Nutrition-Related Disease Risk in Pediatric Cancer Survivors

Thesis

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By

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Abstract

The prevalence of overweight and obesity and other nutritionally related disease development among pediatric cancer survivors is well known to be above national norms. This is a retrospective cohort study designed to investigate the relationship between childhood cancer survivorship and nutritionally related disease development. The objective of this study was to gather data from existing pediatric cancer survivors in order to study disease development in relation to the type of cancer the patient had, the course of treatment, and to nutrition care that patient may have received. Seventy five subjects, with diagnoses of ALL, AML, Burkitt’s lymphoma, neuroblastoma, or Wilm’s tumor, 2 or more years into survivorship, and meeting the other stated criteria, were admitted to the study. Body mass index (BMI) was calculated for each subject using the most recent height and weight, and prevalence of overweight or obesity was established using the current CDC growth charts and guidelines. Of the 75 subjects in the study, 30 (40%) were found to be overweight or obese overall, with relatively equal distribution in those categories (16 overweight vs. 14 obese). When separating subjects into their respective diagnosis categories, the rate of overweight and obesity was higher than the overall number in all groups except the neuroblastoma group (ALL 42%, AML 57%, Burkitt’s 50%, Wilm’s 56% vs. Neuroblastoma 21%). Subject data was analyzed for development
of nutritionally related diseases since diagnosis of cancer. Forty nine (65%) were found to have developed these types of diseases including overweight/obesity, osteoporosis, restrictive airway disease, hypothyroidism, hypertension, gallbladder disease, hypercholesterolemia, and anemia. When overweight and obesity were excluded, 20 subjects (27%) remained. Forty seven (63%) of the 75 total subjects in the study had some type of nutrition education, 45 (60%) received nutrition intervention, and 25 (33%) received nutrition support. In the overweight and obese group (30 subjects), 20 (67%) received nutrition education, 19 (63%) received nutrition intervention, and 8 (27%) received nutrition support. When the overweight and obese subject data was removed from the overall sample, 45 subjects remained and 27 (60%) were found to have received nutrition education, 26 (58%) had nutrition intervention, and 17 (38%) had nutrition support during or after treatment. The results of this study corroborate with the results of previous studies. The rates of overweight and obesity, along with other nutritionally related diseases, are high in this sample even though most subjects are 5 years post-therapy or less. The nutrition education and intervention provided to the overweight and obese group was slightly higher than those who were not in this category, possibly indicating that the timing and quality of nutrition care plays a role in prevention of disease. More research is needed in this area to delineate the appropriate quality and quantity of nutrition care in the prevention of late effects of cancer treatment.
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Chapter 1: Introduction

1.1 Background of Problem

Technology has advanced far enough in this country so that pediatric cancer, which was once a death sentence for most, is now something that children recover from quite readily. It has been said that for every 100,000 people under the age of 21, 16 are diagnosed with cancer every year (Oeffinger1). This translates to a yearly number of 48,913 cases in the United States. While this may seem like a relatively small number compared to an overall population of 305 million (US Census), it is important to keep in mind that approximately 80% of those diagnosed with a childhood cancer will become long-term survivors, living 10-30 years or more (Oeffinger1, Mertens). These patients do not just die and leave the population, but survive and become active members of society.

Unfortunately, with this lengthened survival comes the increased risk of death from a second cancer, cardiovascular disease, pulmonary disease and other, non-cancer causes well beyond 30 years after initial diagnosis (Oeffinger1, Mertens). These subsequent diseases and other causes of death may be directly related to modalities used in cancer treatment and to the various lifestyle habits that are developed during treatment and after the cancer has been resolved (Oeffinger1, Offinger2, Florin, Asner). Development of obesity, cardiovascular disease, and diabetes in particular as late effects
of cancer and its treatment, are closely linked with lifestyle habits including nutrition and physical activity in these survivors (Florin, Oeffinger1). As can be seen, cancer treatment not only affects the patient at the time of diagnosis, but can also have many long-term detrimental effects.

So, in order to assure that these children who have recovered are able to reach their full potential and achieve a normal life span, we need to think about what things will help them to do so. Oeffinger and colleagues suggest that a more systematic plan for health care follow-up be implemented to support these patients throughout the rest of their lives (Oeffinger1). Since nutrition is a key component in the development of further disease after cancer diagnosis (Oeffinger1), inclusion of formal nutrition education and interventions from the first diagnosis, throughout treatment, and in remission are logical steps in ensuring the health of these individuals both during treatment and for years after.

1.2 Statement of Problem

In light of these late effects of cancer and cancer treatment, and the increasing longevity of cancer survivors, there needs to be a more structured program for health care follow-up in this area as mentioned previously (Oeffinger1). Often times, in the case of obesity, general pediatric medical weight loss programs will not admit those patients with significant medical history such as cancer diagnosis. So, it becomes the responsibility of those involved in the care of these patients to find alternative means to help them recover and have the best quality of life possible. It is the aim of the present study to establish a need for a more comprehensive approach to pediatric cancer treatment and follow-up in the central Ohio area, and to set the stage for further development of a health care
program designed towards maintaining a healthy lifestyle through nutrition education for those dealing with and recovering from cancer treatment beyond the traditional inpatient and outpatient visits of a routine cancer treatment regimen.

1.3 Purpose of the Study

Within the context of a major medical center devoted to pediatric health care, this study seeks to establish the need for a specific program and policy regarding nutritional education and treatment of pediatric cancer patients and their families in both the inpatient and outpatient settings, throughout the full course of their treatment, and beyond. The objective of this study was to gather data pertaining to pediatric cancer survivors relating to nutrition specific disease and possible avenues of prevention following cancer treatment. The collection of the data was a two-fold process involving a thorough literature review looking at general characteristics of the target population and an extensive chart review of the selected subjects.

Research Questions

1. What pediatric cancer patient populations in general have the propensity for obesity and related diseases?

2. Where are obesity and these other diseases commonly seen in these populations (i.e.-with specific treatment regimens)?

3. What is the percentage of patients in the survivorship stage that are overweight/obese and/or have developed diabetes, cardiovascular, and other nutritionally relevant diseases?
4. What nutrition education have these patients already received and how is it related to their disease status?

1.4 **Research Approach**

The literature review served as a guide for data collection. This part of the research answered questions concerning what pediatric cancer patient populations in general have the propensity for obesity and related diseases, and where obesity and these other diseases are most commonly seen in these populations. Discussion in the literature of the late effects most commonly seen in these populations molded the criteria governing data collection. The subsequent data collection process from chart review determined what percentage of patients in remission are overweight/obese and/or have developed diabetes, cardiovascular disease, and other nutritionally relevant diseases. Data collection included such things as height, weight, age, type of cancer, length of remission, risk factors for these diseases, and other pertinent figures deemed significant to this study. With these results, the establishment of the need for nutrition education in the cancer treatment process will be addressed. The data was analyzed for significance of disease as well as what subject populations show the highest propensity for these diseases.

1.5 **Significance of Study**

The focus of this study is to establish the need for more comprehensive care for pediatric cancer patients both during treatment and following remission. An essential part of this care should include education on adopting healthy lifestyle behaviors through
both nutrition and physical activity. As there is not a significant amount of research on this topic that is focused on nutrition education specifically, this study is important for both the establishment of policies regarding patient nutrition education within the study setting as well as for the pediatric cancer population in general.

1.6 Limitations of Study

The population of this study is limited to those subjects who have received cancer treatment and/or follow-up treatment at an outpatient clinic of a major pediatric medical center serving the central Ohio area. Although the results may not be directly applicable to the entire pediatric cancer population, the aim is to corroborate with findings of other studies that there is a significant increased risk of nutritionally related late effects in this population overall.

