to examine factors related to the survivor, the health care provider, and the health care system and to investigate relationships between these domains is proposed in Figure 1. Barriers and enablers within each of these three domains are described. Relevant literature is discussed and "unstudied" questions pertinent to survivorship are emphasized.

5.1 Survivor-Related Barriers and Enablers

5.1.1 Cancer Experience

Understanding and predicting health behaviors, such as seeking longitudinal health care, is complicated in the survivor by the cancer experience. This concept is not a simple reflection of a disease that was treated, but rather a process through which the illness was interpreted by the survivor. As stated by Kleinman (1978), "Illness is culturally shaped in the sense that how we perceive, experience, and cope with disease is based on our explanations of sickness, explanations specific to systems of meaning we employ." Further, the cancer experience is different than the illness experience with a chronic health condition. The cancer experience can be thought of as an illness experience in which the cancer collides with one's health, resulting in extreme emotional swings, conflicting desires to fight or run, and heightened fears and joys. After the celebration of the "cure", there is the inevitable aftermath of sorting through continued fears and concerns about the unknown and dealing with the sequelae of treatment. Thus, the cancer experience is a process that extends throughout a lifetime, a looking glass through which all future health and illness behaviors of the survivor must be interpreted.

Psychological Factors

Any assessment of factors related to the likelihood that an "asymptomatic" survivor will seek longitudinal health care must consider the psychological stresses that result or are modified through the cancer experience. These include the perception of being well versus ill, use of confrontation/avoidance as a coping mechanism, experiencing post-traumatic stress or growth, the feelings of invincibility and vulnerability, and trust versus mistrust of doctors and the medical system.

As noted earlier, Kasl and Cobb (1966) describe positive health behaviors arising from whether one perceives himself to be "healthy" and intent upon maintaining health or to be "ill" and intent on defining and treating the illness. However, cancer survivors are cast somewhere in between, having survived the cancer but facing lifelong health risks related to the cancer treatment. Some survivors view themselves as "well" with no chance for residual problems and avoid preventive cancer-related follow-up, because that chapter in life is over. Others may feel damaged by the unknown effects of radiation and chemotherapy and think of themselves as sick or ill, constantly worrying that a sore throat is a return of the cancer. Many survivors vacillate between these extremes.

Van Dongen-Melman and colleagues (1998) conducted in-depth interviews with 87 parents of survivors who were a median of four years post treatment. A confrontation-avoidance strategy was a primary coping process that emerged. Confrontation strategies included seeking information about the disease, seeking help and assistance, and accepting the disease and its late effects. In contrast, avoidance was characterized by distancing oneself from the disease, striving towards normality, and avoiding information about the disease and its long-term consequences. Bauld et al (1998) similarly found that survivors have a tendency to employ avoidance strategies.

A substantial subset of survivors and their parents may experience post-traumatic stress disorder (Stuber, 1996; Stuber, 1997; Kazak, 1998). Uncertainty and loneliness persist long after the completion of treatment in many parents of survivors (Comaroff, 1981; Van Dongen-Melman, 1995). Anxiety and fears related to clinic visits combined with a sense that one does not control his health may contribute to avoidance of follow-up and an increase in unhealthy behaviors. Feelings of invincibility and vulnerability are common in adolescence and young adulthood in the general population. These emotions may be accentuated through the cancer experience. Having conquered cancer, some survivors feel that they are invincible and practice risky behaviors such as smoking (Tyc, 1997). In contrast, some will feel quite vulnerable and may feel that they have no control over their health.

The concept of trust-distrust has not been studied in survivors of childhood cancer. If one has a negative attitude towards health authorities or does not trust the health care provider, he is less likely to seek preventive services. American ethnic minorities often distrust the health care system (Roberson, 1994; Gorelick, 1998; Bell, 1999). Telephone surveys of African Americans, Hispanics, and Native Americans showed a common thread of "mistrust of white people" and the medical care team. Harris et al (1996) reported that mistrust of the medical system was one of the four major barriers to participation in clinical trials of African Americans. African American adults interviewed in focus groups described a distrust of the medical community as a prominent barrier to participation in clinical research (Corbie-Smith, 1999). Die Trill and Kovalcik (1997) described cross-cultural conflicts between family and health-care providers that may arise when there are differing beliefs about the frequency of medical procedures and the need for medical follow-up. If a survivor/family had a negative experience during cancer treatment, such that they

felt that questions were not adequately answered or that feelings/fears of the patient and family were not taken into account, a mistrust of the medical institution could arise.