The study is also limited by the detail of information able to be obtained from chart review of the subject’s medical history. The patients may not have all had the same type of cancer, undergone cancer treatment under the same protocols and policies, and gatherable data may differ significantly between subjects.

1.7 Definition of Terms

Childhood cancer survivor-

A patient, aged 0-17 years at diagnosis, who has survived cancer and its treatment into the remission phase and may remain in the remission phase or be undergoing further treatment at time of study. For the purposes of this study, patients who have survived 5 or more years after initial diagnosis will be the main focus of discussion.
Late effects of cancer and its treatment-

Therapy-related complications or adverse effects that persist or arise after completion of treatment for a pediatric malignancy (COG). Outcomes that tend to occur greater than 5 years from time of cancer diagnosis as a result of the previous cancer treatment and may be physical, psychological, or social in nature (Miller). In the context of this study, they are mainly physical in nature ranging from weight gain and obesity to diabetes and cardiovascular disease. Other nutritionally related effects may also be referred to within this context.

Chronic effects of cancer and its treatment-

Outcomes that occur as a result of cancer treatment, either during or after treatment, and persist for longer than 3 months after the time of initial presentation. These may also persist into the survivorship period (Miller). Primary discussion will focus on late effects in this study.

Nutritionally related diseases-

Diseases and disorders, including cardiovascular disease, diabetes, endocrine disorders, overweight/obesity, and risk factors associated with metabolic syndrome including hypertension and dyslipidemia generally considered to be related to diet and nutrition in some way.
Chapter 2: Literature Review

Introduction

Approximately 80% of pediatric patients diagnosed with cancer between the ages of 0 and 18 years will become long-term survivors, living 5 or more years after diagnosis (Offinger1, Kurt, Mertens, Miller). A recent survey of the demographics this childhood cancer survivor population revealed that 1/3 of these survivors are <20 years of age, 46% are 20-40 years old, and an additional 18% are >40 years old (Landier). We can attribute this increased longevity to improvements in treatment of the cancer itself along with some improvements in and addition of post-treatment, follow-up care (Offinger1, Landier).

Unfortunately, morbidity and mortality in this population still remain higher than the normal population for this group (Landier, Mertens, Offinger1, Miller). The Childhood Cancer Survivor Study, one of the largest studies in this area of cancer treatment, found that the sample of 20,483 survivors had 8.4 times higher mortality risk following their 5-year survival after diagnosis compared with an age-, sex-, and year-matched US population (95% CI= 8.0-8.7; P < 0.001) and continued to be higher throughout the survival period (Mertens). Figure 1 of the Mertens, et al article is fairly descriptive, showing a significant reduction in the survival rates of survivors over time as
compared with the matched US population mortality rates (Mertens). Those survivors diagnosed before age 4 had a higher risk of late mortality (Mertens). The highest standard mortality ratios (SMRs) were found in survivors of other leukemias (non-ALL and –AML, medulloblastoma, or PNET), other CNS malignancy, and Ewing sarcoma (Mertens). And, the highest mortality rate was observed within the first 5 years of entering the cohort, approximately 5-9 years after diagnosis, when the risk of death due to recurrence or progressive disease would be expected to be the greatest (Mertens). Although recurrence and/or progressive disease accounted for the majority of deaths (57.5%) in this study, it is interesting to note that as the cancer survivor survived longer, the risk of death from these decreased (Mertens). Secondary malignancy and non-external related mortality became more significant as this population aged, especially in females (Mertens). This is consistent with other research findings showing that compared with male survivors, female survivors are at higher risk for many adverse long-term outcomes including obesity, poor cardiac outcomes, and other secondary malignancies including breast cancer (Mertens).

Questions as to why this increased morbidity and mortality is seen relating to causes other than the primary disease itself have been raised, and much research has been done examining late and chronic effects of cancer treatments. A multitude of effects have been related to chemotherapeutic agents, radiation therapy, and surgical procedures involved in treatment and involve every organ system in the human body (Landier, Kurt). And, many of these effects are not seen until later in life, for example during puberty 10 years after cancer diagnosis (Kurt, Landier, Oeffinger1).
Interestingly, there is not much research to be found on the role of dietitians and nutrition education in the treatment of pediatric cancer. In fact, many of the recommendations do not address nutrition’s role in disease prevention or development in pediatric cancer survivors at all (Oeffinger, Mertens, Landier). The Children’s Oncology Group (COG) does address nutrition education within their published guidelines (COG), but little dietary intervention information is seen in any research not sponsored or published by this group. As the aim of this study is to look at the incidence of nutritionally related effects of cancer and the role nutrition education may have played in the development of disease following treatment, the hope is that this research will be able to contribute increased knowledge of childhood cancer survivorship and promote successful treatment and care of these individuals.

Providing adequate and appropriate health care for these survivors is becoming one of the biggest challenges in medicine today (Landier). Because of the high morbidity and mortality experienced by these patients (Mertens, Landier), it is important to look at the reasons behind this increased risk as well as the possible solutions to preventing development of disease after cancer treatment. Improvements in cancer treatment therapies have allowed for cancer remission with less rigorous regimens of chemotherapeutic agents, surgical procedures, and radiation therapies (Kurt, Miller). But, these treatments still have lasting effects regardless of improvement in therapies and treatment aesthetics.
2.1 Late Effects of Cancer Treatment

The effects of childhood cancer treatment are many, varied, and may often times be severely disabling to the individual affected (Oeffinger 1, Miller, Kurt). They can range from physical effects resulting from toxicity of different cancer treatments on the body, to psychosocial and emotional effects for both the patient and family (Oeffinger 1, Miller, Kurt). When discussing these effects, especially those that are physical and medical in nature, it is important to differentiate between chronic effects and late effects (Miller). Chronic effects of cancer treatment are outcomes that occur as a result of the treatment itself, either during or after the treatment, and they persist for 3 months or more after initial presentation often into the survivorship period (Miller). Late effects of cancer treatment tend to occur more than 5 years from the time of diagnosis as a result of the treatment regimen, and can be physical, psychological, or social in nature (Miller). For the purposes of this study, we will be focusing mainly on the physical late effects of childhood cancer treatment, including obesity and cardiovascular, endocrine, neurological and pulmonary diseases, as they are highly related to and can be affected by nutrition both during treatment and into survivorship (Oeffinger 1, Landier, Miller).

A brief description of cancer treatment modalities that are important to our discussion is in order here, as it is essential to our understanding of why some of the late effects of treatment may occur. Chemotherapy and radiation therapy are the two most common types of cancer treatment used in the pediatric population (Kurt). Chemotherapy, or the introduction of antineoplastic agents to the body, is used to chemically alter the progression of the cancer cells and is often times associated with various toxicities to the body systems. Acute side effects include fatigue, anemia, and
chronic nausea, and late effects encompass all body systems including neurocognitive and neurosensory deficits (Kurt). Radiation therapy, or the introduction of radioactive particles to the cancer affected area, tends to affect only the target area (Kurt).

Oftentimes radiation therapy involves subjection of the cranium to this radiation, termed cranial radiation therapy (CRT), and can result in severe neurosensory and neurocognitive difficulties (Kurt). As this therapy may also affect various endocrine structures in the brain, it can also have lasting effects on other systems of the body (Kurt). Kurt, et al. have compiled two comprehensive tables, Table I and Table II in the article, describing common therapeutic interventions for pediatric cancer as well as late effects and high-risk features by body system of these interventions (Kurt). As one of the most common childhood cancers, it is interesting to note that treatment modes for acute lymphoblastic leukemia (ALL), including hematopoietic stem cell transplantation (HSCT), have effects that encompass almost every body system described (Kurt).

2.2 Obesity in Survivors

Obesity and co-morbid conditions such as cardiovascular disease, hypertension, diabetes, and metabolic syndrome are on the rise in the pediatric population of this country at an alarming rate (Nathan, Meacham), so it is natural to see the study of this disease in relation to cancer survivors. Much research has been done on all pediatric cancer populations, and the results point towards those having a diagnosis of ALL to be the most at-risk for overweight and obesity (Nathan, Meacham, Oeffinger2, Janiszewski). Several cohort and cross-sectional studies have examined the late effects of cancer treatment in pediatric acute lymphoblastic leukemia patients. All have noted a significant
propensity for increased fat mass in the body resulting in overweight and obesity long after treatment has concluded in this population (Janiszewski, Asner, Florin, Offinger2, Jarfelt). Many reasons for this have been postulated, with an overwhelming majority of data pointing towards the type of treatment as the culprit; namely CRT especially in young, female subjects (Janiszewski, Asner, Florin, Offinger2, Jarfelt). Those patients receiving CRT, commonly those with ALL and central nervous system (CNS) involvement or some type of brain tumor, are believed to be at particular risk because radiation, surgery, or the tumor itself may damage the hypothalamic-pituitary axis (Nathan). Proposed mechanisms affected by this damage include growth hormone regulation and deficiency, leptin insensitivity, and satiety cues controlled by the satiety center of the ventromedial hypothalamus (Nathan). Exposure to corticosteroids during treatment has also been implicated in obesity after treatment (Chow). Other possible reasons for this weight gain include the effects of therapy on the developing brain resulting in growth hormone and other hormone imbalance, genetics, maternal and familial tendencies, environmental causes, dietary practices, and lifestyle habits (Janiszewski, Asner, Florin, Offinger2, Jarfelt).

We know that obesity and overweight are implicated in the development of other co-morbid conditions such as cardiovascular disease and diabetes. Excess weight also has strong implications in the development of cancer itself (Calle). In a study of more than 900,000 U.S. adults, it was found that increased body weight was associated with increased death rates for all cancers (Calle). In those with a body mass index (BMI) of 40 kg/m² or greater, women had a 62% higher death rate and men had a 52% higher death rate from cancer than the normal weight comparisons (Calle). BMI was also significantly
associated with higher rates of death from specific cancers including cancer of the esophagus, colon and rectum, pancreas, kidney, liver, non-Hodgkin’s lymphoma, multiple myeloma, cancers of the stomach and prostate for men, and cancers of the breast, uterus, cervix, and ovary in women (Calle). In this study, it was also estimated that overweight and obesity in the U.S. could account for 14% of all deaths from cancer in men and 20% of all deaths from cancer in women (Calle). In relation to cancer survivors, this is important from the standpoint that they may be at an even higher risk for development of secondary malignancies because of their weight status. With studies showing that secondary malignancies as a significant cause for late mortality after diagnosis (18.6% in one study), we need to look at all aspects of the role of overweight and obesity in cancer survivorship. Further research into the causes and prevention of weight gain, with focus on nutrition intervention, during and after cancer treatment in this population is warranted to prevent further disease development (Janiszewski, Asner, Florin, Oeffinger2, Jarfelt).

2.3 Other Related Diseases

Worth noting are other diseases and disorders seen as late effects in pediatric cancer treatment, including cardiovascular disease, diabetes, osteoporosis/osteopenia, and neurocognitive deficits as they have been shown to be highly correlated with nutrition both in prevention and treatment of the specific disorder and in relation to other diseases (Oeffinger1, Robien, Arroyave, Demark-Wahnefried1).
Cardiovascular Effects.

Exposure of the developing cardiovascular system of pediatric patients to the various harsh treatments of cancer therapy is extremely detrimental to the health of that system (Oeffinger1). Analysis of data from the Childhood Cancer Survivor Study has shown that the SMR for cardiac-related deaths was 8.2 (95% CI, 6.4-10.4) among long-term survivors of pediatric cancer (Mertens, Baker). Some treatments seem to elicit specific etiologies, while others produce multifactorial disease. For example, anthracyclines including doxorubicin and daunorubicin commonly used in pediatric cancer treatments can elicit cardiomyopathy following exposure to these agents (Oeffinger1). Late effects of exposure to anthracyclines can manifest as left ventricular dysfunction, clinical heart failure, or cardiac death (Oeffinger1). The cardiotoxicity of these agents is often late-onset, occurring after the first year of survivorship, is progressive, and has not been shown to be reduced with reductions in therapy (Oeffinger1).

Another treatment in childhood cancer is mantle radiotherapy. Used in the treatment of Hodgkin’s lymphoma, it has been shown to promote coronary and carotid artery disease because the focus of the radiation encompasses the primary lymph node regions of the neck, supraclavicular, infraclavicular, axillary, and mediastinal areas (Oeffinger1). Despite efforts to shield the heart from radiation, primary vessels are still exposed and are at increased risk to produce myocardial infarction (Oeffinger1).

Hematopoietic stem cell transplantation (HSCT) seems to elicit cardiovascular events, namely hypertension, in survivors of this procedure (Baker). A study of 1089 HSCT survivors showed that allogenic HSCT survivors were 2.06 times (95% CI, 1.82-
7.32) more likely to report hypertension compared with siblings, but did not report other cardiovascular outcomes with any greater frequency (Baker). These allogenic HSCT survivors were also 2.31 times more likely to develop hypertension than autologous recipients (95% CI, 1.45-3.67).

Multifactorial cardiovascular disease is often seen following childhood ALL (Oeffinger1). This is due to a variety of reasons, including increased physical inactivity, obesity, increased visceral adiposity, insulin resistance, and dyslipidemia seen after treatment (Oeffinger1). These risk factors are seen primarily in those who have had CRT, but are also seen in patients that have undergone chemotherapy alone (Oeffinger1). Correlations are seen between high levels of corticosteroid exposure, obesity, and hypertension (Chow). Similar outcomes have been reported in those treated with HSCT and brain tumor survivors (Oeffinger1).

**Diabetes and Endocrine Diseases.**

Cancer treatment has significant effects on the endocrine system of the body and can severely disrupt normal development in pediatric patients. This is especially detrimental to the child receiving treatment as this is the period when people are still developing and reach their maximum height (Miller). Cancer treatment, and central nervous system radiation in particular, can cause a host of disruptions in the brain including pituitary dysfunction, resulting in deficiency in hormones produced by this structure (Miller). Growth hormone (GH), thyroid-stimulating hormone, luteinizing hormone, follicle-stimulating hormone, gonadotropin-releasing hormone, and corticotropin-releasing hormone are all affected by damage to the pituitary with GH
being the most vulnerable to the effects of radiation (Miller). Along with growth, some of these hormones can affect fat storage and increase risk for metabolic syndrome and obesity (Miller, Gurney).

One study looking at survivors of ALL found GH deficiency in 64% of subjects, and in 84% of those receiving cranial irradiation (Gurney). They also reported that 60% of subjects treated with cranial irradiation had 2 or more of the 5 components of metabolic syndrome (Gurney). The researchers found that cranial irradiation is strongly related to GH deficiency, and in turn lower insulin-like growth factor 1, higher fasting insulin, abdominal obesity, and dyslipidemia (Gurney). In another study looking at HSCT patients, survivors who had had total body irradiation had 3.42 times increased risk for developing diabetes (Baker). Thyroid disease has also been seen, particularly in the Hodgkin’s disease survivor population as a result of mantle radiation (Miller). And, the greatest risk for hypothyroidism occurs within the first 5 years after the completion of therapy but can occur as far out as 20 years (Miller). So, the effects of cancer treatment on the endocrine system can lead to growth and development disruptions along with increased risk of development of diabetes and cardiovascular disease (Gurney, Baker).