Family and cultural myths or superstitions likely affect the health behaviors of some survivors. A young adult female followed in our long-term program had recurrent somatic complaints. With further discussion, she explained that she feared that her adolescent cancer had been given to her by God as a punishment for allowing her stepfather to sexually abuse her. She had never shared this fear with anyone. This is not an unusual conclusion about the cause of cancer. Wardlow and Curry (1996) illustrate this process in their description of the beliefs about breast cancer and mammograms among low-income urban black women in Atlanta. Some women associated breast cancer with domestic violence, believing that bruises resulting from physical abuse, which are not reported or given medical attention, can later turn into cancer.

Further study is needed to determine how these psychological factors and coping mechanisms influence the development of the health beliefs of a survivor and the subsequent practice of preventive or risky behaviors.

Knowledge of Risks

A significant proportion of survivors are likely unaware of their risks. This is, in part, understandable. From the 1960's to the 1980's, as the survival rates were increasing, there was not the current recognition of late effects. Often, parents of children who made it through their cancer were told that they had "beat the odds" and were instructed to follow-up in twenty years; in other words, when the survivor had a problem. As the prevalence of late effects began to surface, long-term follow-up programs were developed. However, many institutions did not/do not have such programs and care is focused on the immediate acute care needs or assessing for recurrence of the cancer. Illustrating this acute care focus, only 19% (83/441) of the respondents

to the RWJ Barriers study reported having a copy of a summary of their cancer type and previous treatment, and these were generally in medical rather than lay terms. Then, inevitably, there are the parents who listened to the discussions regarding the potential for late effects, but later did not transmit this information to their child as he grew into adulthood. To date, there is no data regarding the extent to which this may or may not be a problem. Illustrating experiences common to many, one survivor stated,

"According to doctors, my heart failure was most likely caused by adding stress to a heart that was already weak from chemotherapy treatments. Although I remember being told that some of my treatments could cause heart damage, kidney failure, or bladder damage, I don't recall being told to monitor heart status after being released from treatment and especially during pregnancy. I am being compensated with medicines now, however, my doctors feel that I will probably need a heart transplant in the next two years."

Or another who said,

"I am a survivor of Hodgkin's Disease diagnosed in 1971 at age 16. My mother died of HD when I was 4. I was treated with high dose radiation only. I do not know my stage or level of rads. I have no documentation from [treating institution]. I asked for it a couple of years ago and they said it was in storage somewhere."

Thus, lack of knowledge of risks and the potential for late effects is likely an important barrier to survivors deciding to seek periodic preventive health care.

5.1.2   Core Health Beliefs

The three core components of one's health beliefs include general motivation towards health, perceived susceptibility to disease (or in this case, to late effects), and perceived seriousness of disease/late effects. Lack of motivation or perception of susceptibility or seriousness of late effects will result in inadequate follow-up. How the cancer experience affects the development of these three core beliefs has not been studied.

5.1.3 Internal Modifying Factors

Innate sociodemographic factors such as age, gender, and race/ethnicity are often associated with health and preventive care utilization. These may be modified by income and education. In the CCSS analysis, when adjusted for socioeconomic factors, males were less likely to have general medical contact, a general physical examination, or a cancer-related visit in comparison with females (Oeffinger, 2002a). Adjusted for gender, income, and age, ethnic minority survivors were less likely to have general medical contact, but more likely to have cancer center visits. These factors may be further modified by cultural and spiritual beliefs and social support structures that affect the survivor's response to positive or negative peer pressure.