**Bone Mineral Density.**

Osteopenia and osteoporosis have been found to occur more frequently in the cancer survivor population as compared to normal individuals (Miller). Research on this is in agreement that the etiology for osteopenia in this population is most likely a multifactorial process including exposure to various treatment agents like corticosteroids, methotrexate, chemotherapy, and cranial irradiation (Miller, Kaste, Rai). Lifestyle
factors likely contributing to this process include physical inactivity, inadequate dietary amounts of calcium and vitamin D, smoking, and alcohol consumption both during treatment and into survivorship (Miller, Kaste, Rai). In one study looking at bone mineral density (BMD) in ALL survivors, it was found that low body weight, nutritional supplement use, and alcohol all had negative effects on BMD (Kaste). Exercise participation at enrollment seemed to point to a more positive BMD status (Kaste). As this was a small study with only 57 participants, more research is needed for more comprehensive evaluation of the causes of low BMD in survivors. To address this, Rai et al. have designed a study, termed the BONEII study, to look at a larger cohort of childhood cancer survivors and obtain more evidence relating to BMD status of these patients and to investigate the effects of calcium and vitamin D supplementation over a 2 year follow-up period (Rai).

**Neurological Effects.**

Although the neurological effects of various cancer therapies may not have direct effect on the other body systems, it is important to note these effects as being nutritionally related. This is because some of these effects may affect the patient’s ability to understand appropriate nutrition, see and obtain this nutrition, and the effects may also alter the energy requirements depending on the individual. For example, neurocognitive effects of methotrexate and CRT can produce neurocognitive deficits in executive function, memory, and learning along with promoting adverse behavioral changes (Miller, Kurt). Visual impairment can happen as a result of bisulfan and glucocorticoid therapy along with radiation applied to related areas (Kurt). Peripheral neuropathy and
motor deficits can occur resulting from vincristine and vinblastine therapy resulting in altered motor skills that may affect the patient’s ability to obtain food and also alter their energy requirements (Kurt).

2.4 Multidisciplinary Models of Care: The Follow-up

With the myriad of late effects of cancer treatment, it is essential to have a comprehensive, multidisciplinary follow-up plan for these patients as many researchers suggest (Oeffinger1, Landier, Miller). Patients with complex medical needs may not be adequately served by an annual visit to a traditional hospital-based late effects clinic or by a primary care physician, and most may need access to oncology/survivorship, endocrinology, pulmonology, cardiology, nutrition, and psychology professionals in a same day visit (Carlson, Landier, Oeffinger1). The Children’s Oncology Group has come up with a set of guidelines for clinicians involved in survivorship care, ‘Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers’ available at www.survivorshipguidelines.org, which suggest recommendations for periodic evaluations based on different treatment exposures and include modifying risk factors (Oeffinger1, COG, Landier). Each late effect is presented with supporting evidence and a score for the quality of evidence is provided (Oeffinger1, COG). As a nutritionally related example, on page 56 of the guidelines, nutrition related counseling is recommended for those patients that have received CRT due to the propensity for overweight related issues (COG). The idea of tailoring follow-up care to the patient’s specific diagnosis and treatment is a good one, and is worth expanding upon with further research.
A structured follow-up program may provide for survivors to seek medical contact more frequently, thereby becoming a sort of preventative maintenance instead of only seeking care when things go wrong. It may also help primary care practitioners care for these patients more effectively if more specialized care is unavailable (Landier). Inquiry into health care use by a large cohort of long-term survivors of childhood cancer revealed that 87% of the survivors reported general medical contact within the past 2 years and 72% reported a general physical examination within the same period, however only 42% reported a cancer-related visit and only 19% reported a visit to a cancer center (Landier). This indicates that primary care practitioners are the ones most involved in care of these childhood cancer survivors and need appropriate resources when caring for these individuals. Another study, looking at information and service needs of those patients diagnosed between ages 15-35 years, found that these survivors had high demand for information and assistance regarding diet and nutrition, but 40-50% of these patients reported these needs being unmet (Zebrack). Although this demographic does not quite fit the population of interest in this study, it does provide insight into the needs of childhood survivors.

2.5 Nutrition and Health Promotion in Survivors

As can be seen, there is a vast body of evidence that childhood cancer survivors are at increased risk of developing diseases such as cardiovascular disease, diabetes, osteoporosis, and obesity along with secondary malignancies. These conditions share modifiable risk factors that are recognized and lifestyle interventions, such as consuming a well-balanced diet, maintaining appropriate weight, and engaging in physical activity,
have shown benefit in reducing co-morbid illness and functional decline in these individuals (Demark-Wahnefried2, Arroyave). Unfortunately, most research on this topic is focused on the medical procedure and outcomes involved in cancer treatment, and assessing need for nutrition education and lifestyle behavior interventions tend to be neglected (Donze). And, the focus of the few studies that do look at nutrition and lifestyle behaviors of this population seem to look more at barriers to attaining healthy behaviors rather than on promotion of these behaviors in the first place (Demark-Wahnefried2, Arroyave, Robien).

Although these studies do not tell us much on the effective implementation of nutrition education and dietary behavior interventions in childhood cancer treatment, they do highlight areas where this type of intervention may be beneficial. The three studies reviewed here show overwhelmingly that this population does not meet recommended dietary guidelines in areas of fruit and vegetable consumption, calcium intake, whole grain consumption, making low-fat choices, appropriate intake of sodium, and appropriate intake of sugar-containing foods (Demark-Wahnefried2, Arroyave, Robien). Barriers to meeting these recommendations include difficulty in making healthy choices while dining out, peer pressure, taste, time constraints, and cost (Arroyave).

What is interesting here is that most, if not all, of these barriers can be ameliorated by appropriate nutrition intervention and education. Food label education, food preparation techniques, instruction on what to look for when dining out, and budget friendly food choices along with the traditional dietary recommendations are all areas that can be discussed with these patients (Donze, Arroyave). Donze and Tercyak offer a fairly simple nutrition education plan for childhood cancer survivors (SHARE Program),
which involves a 3-4 hour workshop for health promotion focusing on nutrition (Donze). With the aforementioned discussion of unmet health care needs focusing on diet, nutrition, and healthy lifestyle education (Zebrack), more research, including this study, should prove to be useful in expanding both our knowledge of the need for nutrition education and intervention as well as development of follow-up care focusing on health promotion and disease prevention in this population.
Chapter 3: Methodology

3.1 Research Design

Within the context of a major medical center devoted to pediatric health care, this study seeks to establish the need for a specific program and policy regarding nutritional education and treatment of pediatric cancer patients and their families in both the inpatient and outpatient settings, throughout the full course of their treatment, and into the survivorship period. This is a retrospective cohort study designed to investigate the relationship between childhood cancer survivorship and nutritionally related disease development. The objective of this study was to gather data from existing pediatric cancer survivors in order to study nutritionally related disease development in relation to the type of cancer the patient has, the course of treatment, and to nutrition education and intervention that patient may or may not have received.

3.2 Research Questions

The data collection and data analysis process will answer the following questions:

1. What pediatric cancer patient populations within this sample have the propensity for obesity and related diseases?

2. Where are obesity and these other diseases commonly seen in these populations (i.e.-with specific treatment regimens)?
3. What is the percentage of patients in the survivorship stage that are overweight/obese and/or have developed diabetes, cardiovascular, and other nutritionally relevant diseases?