5.1.4 External Modifying Factors

Subjective Norms

Family, friends, and employers may influence a survivor's decision to seek longitudinal health care or practice healthy behaviors. The interaction of these subjective norm groups and the survivor has not been explored and is likely complex. Take for example the mother who brings her young adult son/survivor to a physician for a check-up, almost "pulling him in by the ear". The mother has gone through the trauma of the cancer diagnosis and treatment and has a desire to know that "all is ok". As the bond between the mother and son begins to weaken, the survivor may avoid the previous preventive health-seeking behavior, equating it as a product of his previous dependence upon his mother.

Similarly, how does a survivor interact with his or her peers? Do survivors have a desire to "get on with life" and align themselves with their peers and their behavior? Since their peers don't seek preventive health care, why should the survivor? If they smoke, why shouldn't the survivor? Do peer norms recognize the six-fold increase in the prevalence of lung cancer in

survivors who smoke and were previously treated with chest or mantle radiation? It is doubtful

that peers and even spouses recognize the increased risk that survivors face, and so may instead

encourage or fail to discourage the adoption of a risky behavior.

Cues to Action

External cues, such as a newspaper article, a television report, or a cancer survivor

newsletter, may serve to inform the survivor regarding risks and either positively or negatively

influence the preventive health seeking behavior of a survivor.

5.1.5   *Health Locus of Control*

If the survivor is strongly influenced by the belief in chance outcomes of health, he may

be less motivated to be proactive regarding health. Greenberg (1989) suggested that survivors of

childhood cancer may have a more external locus of control, or a belief that one is not in control

of his health. Whether or not the cancer experience influences the development of health locus of

control and if survivors are different from the general population is not known. Further, the

relative importance of the locus of control in moving from an intended to a successful health

action has not been studied.

5.2   Health Care Provider-Related Barriers and Enablers

5.2.1   *Core Preventive Beliefs of Health Care Provider*

The demographics of the health care provider have received recent attention in the

provision of preventive health care services in the general population and may be important in

the care of survivors. Younger, more recently trained physicians may be more preventive-minded

than those trained many years ago. Gender differences between provider and survivor may also

lead to different preventive services offered.

5.2.2   Knowledge of Risks

As noted above, there is little in primary care training curricula, journals, or textbooks discussing the risks of this population, and so it is likely that there is a knowledge gap regarding the health care needs of adult survivors. The mother of one survivor wrote,

"If my son, who is now 21, remains in this geographical area and the clinic

at his children's hospital does not improve its services, I honestly do not

think that he will be able to visit a doctor who will be able to handle

specific late effects that he might experience. In my opinion, he should

always have his care directed by a person who specializes in late effects.

Our current PCP barely knew the treatment for leukemia, for heaven's sake,

and did not bother to look it up before my son went to him for a minor

complaint while he was still on treatment."

The training and literature base is no better for specialists in adult medicine, including oncologists, cardiologists, and obstetricians. Because this area of research is continually changing, even many pediatric oncologists who are not involved in regular follow-up of childhood cancer survivors are less likely to be aware of the extent of risks. As described by a survivor,

"Many patients attempt getting long-term care via oncologists. Yet it seems that oncologists have

enough to do to keep up with current acute care issues, and are not interested in long-term care –

in particular where it involves the psychologically difficult recognition that long-term effects are

often treatment effects, and that the science of what to do is murky."

5.2.3   Attitudes Towards Cancer Survivors

Health care providers may interact with young adult survivors differently than other patients with chronic health care needs. Either consciously or unconsciously, some may treat the survivor in a way that implies that the cancer experience is long over, to see the disease as

successfully treated. And so when a survivor comes in for a check-up or complaining of vague

symptoms, physicians may sometimes minimize the likelihood of current or future problems.

Illustrative remarks by two survivors were,

> "I have been disregarded by many doctors. One doctor said to me that doctors don't know how to
>
> deal with a survivor such as myself"

and

> "I feel all physicians should provide and encourage clear instructions for preventative health
>
> measures. Most I've met seem only concerned with treating the illness only when it arises."