4. What nutrition education have these patients already received and how is it related to their disease status?

3.3 Sample

The goal of this study was to obtain the current medical records of approximately 150 pediatric cancer survivors seen at a specialized pediatric oncology clinic in Columbus, OH. Inclusion criteria were as follows: age 0-10 years at time of diagnosis, 2 or more years into survivorship, and the medical record must contain current height, weight and age, type of cancer, date of diagnosis, length of remission or treatment stage, type of treatment(s) received, presence of secondary malignancy, presence or absence of nutritionally related diseases and risk factors pertaining to those diseases, and, if possible, information on nutrition intervention or education received through nutrition services/dieticians. The subject was excluded if not meeting these criteria.

3.4 Procedures/Data Collection

Identification of suitable subjects began with a thorough review of each potential subject’s medical record. During this screening process, it was ascertained whether or not the patient fits the inclusion criteria previously mentioned. Once confirmation of suitability for enrollment to this study was confirmed, data collection began. Included in this collection were such things as most recent height, weight and age, type of cancer,
date of diagnosis, years post-therapy, type of treatment, presence of secondary malignancy, presence or absence of nutritionally related diseases and risk factors pertaining to those diseases, information on nutrition intervention or education received through nutrition services/dieticians, and any other pertinent figures deemed significant to the study. See Appendix A for the form used in data collection.

3.5 Data Analysis/Statistical Analysis

Analysis of data was done to investigate relationships between cancer diagnosis, survivorship status, type of treatment, weight/BMI, nutrition education, progression of disease, and development of secondary malignancies and new nutritionally related diseases including overweight and obesity. Body mass index (BMI) was calculated with the most current height/weight data using the formula BMI = weight(kilograms) ÷ height(meters)^2. The most recent published CDC growth charts, appropriate for age and gender, were used in determination of percentile rank of BMI for each subject (CDC). In the case of those subjects with Down syndrome, the standard growth charts published by Cronk, et al. were utilized (Cronk). Overweight and obesity were defined according to the CDC guidelines for children, where overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile, and obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex (CDC). Nutrition involvement was categorized into three groups: 1) Education-where education on diagnosis and age appropriate dietary practices and/or educational materials were provided to the subjects; 2) Intervention-where consultation from a dietitian was requested and/or full assessment including macronutrient needs and diet
recommendations were provided and/or special diets/calorie counts/daily weights were requested or recommended; and 3) Support-TPN or enteral feeds were initiated.

Percentages were used when analyzing data pertaining to the number of subjects who have developed a particular disease and were then compared with previous research and population norms.

3.6 Ethical Issues

As there was no involvement of the patient, other than obtaining usable data from the patient’s current medical record, no consent will be signed. Every effort was made to protect the patient’s confidentiality and no identifying marks were used in the collection or publication of this data.
Chapter 4

Nutrition Related Disease Risk in Pediatric Cancer Survivors

Buegel, A., Martin, L., Wolf, K., Clutter, J.

Introduction.

Technology has advanced far enough in this country so that pediatric cancer, which was once a death sentence for most, is now something that children recover from quite readily. It has been said that for every 100,000 people under the age of 21, 16 are diagnosed with cancer every year (Oeffinger1). This translates to a yearly number of 48,913 cases in the United States. While this may seem like a relatively small number compared to an overall population of 305 million (US Census), it is important to keep in mind that approximately 80% of those diagnosed with a childhood cancer will become long-term survivors, living 10-30 years or more (Oeffinger1, Mertens). These patients do not just die and leave the population, but survive and become active members of society.

Unfortunately, with this lengthened survival comes the increased risk of death from a second cancer, cardiovascular disease, pulmonary disease and other, non-cancer causes well beyond 30 years after initial diagnosis (Oeffinger1, Mertens). These subsequent diseases and other causes of death may be directly related to modalities used in cancer treatment and to the various lifestyle habits that are developed during treatment and after the cancer has been resolved (Oeffinger1, Offinger2, Florin, Asner). Development of overweight, obesity, and related diseases as late effects of cancer and its
treatment, are closely linked with lifestyle habits including nutrition and physical activity in these survivors (Florin, Oeffinger1). As can be seen, cancer treatment not only affects the patient at the time of diagnosis, but can also have many long-term detrimental effects.

Of particular interest in this study is the occurrence of obesity and other nutritionally related diseases during cancer survivorship. Obesity and co-morbid conditions such as cardiovascular disease, hypertension, diabetes, and metabolic syndrome are on the rise in the general pediatric population of this country at an alarming rate (Nathan, Meacham), so it is natural to see the study of this disease in relation to cancer survivors. Much research has been conducted on all pediatric cancer populations, and the results suggest those having a diagnosis of ALL (acute lymphoblastic leukemia) to be the most at-risk for overweight and obesity (Nathan, Meacham, Oeffinger2, Janiszewski). Several cohort and cross-sectional studies have examined the late effects of cancer treatment in pediatric ALL patients (Janiszewski, Asner, Florin, Offinger2, Jarfelt). And, all have noted a significant propensity for increased fat mass in the body resulting in overweight and obesity years after cancer treatment has concluded in this population (Janiszewski, Asner, Florin, Offinger2, Jarfelt). Many reasons for this increased fat mass have been postulated, with an overwhelming majority of data pointing towards the type of treatment as the culprit; namely CRT (cranial radiation therapy), especially in young, female subjects (Janiszewski, Asner, Florin, Offinger2, Jarfelt). Those patients receiving CRT, commonly those with ALL and central nervous system (CNS) involvement or some type of brain tumor, are believed to be at particular risk because radiation, surgery, or the tumor itself may damage the hypothalamic-pituitary axis which has roles in growth hormone regulation, leptin sensitivity, and satiety cues
(Nathan). Exposure to corticosteroids during treatment has also been implicated in obesity after treatment (Chow). Other possible reasons for weight gain include the effects of chemotherapy on the developing brain resulting in other hormone imbalances, genetics, maternal and familial tendencies, environmental causes, dietary practices, and lifestyle habits (Janiszewski, Asner, Florin, Oeffinger2, Jarfelt).

In light of these late effects of cancer and cancer treatment, and the increasing longevity of cancer survivors, it is logical to conclude that there needs to be a more structured program for health care follow-up in this area (Oeffinger1). Often times, in the case of obesity, general pediatric medical weight loss programs will not admit those patients with significant medical history such as cancer diagnosis. So, it becomes the responsibility of those directly involved in the care of these patients to find alternative means to help them recover and have the best quality of life possible. It is the aim of the present study to establish a need for a more comprehensive approach to cancer treatment, and to set the stage for further development of a health care program designed towards maintaining a healthy lifestyle through nutrition education for those dealing with and recovering from cancer treatment beyond the traditional inpatient and outpatient visits.

Within the context of a major medical center devoted to pediatric health care, this study seeks to establish the need for a specific program and policy regarding nutritional education and treatment of pediatric cancer patients and their families in both the inpatient and outpatient settings, throughout the full course of their treatment, and beyond. The objective of this study was to gather data pertaining to pediatric cancer survivors relating to nutrition specific disease and possible avenues of prevention following cancer treatment. The collection of data was targeted towards those subjects
suffering from common cancers found in the pediatric population and those known to produce nutritionally related diseases such as overweight and obesity. The diagnoses included in this study were acute lymphoblastic leukemia (ALL), acute myelogenous leukemia (AML), Burkitt’s lymphoma, neuroblastoma, and Wilm’s tumor or nephroblastoma. Subsequent data analysis answers the questions of what percentage of these patients in survivorship are overweight and obese and/or have developed nutritionally relevant diseases such as osteoporosis, restrictive airway disease, hypothyroidism, hypertension, gallbladder disease, hypercholesterolemia, and anemia. The study also looked at what level of nutrition education the patients received during and after treatment.

Methods.

This is a retrospective cohort study designed to describe the nutritional characteristics of childhood cancer survivorship. The objective of this study was to gather data from existing pediatric cancer survivors’ records to describe patients’ nutritionally related disease development and the type of cancer, the course of treatment, and nutrition education and intervention that the patient may or may not have received.

Sample.

The goal of this study was to obtain the current medical records of approximately 150 pediatric cancer survivors seen at a specialized pediatric oncology clinic. Due to availability of patient charts, only 75 subjects were admitted to the study. Inclusion criteria were as follows: age 0-10 years at time of diagnosis, 2 or more years into
survivorship, age of 3-12 years at analysis, diagnosis of ALL, AML, Burkitt’s lymphoma, neuroblastoma, or Wilm’s tumor, availability of current height, weight and age, date of diagnosis, length of remission or treatment stage, type of treatment(s) received, presence of secondary malignancy, presence or absence of nutritionally related diseases and risk factors pertaining to those diseases, and, if possible, information on nutrition intervention or education received through nutrition services/dietitians and other health care professionals. The subject was excluded if not meeting all criteria.

*Procedures and data collection.*

A tiered exclusion process was used for identification of potential subjects. This process involved the organization of several cohorts of potential subjects through the Cancer Registry at Nationwide Children’s Hospital in Columbus, OH using the initial criteria of age 0-10 years at time of diagnosis, age of 3-12 years at analysis, and diagnosis of ALL, AML, Burkitt’s lymphoma, neuroblastoma, or Wilm’s tumor. Then a screen of each potential subject’s medical record for more information was completed. Once confirmation of inclusion criteria for enrollment to this study was obtained, data collection began. Included in this collection were most recent height, weight and age at diagnosis, current age, end of therapy date, type of cancer, date of diagnosis, years post-therapy, type of treatment, presence of secondary malignancy, presence or absence of nutritionally related diseases and risk factors pertaining to those diseases, and information on nutrition care received through nutrition services, dietitians, dietetic technicians, physicians, nurses, and pharmacists.
Data analysis/statistical analysis.

Analysis of data was conducted to describe cancer diagnosis, survivorship status, type of treatment, weight/BMI, nutrition education, progression of disease, and development of secondary malignancies and new nutritionally related diseases including overweight and obesity. Body mass index (BMI) was calculated with the most current height/weight data using the formula BMI = weight(kilograms) / height(meters)^2. The most recent published CDC growth charts, appropriate for age and gender, were used in determination of percentile rank of BMI for each subject (CDC). In the case of those subjects with Down syndrome, the standard growth charts published by Cronk, et al. were utilized (Cronk). Overweight and obesity were defined according to the CDC guidelines for children, where overweight is defined as a BMI at or above the 85th percentile and lower than the 95th percentile, and obesity is defined as a BMI at or above the 95th percentile for children of the same age and sex (CDC). Nutrition treatment or care was categorized into three groups: 1) Nutrition Education—where education on diagnosis and age appropriate dietary practices and/or educational materials were provided to the subjects; 2) Nutrition Intervention—where consultation from a dietitian was requested and/or full assessment including macronutrient needs and diet recommendations were provided and/or special diets/calorie counts/daily weights were requested or recommended; and 3) Nutrition Support—TPN or enteral feeds were initiated. Percentages were used when analyzing data pertaining to the number of subjects who have developed a particular disease and were then compared with previous research and population norms.
Ethical issues.

As there was no involvement of the patient, other than obtaining usable data from the patient’s current medical record, no separate consent was needed for this research. Every effort was made to protect the patient’s confidentiality and no identifying marks were used in the collection or publication of this data.

Results.

A total of 75 predominantly white subjects with a history of ALL, AML, Burkitt’s lymphoma, neuroblastoma, and Wilm’s tumor were included in this study. The age range at analysis of this sample was 3 years 11 months to 12 years old. Age at diagnosis of these subjects ranged from a few days to 6 years 5 months. The years post-therapy of these subjects ranged from 2 years to 9 years 9 months, with a median time period of 3 years 2 months, and the majority of subjects were 5 years or less post-treatment. See Table 1 for descriptive characteristics of this sample at diagnosis.

Overweight and obesity.

Of the 75 subjects in the study, 30 (40%) were found to be overweight or obese overall at their most current follow-up visit, with relatively equal distribution in those categories (16 overweight vs. 14 obese). While only 14 (22.5%) of subjects were overweight or obese at diagnosis, also with equal distribution in those categories (7 overweight vs. 7 obese)—see Table 1. Further breakdown of the most current data revealed that 6 (37.5%) of the 16 subjects ages 2-5 were overweight or obese, and 24 (40.7%) of the 59 subjects ages 6-12 were overweight or obese. When separating
subjects into their respective diagnosis categories, the rate of overweight and obesity was higher than the overall number in all groups except the neuroblastoma group (ALL 42%, AML 57%, Burkitt’s 50%, Wilm’s 56% vs. Neuroblastoma 21%). Similar equal distribution of overweight and obesity is also seen within those groups with the exception of the AML group with 75% overweight and 25% obese. Table 2 summarizes the overweight/obese rate by group and overall.

The table also presents data on selected cancer treatments, steroids and cranial radiation therapy (CRT), as they relate to the obesity rates in each group. Overall, 57 subjects (76%) received steroid therapy and 6 subjects (8%) received CRT as part of their treatment regimens. High numbers of steroid treatment were seen in the ALL, AML, Burkitt’s, and neuroblastoma groups (100%, 57%, 100%, and 86% respectively). CRT treatment occurrence was low, with 1 subject in both the AML and neuroblastoma (14% and 5%) groups and 4 in the ALL group (11%). CRT treatment did not occur often in the treatment of the overweight and obese individuals (10% overall). However, steroid treatment was more common in these individuals with an overall rate of 67% and 100% in both the ALL and Burkitt’s groups.

Nutritionally related diseases.

Subject data was analyzed for development of nutritionally related diseases since diagnosis of cancer. Out of the 75 subjects studied, 49 (65%) were found to have developed these types of diseases including overweight/obesity, osteoporosis, short stature, failure to thrive, restrictive airway disease, hypothyroidism, hypertension, gallbladder disease, hypercholesterolemia, esophageal varices, anemia, and chronic
gastrointestinal symptoms. When overweight and obesity were excluded, 20 subjects (27%) remained with disease development. Although not included under nutritionally related diseases, 3 subjects (4%) were found to have recurrent malignancy and those subjects were not overweight or obese.

Nutrition-related care.

Table 3 denotes the distribution of subjects who received some type of nutrition-related care during or after cancer treatment. Forty seven (63%) of the 75 total subjects in the study had some type of nutrition education, 45 (60%) received nutrition intervention, and 25 (33%) received nutrition support. In the overweight and obese group (30 subjects), 20 (67%) received nutrition education, 19 (63%) received nutrition intervention, and 8 (27%) received nutrition support. When the overweight and obese subject data was removed from the overall sample, 45 subjects remained and 27 (60%) were found to have received nutrition education, 26 (58%) had nutrition intervention, and 17 (38%) had nutrition support during or after treatment. Nutrition education, nutrition intervention, and nutrition support are defined for the purposes of this study in the methods section.

Discussion.