The opposite is equally important, as expressed by a survivor who wrote,

> "I believe many doctors simply do not have the experience needed to address serious illnesses. If
>
> they find out you have had cancer, a red flag comes out and clouds his or her judgment towards
>
> the current health issue. My health is great. I feel like a marked man when I do have a slight or
>
> 'normal' health problem."

5.2.4 Organizational Structure of Practice

Even when a health care provider has the knowledge and is interested in assisting a

survivor to develop a plan for follow-up, organizational barriers of practice, such as lack of time,

may negatively influence the likelihood of optimal cancer-related care. As stated by a survivor,

> "They always seem to be running out the door. I only get results when I am pushy and forceful
>
> with my requests and concerns. Most information I have heard is through other people rather than
>
> my own doctors. They never seem to be informative with me."

This is a commonly reported barrier in studies in the general population assessing the prevalence

of cancer screening tests and counseling about risky behaviors.

To effectively provide longitudinal cancer-related health care for survivors, it is

necessary to develop a network of knowledgeable and available consultants and service

providers, as noted by a survivor and the mother of a survivor,

"What do I think would be a good model for follow-up care for survivors? Make sure there is a doctor in charge who can orchestrate all of the other specialists that the patient will need in the future."

and

"My daughter and I have been stumbling blindly trying to find someone to help her with her many deficits. She needs a good ENT, oncologist, neurologist, psychologist, PT and OT, sign language teacher and special ed teacher ECT. We need a coordinator, that's what a survivor needs, a good COORDINATOR. Also some counseling for the siblings. It is a family illness not just one person's."

With the stressful, time-constrained practice of medicine, this may be a significant impediment to the delivery of longitudinal cancer-related health care.

5.3   Health Care System-Related Barriers and Enablers

5.3.1   Health Care Policies Regarding Survivorship

In the past decade, the National Institutes of Health have embraced the concept of survivorship and the need for further study with the creation of the Office of Cancer Survivorship and work of the National Cancer Policy Board through the Institute of Medicine. The literature base and number of studies funded investigating the health care needs of this population have grown significantly, but much is still needed. There are still too many unanswered questions and critical gaps in the understanding of methods to optimally care for this population.

A notable gap is the lack of any evidence-based recommendations for type and frequency of surveillance and screening tests, such as echocardiography and mammography. Each long-term follow-up program has developed institution-specific protocols, but these are generally based upon consensus. Lacking are rigorous studies to assess the cost and benefit of testing, both in terms of reduced morbidity or mortality and in quality of life. Even tests that are universally

recommended, such as a complete blood count in survivors who received an epipodophyllotoxin, have not been studied to determine optimum frequency and duration of testing. At what time is it appropriate to stop checking yearly blood counts? Only through national policy leading to an increase in funding mechanisms can these questions be addressed.

5.3.2 Health Care System

The U.S. health care system is complex and ever changing. One of the greatest crises in the general population is the difficulty in maintaining a single source of care because of changing insurance plans. This problem is an even greater barrier to optimal longitudinal health care of adult survivors. Having to "re-educate" each new health care provider can be frustrating, even for the most persistent of survivors. Unfortunately, many survivors, including those from lower socioeconomic backgrounds, those with cognitive dysfunction from previous therapy, and those who culturally find it difficult to navigate the system, will become disenfranchised and essentially lost to follow-up until symptomatic disease occurs.

5.3.3 Health/Medical Insurance

It is rare for medical insurance to be affordable to the self-employed survivor or one who works in a small company. Needless to say, under and uninsured survivors will face significant impediments to timely and appropriate longitudinal care. Medical insurance companies are even more likely to react in the extremes regarding the long-term risks of adult survivors. More often than not, a cancer history can be a cause for discrimination, regardless of treatment. At the other extreme, insurance companies are likely unaware of the screening needs for younger populations, and frequently deny tests such as a mammogram for thirty-year old females who was treated with mantle radiation or bone densitometry for a thirty-five year old with premature ovarian failure secondary to chemotherapy.