Overall, the results of this study corroborate with the results of previous studies. The rates of overweight and obesity, along with other nutritionally related diseases, are high in this sample, supporting previous findings. In this study, it was found that 40% of the subjects overall were overweight or obese (with a BMI ≥ 85th percentile of the CDC
growth charts). Further breakdown revealed that 37.5% of subjects ages 2-5 years and 40.7% of subjects ages 6-12 were overweight or obese. These numbers are noticeably above the national averages of 24.4% for ages 2-5 years and 33.3% for ages 6-11 years, published last year from the National Health and Nutrition Examination Survey data for 2003-2006 (Ogden) and well above the rates of overweight and obesity at cancer diagnosis. Of note, however, is that steroids and CRT provided as part of cancer treatment seemed to have little relationship to the development of overweight and obesity where most of the subjects who were overweight/obese were equally or even less likely to have had these treatments than the rate in the entire group or sample as a whole. The other piece of this study looking at provision of nutrition-related care during and after treatment showed that there was very little difference in the number of subjects who were overweight and obese versus those who were not when looking at the amount of nutrition education, intervention, and support provided both during this time. The nutrition education and intervention provided to the overweight and obese group was slightly higher than those who were not in this category, possibly disproving the hypothesis that more education and intervention would be more likely to prevent nutrition related diseases like overweight and obesity. It is possible that the timing and/or the quality of this nutrition care was not optimal and therefore did not help the patient to prevent development of overweight, obesity, and other nutrition-related problems.

There are limitations that could be improved upon in further research and may give more insight into the intricacies of the role of nutrition in pediatric cancer treatment. The subjects in this study were mainly 5 years or less post-therapy and may not be well compared to other studies focusing on the standard 5 years or more. There may not have
been adequate time for post-treatment disease to develop, and we may have found more significant results than already found had we been able to use subjects that were further into survivorship. It was difficult to obtain updated records for those 5 or more years in survivorship because they tended to not be as diligent with follow-up visits. We did not perform correlation analyses on the data, and instead focused more on the raw data. The intent of the study was to describe incidence of nutritionally related disease in a specific population to support the need for revision and development of cancer treatment programs. Further research and analysis may be needed for the next step of actual change and development of these policies and plans.

With limitations aside, the important thing to take away from our study is that it was done on a pediatric cancer population with little research surrounding it. Our subjects were younger than those normally studied, and they had a shorter follow-up period post-treatment, 5 or fewer years vs. the standard 5 or more years. What we found is that late effects, like overweight and obesity are seen sooner than previously thought. We already know that obesity and overweight are implicated in the development of other co-morbid conditions such as cardiovascular disease and diabetes. Excess weight also has strong implications in the development of cancer itself (Calle). In a study of more than 900,000 U.S. adults, it was found that increased body weight was associated with increased death rates for all cancers. In those with a body mass index (BMI) of 40 kg/m² or greater, women had a 62% higher death rate and men had a 52% higher death rate from cancer than the normal weight comparisons. In the study, it was also estimated that overweight and obesity in the U.S. could account for 14% of all deaths from cancer in men and 20% of all deaths from cancer in women. In relation to pediatric cancer
survivors, this is important from the standpoint that they may be at an even higher risk for
development of secondary malignancies because of their weight status. With studies
showing that secondary malignancies as a significant cause for late mortality after
diagnosis (18.6% in one study), we need to look at all aspects of the role of overweight
and obesity in cancer survivorship. Although our study only reported 3 subjects with
recurrent malignancy, a longer survivorship period may have produced more recurrences
in those with overweight or obesity. Further research into the causes and prevention of
weight gain, with focus on nutrition intervention, during and after cancer treatment in this
population is warranted to prevent further disease development (Janiszewski, Asner,
Florin, Oeffinger2, Jarfelt). The tendency for disease development to occur later on into
survivorship may mean that we can do more in the early stages of disease and
survivorship to prevent this from happening.

In order to assure that these children who are recovering or have recovered are
able to reach their full potential and achieve a normal life span, we should consider
including more preventative measures for late effects of treatment within their treatment
regimens. Oeffinger and colleagues (2008) state that a more systematic plan for health
care follow-up should be implemented to support these patients throughout treatment and
the rest of their lives. Demark-Wahnefried and Jones (2008) relate that promoting a
healthy lifestyle through health behavior change in cancer patients and survivors while
focusing on weight management through energy restriction and macronutrient balance,
healthy diets including phytochemical, antioxidant, and fiber containing fruits and
vegetables, regular exercise, and smoking cessation has proven effective. However, there
is little in the way of research to support when the best time is to introduce this
information and behavior change (Demark-Wahnefried1). Since nutrition is a key component in the development of further disease after cancer diagnosis (Oeffinger1, Demark-Wahnefried1), inclusion of formal nutrition education and interventions from the first diagnosis, throughout treatment, and in remission may be logical steps in ensuring the health of these individuals both during treatment and for years after.
References.


Pui, C., Kaste, S. Implementing an intervention to improve bone mineral density in survivors of
childhood acute lymphoblastic leukemia: BONEII, a prospective placebo-controlled double-blind
randomized interventional longitudinal study design. *Contemporary Clinical Trials*. 2008; 29(5):
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### Table 1.

Descriptive characteristics of the sample (N=75) at the time of cancer diagnosis. Data include age range at diagnosis, sex, race, pre-existing unrelated conditions, and weight status at diagnosis. Age is depicted in years and months for clarity. MDS = Myelodysplastic syndrome. ADHD = Attention Deficit/Hyperactivity Disorder.
<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Total Subjects in Group</th>
<th>Ovwt/Obese(%)</th>
<th>Steroid Tx(%)</th>
<th>CRT Tx(%)</th>
<th>Ovwt/Obese and Steroid Tx (% of #ovwt/obese)</th>
<th>Ovwt/Obese and CRT Tx (% of #ovwt/obese)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Cancers</td>
<td>75</td>
<td>30 (40)</td>
<td>57 (76)</td>
<td>6 (8)</td>
<td>20 (67)</td>
<td>3 (10)</td>
</tr>
<tr>
<td>ALL</td>
<td>38</td>
<td>16 (42)</td>
<td>38 (100)</td>
<td>4 (11)</td>
<td>16 (100)</td>
<td>1 (6)</td>
</tr>
<tr>
<td>AML</td>
<td>7</td>
<td>4 (57)</td>
<td>4 (57)</td>
<td>1 (14)</td>
<td>2 (50)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Burkitt’s</td>
<td>2</td>
<td>1 (50)</td>
<td>2 (100)</td>
<td>0 (0)</td>
<td>1 (100)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>19</td>
<td>4 (21)</td>
<td>13 (68)</td>
<td>1 (5)</td>
<td>1 (25)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Wilm’s</td>
<td>9</td>
<td>5 (56)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Table 2. Subjects who are overweight and obese by cancer diagnosis and specified treatment. Numbers in parentheses denote percentages. Ovwt/Obese = Overweight/Obese (≥85th%ile of BMI for age), Tx = treatment, ALL = Acute Lymphoblastic Leukemia, AML = Acute Myelogenous Leukemia, Burkitt’s = Burkitt’s Lymphoma, Wilm’s = Wilm’s Tumor or Nephroblastoma.

<table>
<thead>
<tr>
<th></th>
<th>Total Subjects in Group</th>
<th>Nutrition Education (%)</th>
<th>Nutrition Intervention (%)</th>
<th>Nutrition Support (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Subjects</td>
<td>75</td>
<td>47 (63)</td>
<td>45 (60)</td>
<td>25 (33)</td>
</tr>
<tr>
<td>Overweight/Obese</td>
<td>30</td>
<td>20 (67)</td>
<td>19 (63)</td>
<td>8 (27)</td>
</tr>
<tr>
<td>Subjects</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-Overweight/Obese</td>
<td>45</td>
<td>27 (60)</td>
<td>26 (58)</td>
<td>17 (38)</td>
</tr>
</tbody>
</table>

Table 3. Subjects receiving some type of nutrition-related care during or after cancer treatment. Numbers in parentheses denote percentages. Nutrition education, nutrition intervention, and nutrition support are defined in the methods section of this report.
Chapter 5: Summary and Conclusion

As previous research has shown, and our results reflect, the problem of late effects of cancer treatment in pediatric cancer survivors is a significant one (Oeffinger1, Offinger2, Florin, Asner). The gold standard for follow-up periods in research in this population is at the 5 year post-treatment milepost in those patients that have reached puberty (Oeffinger1, Miller). Our research was directed towards a younger, less studied population aged 3-12 years who were mainly 5 years or less past their cancer treatment phase. Interestingly, we found that there is a marked increase in late effects and nutritionally related diseases in this population as well.

Out of the 75 subjects studied, 49 (65%) were found to have developed nutritionally related diseases including overweight/obesity, osteoporosis, short stature, failure to thrive, restrictive airway disease, hypothyroidism, hypertension, gallbladder disease, hypercholesterolemia, esophageal varices, anemia, and chronic gastrointestinal symptoms. When overweight and obesity were excluded, 20 subjects (27%) still remained with disease development. We also found that 40% of the subjects, in the survivorship period, were overweight or obese (with a BMI ≥ 85th percentile of the CDC growth charts) even though a relatively equal number of these subjects had nutrition education and intervention as their non-overweight/obese counterparts and most were not
overweight or obese to begin with. Further breakdown revealed that 37.5% of subjects ages 2-5 years and 40.7% of subjects ages 6-12 were overweight or obese. These numbers are noticeably above the national averages of 24.4% for ages 2-5 years and 33.3% for ages 6-11 years, published last year from the National Health and Nutrition Examination Survey data for 2003-2006 (Ogden). Clearly, more research on this population is needed to ascertain whether this is common in all associated populations, not just this isolated sample.

The implications of our findings are profound. We are seeing an increased number of late effects of cancer treatment before the 5 year follow-up milestone, so we need to consider why this is happening and what can be done to prevent this development of nutritionally related disease in pediatric cancer survivors. Experience suggests that these late effects do not just occur from the cancer treatment itself, but also involves the type and quality of nutrition care received both during and after treatment, psychological cues for eating habits, and unhealthy eating behaviors during therapy. Because patients are surviving cancer and living a significant number of years past diagnosis, we need to make a shift to prevention of these diseases instead of thinking in the short term during treatment.

Nutrition care for a newly diagnosed cancer patient can often times be a sort of hit-or-miss type of care. The patients and their families are overwhelmed with learning all of the intricacies of the disease and treatment, there are multitudes of tests, procedures, and visits from various health care professionals, and they are inundated with inquiries of the patient’s health by family and friends. In the beginning, there is rarely time for a dietitian or other professional to visit the patient and family and discuss
nutrition and healthy eating during treatment. What tends to happen is that the family is given some handouts on the topic and they are left to decipher them on their own. Then, when the patient is discharged, the same bustle of activity happens and the opportunity for nutrition education is again missed. Whether it involves making a specific appointment with a dietitian or waiting a month or so into treatment to address nutrition, it is important that we make nutrition education for cancer patients more prominent in their care.

Psychological cues and behavior promotion also play a role in dietary habits developed during cancer treatment. Oftentimes, chemotherapy and other cancer treatments adversely affect the patient’s appetite. Nausea lowers the appetite, and the patient is then encouraged to eat anything just to get them to eat. When you are a parent and your child is sick, you want your child to eat, because eating equates to health, and it doesn’t matter what the child eats as long as he or she eats. When it comes to pediatric cancer treatment, both the family and the health care professionals are guilty of this behavior. Then, because nutrition education and intervention has not followed through to discharge, these behaviors continue and diseases like overweight and obesity develop as a result. We, as professionals, already know that obesity and overweight are linked to the development of other co-morbid conditions such as cardiovascular disease and diabetes, and excess weight has strong associations with the development of cancer itself (Calle). But, are we communicating this to the patients and family members effectively? As with the general population, there seems to be a knowledge deficit when it comes to association of eating habits and long term disease risk. Obviously, effective
communication of disease risk is something that health care professionals need to work on.

As far as prevention of late effects and nutritionally related disease in pediatric cancer survivors, Oeffinger and colleagues (2008) state that a more systematic plan for health care follow-up should be implemented to support these patients throughout treatment and the rest of their lives by including nutrition education and intervention at each step. Demark-Wahnefried and Jones (2008) relate that promoting a healthy lifestyle through health behavior change in cancer patients and survivors, while focusing on weight management through energy restriction and macronutrient balance, healthy diets including phytochemical, antioxidant, and fiber containing fruits and vegetables, regular exercise, and smoking cessation (generally not a concern in pediatric populations) has proven effective. However, there is little in the way of research to support when the best time is to introduce this information and behavior change (Demark-Wahnefried1). Since nutrition is a key component in the development of further disease after cancer diagnosis (Oeffinger1, Demark-Wahnefried1), inclusion of formal nutrition education and interventions from the first diagnosis, throughout treatment, and in remission may be logical steps in ensuring the health of these individuals both during treatment and for years after.

The intent of the study was to describe the incidence of nutritionally related disease in a specific population to support the need for revision and development of cancer treatment programs. We found that there is a marked increase in this disease in a younger population even before the expected cut off of 5 years into survivorship. Further research and analysis is needed for the next step of actual change to elucidate appropriate
timing and quality of nutrition care, and for subsequent development of these policies and plans regarding care of pediatric cancer patients.
References


Data Gathering Sheet (2 sided)

<table>
<thead>
<tr>
<th>Gender (circle):</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
</table>

**Age Data (years with months):**
- Age at diagnosis:______y______mo.  **Date of diagnosis:**____________
- Age therapy ended:______y______mo  **Date of therapy end:**____________
- Age at analysis:______y______mo  **Years post-therapy:**____________

**Height and Weight:**
- At diagnosis: ___________cm ___________kg  BMI:______________kg/m²
- At therapy end: ___________cm ___________kg  BMI:______________kg/m²
- Most current: ___________cm ___________kg  **Date:**______  BMI:______________kg/m²

**Obesity/Overweight?**  Y  N  **Underweight?**  Y  N

**Initial Cancer Diagnosis:**  Acute Lymphoblastic Leukemia (ALL)?  Y  N
__________________________________________
__________________________________________
__________________________________________
__________________________________________

**Other/Secondary Diagnoses at Initial Diagnosis (if known):**
__________________________________________
__________________________________________
__________________________________________
__________________________________________

**Cancer Treatment Regimen:**  CRT?  Y  N  *(If Y, provide numerical data of exposure.)*
__________________________________________
__________________________________________
__________________________________________
__________________________________________

**Current Diagnoses:**  Any nutritionally related?  Y  N
__________________________________________
__________________________________________
__________________________________________

**Bone Health Data:**  
- **Osteoporosis/Osteomalacia present?**  Y  N
- Describe bone status if known:

**Living Circumstances:** *(i.e.-lives with both parents, one parent, foster child, etc. at diagnosis, during treatment, and in survivorship)*
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54
Nutrition Intervention:

Has patient received nutrition education/intervention/support at any time since diagnosis?  Y  N

If so, please describe:

<table>
<thead>
<tr>
<th>Date(s)</th>
<th>Intervention <em>(describe type of education, intervention, support, etc.)</em></th>
<th>By whom? <em>(dietician, physician, etc.</em>)</th>
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