6.0   SUMMARY AND POLICY/RESEARCH RECOMMENDATIONS

In summary, adult survivors of childhood cancer are a growing, at-risk population with health care needs that are not being met by the current system. Cancer centers and pediatric oncologists do not follow most adult survivors. Survivors will usually have contact with a primary care physician, most of whom are unfamiliar with the risks of this population. Navigating through the complexities of the health care system is difficult, even for the persistent and savvy survivor. Hence, the current status of cancer-related health care provided to adult survivors of childhood cancer is dismal. The choice, then, is to continue in this haphazard fashion and witness the devastation of preventable or modifiable late effects as our survivors age or to develop a cohesive national plan with the necessary resources to facilitate optimal health care delivery to survivors, with the intent of maximizing health and quality of life. To this end, one policy and three focuses of research are critical.

6.1   National Health Care Policy for Adult Survivors of Childhood Cancer

Change will not occur without national policy that highlights the problem, facilitates the collaboration of involved parties, and provides the necessary resources to develop and implement an action plan. The involved parties include federal policy makers, childhood cancer specialists, health care providers experienced in long-term follow-up of survivors, primary care physicians, survivor and patient advocacy groups, and, most notably, survivors and their families.

6.2   Evidence-Based Guidelines for Screening and Surveillance

Funding must be provided for rigorous and well-designed studies to assess and compare different strategies of surveillance and prevention needed to develop evidence-based guidelines for longitudinal care. Appropriate timing and frequency of testing in asymptomatic survivors should be evaluated. Until then, guidelines will remain an effort of consensus and fall prey to

unexamined tradition, increasing the cost of care of this population while failing to improve health outcomes.

6.3   Develop Interventions to Minimize Barriers and Maximize Enablers

Determination of survivor, provider, and medical system-related factors involved in the longitudinal cancer-related care of survivors will provide a foundation for developing and testing interventions to facilitate and enhance care. A multi-method approach is needed, exploring the depth and breadth of issues with qualitative methodologies and generalizing to the wider population of cancer survivors with more quantitative approaches.

6.4   Models for Center of Care of the Survivor

Models for providing longitudinal cancer-related health care for adult survivors need to be further developed and compared. In the long run, there are three viable centers for care for adult survivors, each needing an infusion of resources to be successful. Each of these models has distinct advantages and disadvantages, and thus a hybrid of models may be necessary.

First, longitudinal care can be provided through a comprehensive program in an academic health center that partners the childhood cancer center with academic primary care physicians. This route facilitates the continuum of care of the survivor within a familiar set of institutions and joins the expertise of those involved in the care of childhood cancer with those experienced in prevention and coordination of care. Further, it provides the necessary ancillary resources generally found in a medical center. Finally, this model can benefit from the integration of patient care, education, and research. However, it must be recognized that most survivors do not live near an academic health center and may prefer instead to be followed in their neighborhood near home or work.

Second, care can be provided through a primary care provider's office. To be effective, this will require development of an ongoing, two-way relationship between the primary care provider and the childhood cancer center. Methods to enhance educating and updating primary care physicians about recommended guidelines and the evolving knowledge base of late effects is critical. Resources to assist with coordination of the different health care services are also important. Learning from those involved in the establishment of "medical homes" and adapting their tenets and concepts would be prudent.

A third novel, and as yet unexplored, model would be work directly through the survivor, linking him to a nationally supported center that would be responsible for facilitating health care needs. Distance networking, facilitated through rapidly advancing Internet and telecommunication technologies, provides the foundation for this model. The center would have four components: a national cancer registry, care coordinators, a repository of information, and a decision-making board. Upon diagnosis of cancer, children would be entered in the registry. When therapy is completed, the cancer center will provide a summary of treatment and complications. Care coordinators would develop a survivor-specific plan of action, assess health care resources in the survivor's environment, and orchestrate care with appropriate health care providers located near the survivor. The repository would include guidelines for screening and surveillance, current literature about survivor-related health care problems and needs, and patient and physician education materials. The board, including health care providers and survivors, would garner necessary resources to facilitate and enhance the process.

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**Figure 1. Theoretical Model of Potential Barriers and Enablers to the Longitudinal
Cancer-Related Health Care of Adult Survivors of Childhood Cancer**